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**Zeolite-Encapsulated UV-filters:
the key for more safe, effective and ecofriendly
sunscreens**

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Ph.D. Course in
Models and Methods for Materials and Environmental Sciences
XXXIV Cycle – Academic Year 2020-2021

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1 Abstract

Solar exposure to UVA and UVB radiation is the main cause of skin cancers, whose incidence is nowadays increasing. Thus, the use, empowerment, and research of new sunscreen products containing UV filters is a fundamental topic for the future of material and life sciences.

Ideally, a UV filter should be photostable and convert light into heat, or other forms of energy, once the radiation is absorbed. Nevertheless, if the molecule is photoreactive, it can degrade in other entities of unknown toxicity to human health and the environment. UV filters' stability, and consequently safety, strongly depends on the chemical environment, and particularly on the interaction with other components of sunscreen formulations. Therefore, much effort has been invested in developing more effective and safe sunscreens.

This thesis concerns the preparation and characterization of ZEOfilters, which are hybrid UVfs obtained by the encapsulation of the two organic UV filters octinoxate (OMC), and avobenzone (AVO) into zeolites with MOR, FAU, MFI, and LTL framework topologies, and different Si/Al ratio (low-silica: Na-MOR, LTL, ZSM5-30, 13X-FAU; high-silica: HS-MOR, ZSM5-398, HS-FAU). ZEOfilters were deeply characterized by Elemental Analysis, Thermogravimetric Analysis, UV-visible Spectroscopy, FT-IR spectroscopy, and Synchrotron-X-ray Powder Diffraction. Moreover, the safety of ZEOfilters was evaluated by skin permeation tests, solar exposure tests, and leaching tests into simulated seawater.

The project addressed: i) the optimization of ZEOfilters synthesis; ii) the evaluation of their UV filtering performances; iii) the assessment of the efficacy and safety of ZEOfilters in simulated field conditions; iv) the investigation of host-guest and guest-guest interactions.

A four-step loading procedure was optimized: 1) zeolite dehydration to remove H₂O molecules from channels; 2) UVf loading into the zeolite at 100 °C to promote molecule diffusivity; 3) ZEOfilter washing with acetone to remove unencapsulated UVf molecules; 4) ZEOfilter drying at 60 °C for solvent removal.

The encapsulation was found to be effective, even if strongly variable between different zeolite-UVf combinations. Particularly, OMC was found to be loaded almost evenly in both high- and low-silica zeolites, while AVO is more efficiently trapped in low-silica zeolites compared to their high-silica counterparts.

High silica ZEOfilters, generally display a low UV filtering power and appear colored, possibly due to UVf protonation. Among low-silica zeolites, Na-MOR displays no UVf loading, while the protonated ZSM5-30 presents strong absorption colors alike high-silica zeolites. LTL and 13X-FAU display a high UVf content, an enhanced UV filtering power compared to bare UVfs, and almost complete transparency in the visible range. Thus, LTL and 13X-FAU ZEOfilters were more deeply investigated being the most promising for future applications.

FT-IR experiments and structural refinements were performed on selected samples. FT-IR analysis of HS-MOR/OMC revealed the protonation of OMC (possibly explaining its visible color) together with the inhibition of its trans-cis photoisomerization under UV exposure. In LTL/OMC, FT-IR highlighted a perturbation of the $\nu(\text{C}=\text{O})$ mode of the OMC carbonyl group, then attributed, by structural refinements, to the carbonyl oxygen bonding to K cations of the LTL zeolite; no protonation of OMC was observed. The major role of carbonyl groups in locking organic compounds into zeolites has been already reported in the literature.

Solar UV exposure tests performed on bare UVfs, and LTL and 13X-FAU ZEOfilters demonstrated high stability of all samples when the compounds were tested independently.

Skin permeation tests were performed on bare UVfs, and HS-FAU, HS-MOR, LTL, and 13X-FAU ZEOfilters in aqueous suspensions, showing a very low permeation through pigskin membrane for all systems (less than 0.2% of the starting amount after 26 hours). The skin permeation of LTL ZEOfilters and bare UVfs in

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oil-in-water (O/W) emulsions was also tested, leading again to very low values for all tested samples. Results of accumulation in the skin demonstrated that most UVfs (encapsulated or not) accumulate in the stratum corneum and to a lesser extent in epidermis, while the amount in the dermis is negligible (up to 0.06 $\mu\text{g}/\text{cm}^2$).

In view of future employment, some O/W formulations were prepared with different ZEOfilter content (2 or 20 wt.%) and displayed good rheological properties. The use of ZEOfilters in cosmetics should provide several advantages: i) the UVf-skin interaction should be inhibited by the encapsulation; ii) the UVf-UVf interaction should be prevented by the encapsulation of different UVfs separately; iii) the UVf content of formulation may be reduced thanks to their enhanced filtering power; iv) UVf stabilizers and other co-formulants may be reduced thanks to the improved UVf stability.

During the last decades, UVfs are emerging as a new class of pollutants, especially in the aquatic environment. Leaching tests performed on LTL and 13X-FAU ZEOfilters exhibited very slow but continuous leaching of UVfs (worst-case scenario: 4% after 6 days of testing, for 13X-FAU/OMC). The observed leaching trends do not display an evident flattening up to 160 hours, thus in the future new and more protracted leaching tests should be made.

This thesis is by no means exhaustive of the project, and the development and understanding of these zeolite-based UV filters are still ongoing, and ZEOfilters can be a promising and eco-friendly alternative to traditional UVfs.

2 List of abbreviations

AS	Aqueous suspension	Parsol 1789	Avobenzone
AVO	Avobenzone	Parsol MCX	Octinoxate
BM-DBM	Avobenzone	PFA	UVA protection factor
CDOM	Chromophoric dissolved organic matter	PMOC(s)	Persistent and mobile organic compounds
CE	Chelated keto-enol form of avobenzone	PPD	Persistent pigment darkening
CW	Critical wavelength	PS	Pigskin membrane
D	Dermis	PT(s)	Pemeation test(s)
DC	Donor compartment of the Franz Cell device	RC	Receiving compartment of the Franz Cell device
E	Epidermis	ROS	Reactive oxygen species
E+D	Epidermis and dermis	s.g.	Crystalline space group
EA	Elemental analysis	SC	Stratum corneum
FDA	U.S. Food and Drug Administration (also US FDA)	SE	Soxhlet extraction
FT-IR	Fourier-transform infrared spectroscopy	SG	Specific gravity
HOMO	Highest occupied molecular orbital	SIN	(Italian) contaminated sites of national interest
HS-(zeolite)	High-silica zeolites	SM	Synthetic membrane
IPD	Immediate pigment darkening	SPF	Sun protection factor
IR	Infrared rays	SR-XRPD	Synchrotron radiation x-ray powder diffraction
K (form)	Diketo form of avobenzone	TCI	Tokyo chemical industry
l/s	Liquid/solid ratio (ml/mg) during ZEOfilter washing	TG(A)	Thermogravimetric analysis
LMCT	Ligand-metal charge transfer	TGA-MSEGA	Thermogravimetric analysis with mass spectroscopy analysis of the evolved gas
LUMO	Lowest unoccupied molecular orbital	UAE	Ultrasound-assisted extraction
MED	Minimal erythema dose	UVA	Ultraviolet radiation a
MM	Malignant melanoma	UVAPF	UVA protection factor
MOF	Metal-organic framework	UVB	Ultraviolet radiation b
MOF(s)	Metal-organic framework(s)	UVC	Ultraviolet radiation c
MW	Molar weight	UVf(s)	UV filter(s)
NCE(1)(2)	Non-chelated keto-enol forms of avobenzone	UVR	Ultraviolet radiation
NMSC	Non-melanoma skin cancer	UV-Vis	UV-visible spectroscopy
O/W	Oil-in-Water emulsion and/or formulation	VOC(s)	Volatile organic compound(s)
OMC	Octinoxate, octyl methoxycinnamate	W/O	Water-in-oil emulsion and/or formulation
OXB	Oxybenzone	ZEOfilter(s)	Zeolite-encapsulated UV filters
PABA	Para-aminobenzoic acid	ZIF(s)	Zeolite imidazolate frameworks
		λ_{max}	Absorption maximum in UV-Vis spectra of a given molecule

3 Introduction

3.1 Solar UV exposure

Sunlight is the main external energy source for Earth, greatly affecting Earth's climate and biosphere for better or worse. Just 48% of solar radiation reaches the Earth's surface (1). The solar spectrum is constituted of infrared rays (IR, wavelength range 750 nm – 1 mm), visible light (Vis, 400 - 750 nm), and ultraviolet rays (UVR or UV, 100 – 400 nm). About 8.3 % of the solar radiation at the Earth's surface is represented by UVR, while visible and infrared radiations represent 42.3% and 49.4%, respectively (2). UV rays are further divided in UVA (315 -400 nm), UVB (280 – 315 nm), and UVC (100 – 280 nm), which account for about 6.3%, 1.5%, and 0.5%, respectively. The solar UV irradiance at the Earth's surface is affected by many local factors such as aerosols, clouds, and surface albedo (3) and by other global factors such as the sun's activity and reciprocal Sun-Earth position (4). The ozone depletion induced an increase in UV irradiance at middle-high latitudes in the second half of the 20th century. Fortunately, after the Montreal Protocol (1989), the trend reversed with the recovery of the ozone layer obtained by reducing the emission of halogenated hydrocarbons (5). In 1992 Canadian scientists James B. Kerr, C. Thomas McElroy, and David I. Wardle introduced the UV Index, which two years later, in 1994, was adopted as a standard indicator of UV levels by the World Meteorological Organization and World Health Organization (4, 6). The UV Index is an erythemally weighted irradiance scale correlating the potential for damage to the skin and eye with UV irradiation (3, 4). The UV Index is now commonly employed in daily forecasts for civil protection, and its value varies usually between 0 (minimal risk) and 11 (very high risk), but values higher than 11 are also possible (**Figure 3-1**) (7).

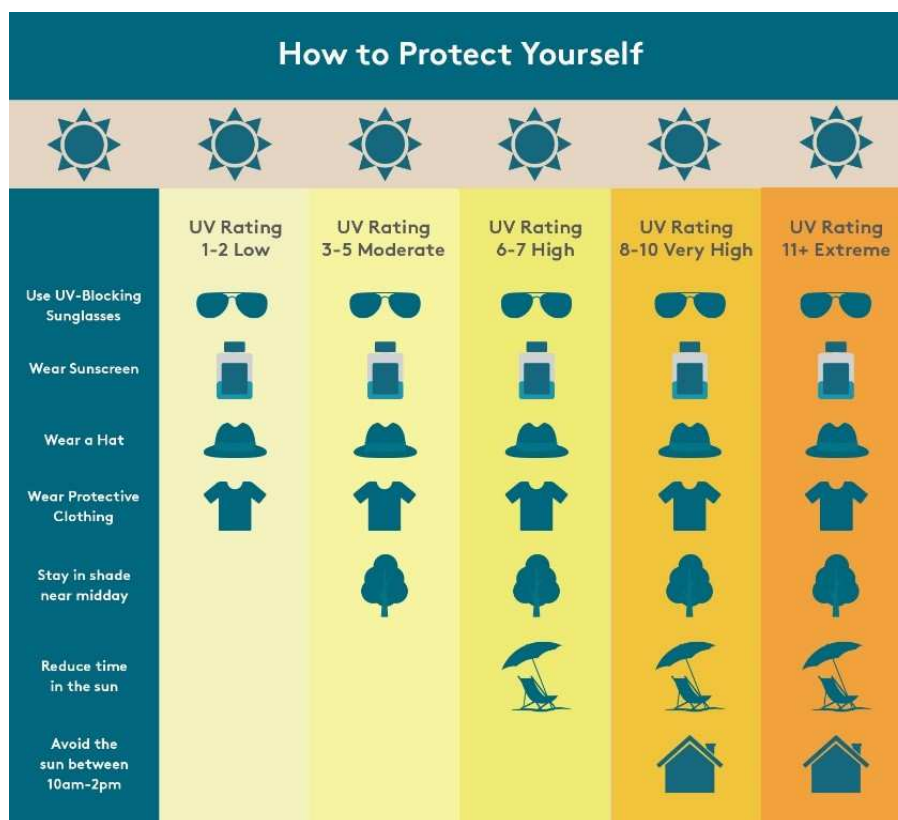


Figure 3-1. Safety guidelines for UV index interpretation. Figure from (7).

Introduction

Despite its quite low contribution to sunlight, UV radiation has an important impact on human health. Indeed, balanced sunlight exposure is of paramount importance in preventing health issues. On one hand, a correct and safe UVR exposure is responsible for the production of about 90% of the requirement for vitamin D in humans (8), and health issues arise from UVB exposure deficit (9). On the other hand, UVR is linked to most of the adverse effects of excessive and unprotected solar exposure and is considered the main cause of skin carcinogenesis and sensitization (10, 11).

3.1.1 UV exposure effects on humans

After the Earth's ozone layer, the skin is the only barrier protecting humans from solar UV rays (**Figure 3-2**). The solar UV rays reaching the Earth's surface may interact with our skin at different levels. The first response of human skin to UV exposure is an immediate pigment darkening (IPD) caused by UVA. IPD occurs rapidly (after 60 s) and disappears (after ~30 min) depending on the subject, i.e. according to phototype, melanotype, and skin color (12). Persistent pigment darkening (PPD) occurs within hours of exposure to UVA and UVB and may last days or weeks. While IPD involves the melanin already present in the skin, PPD requires the production of new melanin (13). Unfortunately, despite the darkening of skin pigmentation, undesired reactions may be induced by overexposure to UV rays, such as erythema (i.e. sunburns), photo-aging, and skin cancer (14). Excessive exposure to solar UVA causes skin photoaging by favoring the production of free radicals and other reactive oxygen species (ROS, **Box 3-1**). The resulting oxidative stress induces the activation of cytokines, matrix metalloproteinases, the enzymes for degrading elastin and collagen, and many others. Moreover, ROS can cause DNA mutations, that may lead to skin carcinogenesis, especially in an already negatively conditioned, wrinkled, and fragile skin (15).

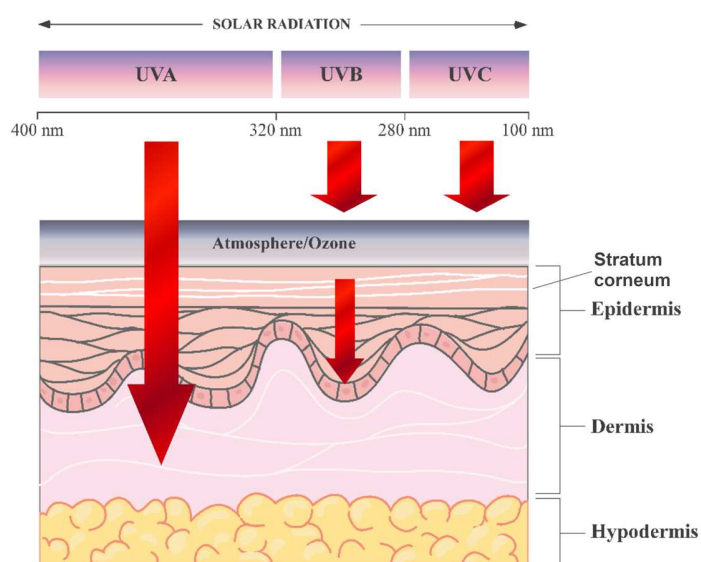


Figure 3-2. Solar UV penetrating the atmosphere and the different skin layers: epidermis, dermis, and hypodermis. The outermost layer of epidermis is the stratum corneum. The figure is modified from (16) and is licensed under the Creative Commons Attribution 3.0 Unported License (www.creativecommons.org/licenses/by/3.0/).

Box 3-1. *Free radicals: oxidative stress and diseases*

Free radicals are chemical species containing one or more unpaired electrons. The unpaired electrons make atoms, or molecules, particularly reactive, both towards radical and non-radical species. Indeed the formation of an electron pair is energetically favorable. The reaction product between a free radical and a non-radical species is often a new, reactive radical, triggering dangerous chain reactions.

In healthy organisms (such as our body), free radicals are always present (generally in low concentrations), produced, and used for many physiological roles, e.g. by activated phagocytes to defend against foreign organisms. As an example, about 1-3% of breathed oxygen is transformed into its superoxide radicals. However, free radicals must be counterbalanced by antioxidant defenses, since an excess of free radicals may be damaging. If this equilibrium is broken, oxidative stress occurs. Free radicals can react with lipids, proteins, and DNA of our organism, causing, e.g., lipid peroxidation, proteolysis, cell death, and DNA mutations. Uncontrolled free radicals are considered responsible for different diseases, such as cardiovascular diseases and cancers. Thus a healthy diet must be rich in fruits, nuts, grains, and vegetables, which are natural sources of antioxidants (e.g., vitamins E and C, carotenoids, and flavonoids) (17-19).

UVA and UVB may both cause erythema formation. UVA effects may be undetectable depending on the subjective response, while UVB causes delayed erythema, which appears within 3-4 hours and intensifies for 12-24 hours. This more severe erythema is usually accompanied by pain, pruritus, and bullae.

A minimal erythema dose (MED) is the amount of UVR needed to induce barely detectable erythema in a given individual (**Box 3-2**) (13). The dose of UVA exposure needed to cause erythema (20-70 J/cm²) is much higher than that required of UVB (20-1000 mJ/cm²). This explains why UVB is responsible for the majority of erythemas even being just about 10-20% of solar UV radiation. Together with erythema, sunburn cells develop, which are necrotic keratinocytes in the epidermis. Sunburn cells are similar to apoptotic cells (i.e. cells that are naturally at the end of their life cycle), indicating that erythema probably causes DNA damages. Thus it may be speculated that sunburn cells could be an indicator of photocarcinogenic potential (13). Indeed, DNA damages trigger a cascade of events that may lead to carcinogenesis. Damaged DNA activates a tumor suppressor protein (p53) that repairs the DNA or induces apoptosis (i.e. death) of the damaged cell. Excessive UV exposure, and thus excessive DNA damage, overwhelms the repairing mechanism, also leading to its deactivation and degeneration. Damaged cells in which the mechanism is compromised become resistant to apoptosis. Apoptosis-resistant cells may undergo clonal expansion being thus the basis of cancer development (20-22).

During the last decades, the number of skin cancers diagnosed annually increased continuously, including both malignant melanoma (MM) and non-melanoma skin cancer (NMSC) (23). The American Cancer Society estimates 106,110 new MM in the United States for 2021, with over 7,000 deaths (24). Also, European countries reported an overall increase in melanoma incidence rate (25). Skin cancer is also a cost burden for many countries (15). Public investment in skin cancer prevention and early detection programs shows thus a strong potential for health and economic benefits.

Fortunately, the public has become more and more conscious of the adverse effects of excessive exposure to UVR. However, UV exposure risk affects the great majority of the population, especially open-air workers (e.g. farmers and bricklayers). Thus, the paramount importance of skin cancer elicited a strong research interest in the development of more effective and safe UV filters (UVFs); UVFs have become almost ubiquitous in personal-care products such as sunscreens, shampoo, shower gels, and body lotions (26).

Box 3-2. Definitions of different UV exposure and protection parameters.

Here, some useful definitions are provided. Some differences may occur in definitions based on competing authorities or geographical areas (e.g. US FDA, European Union, Japan).

Minimal Erythema Dose (MED). MED is a unit adopted to quantify UV exposure. It is defined as “the smallest UV dose that produces perceptible redness of the skin (erythema) with clearly defined borders at 16 to 24 hours after UV exposure” (FDA 2011, in (27)). The MED strongly depends on the individual’s phototype (e.g. skin color and typology, eyes and hair color).

Sun protection factor (SPF). It is the most commonly employed parameter of sunscreen protection efficacy. SPF is the ratio between the amount of solar (UV) radiation needed to cause sunburns on protected skin, and the amount required to cause the same reaction on unprotected skin. SPF values are typically integers, e.g. 8, 15, 30, 50, 50+, with sunburn protection increasing with SPF. It has to be stressed that SPF is not directly related to the time of exposure since, e.g., 1 hour of exposure at 9:00 am may correspond to 15 minutes of exposure at noon. Since SPF is determined by tests measuring sunburns induced by UVB radiation, it mainly indicates sunscreen’s UVB protection. Since June 2011, sunscreens labeled as “Broad Spectrum SPF” are also tested for UVA protection (28, 29).

UVA Protection Factor (UVAPF or PFA). It is the ratio between the UVA dose required to obtain a certain persistent pigment darkening (PPD) on protected and unprotected skin. UVAPF value for a product is obtained as a mean of measurements performed in vivo on different individuals (ISO/DIS 24442 (30)). In vitro tests are also available to evaluate UVA protection (10).

Critical Wavelength (CW). CW is the UVA protection parameter mandated since 2011 by US Food and Drug Administration (FDA) (27), even if the parameter was already employed before (31, 32). Given a UV-visible spectrum (see section 4.5.1) of a compound/formulation in the 290-400 nm range, CW is defined as the wavelength at which the integral of the absorbance curve reaches 90% of the integral over the entire UVB-UVA spectrum (290-400 nm) (**Figure 3-3**). UVfs are divided based on CW between Broad Spectrum (CW > 370 nm) and Not Broad Spectrum (CW < 370 nm) filters (27).

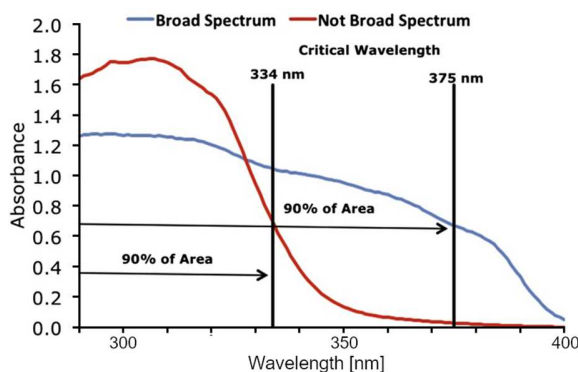


Figure 3-3. Examples of two different sunscreens. Both of them have SPF of 16, but different critical wavelengths, one above and one below 370 nm. Figure from (27).

Water resistance. The water-resistance of a sunscreen indicates its ability in retaining its SPF after water immersion. In the US FDA, sunscreens are classified as “water resistant (40 minutes)” or “water resistant (80 minutes)” if their SPF is retained after 2 or 4 cycles, respectively, of 20 minutes of water immersion separated by 20 minutes of air drying. Similarly, in Europe, a product is labeled as “water resistant” or “extra water resistant” if the retained SPF value is greater or equal to 50% of the stated value after 40 or 80-minute immersions, respectively. Thus, the SPF stated on European products is pre-water exposure, whereas the USA’s products are labeled with the post-immersion SPF (27, 32).

3.1.2 Sunscreen formulations

Sunscreen formulations are the main method of health protection against solar exposure. The main targets of an ideal sunscreen are protection against sunburns, skin aging, skin sensitization, and skin carcinogenesis. Sunscreen must provide broad-spectrum UV protection, filtering both UVB, and UVA, and possibly also the shortest visible light beyond 400 nm. **Box 3-2** details some of the parameters used to determine UV filters and sunscreen properties. The main parameter employed is the Sun Protection Factor (SPF), which indicates the protection from erythema, and thus from UVB rays (**Figure 3-4**). However, SPF needs to be related also to UVA protection, which is more important for skin aging and cancer, thus leading to the Broad Spectrum SPF definition (29). The effects of UVA can be reliably assessed also by in vitro tests, such as the critical wavelength determination (**Box 3-2**) (10).

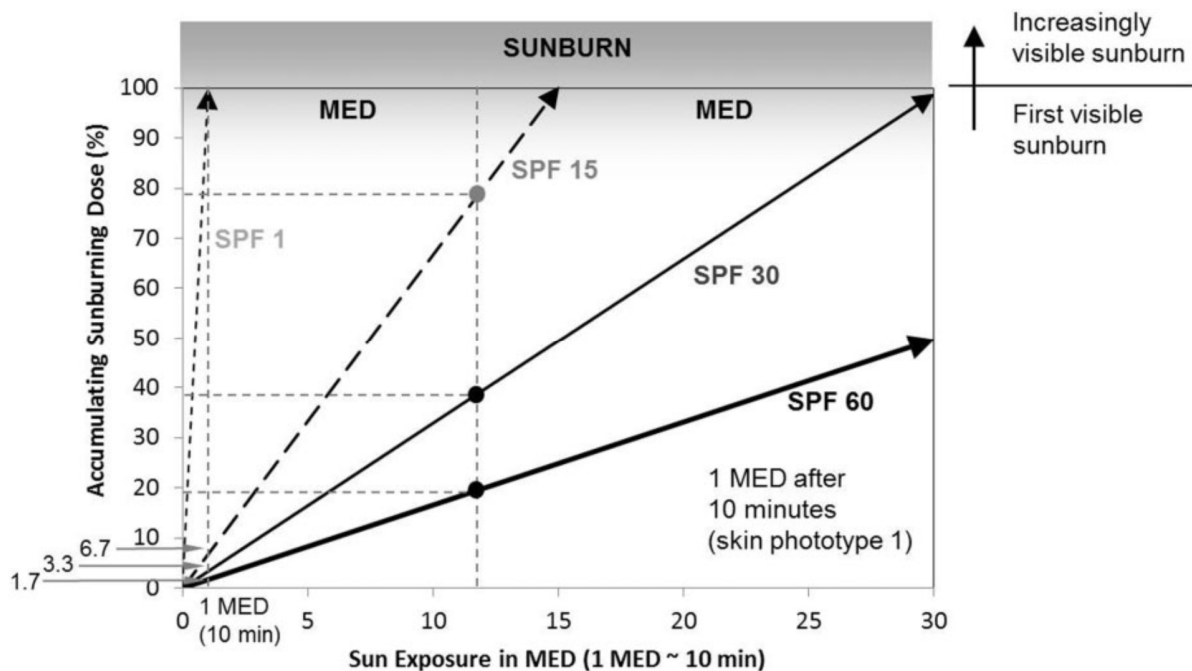


Figure 3-4. How a sunscreen works (according to Australian Standard), given a skin phototype and its related minimal erythema dose (MED). The horizontal axis is the sun exposure dose in MED, but it is also an approximative timescale supposing that 1MED $\approx$ 10 minutes. The vertical axis represents the accumulated sunburning dose in the skin, i.e. the amount of UV dose reaching the skin without being blocked (100% = 1MED). The arrows represent the accumulating sunburn dose (%) upon exposure, of a subject with no protection (SPF 1), and applied sunscreens of SPF 15, 30, and 60, respectively. Of note, unprotected skin leads to erythema (i.e. 100% of sunburning dose) after 1MED of sun exposure for definition. On the contrary, skin protected with an SPF 60 sunscreen is reached by just 0.5MED after being exposed to a 30 MED dose. Figure from (10).

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Sunscreens are available in various product typologies, such as emulsions, oils, gels, sticks, mousses, aerosols, and ointments. The choice of a proper vehicle should be made on both technical and aesthetical grounds (33). For example, water-resistant formulations are needed for bathing activities, while the rendering on the skin and its odor may determine the success of a sunscreen compared to another, appealing more or less to the customers.

Sunscreen formulations are complex mixtures of different compounds (**Figure 3-5**). The three main compounds of sunscreens are UV filters (UVfs), emollients, and emulsifiers. UVfs are the real active component of sunscreens absorbing UV rays and will be discussed in detail in section 3.2. For effective UV protection, UVfs should form a uniform layer on the skin and remain stable and active during the whole UV exposure. Moreover, to prevent undesired allergic reactions, UVfs should not permeate the viable skin (34). Emollients are compounds aiming at the solubilization and photostabilization of other components in the emulsion (especially of UVfs), together with providing enhanced sensory properties. Emulsifiers (e.g. surfactants) are compounds favoring the stability of sunscreen formulations. Other compounds of sunscreens are photostabilizers, film formers, rheology modifiers (e.g. thickeners), boosters, and sensory enhancers (**Figure 3-5**, see (10)).

Emulsions are widely employed for sunscreen products thanks to their almost unlimited versatility. They can be broadly divided between oil-in-water (O/W) and water-in-oil (W/O) emulsions – depending on which of the two unmixable liquid phases prevails – and between creams and lotions depending on their viscosity (i.e. in the range of 150,000-500,000 or below 50,000 centipoises, respectively) (35, 36). W/O emulsions would be preferable thanks, e.g., to their higher water resistance, and higher protection factor for a given UVf concentration. Indeed, W/O emulsions provide a more uniform protective layer, since organic UVfs are generally more soluble in the oil phase and would thus agglomerate in the small oil droplets of O/W formulations. Additionally, W/O emulsifiers (i.e. compounds added to stabilize the emulsions) limit the penetration of sunscreen ingredients in the skin. Nevertheless, despite the favorable properties of W/O emulsions, O/W ones are generally favored by sunscreen producers due to better sensorial appeal, and cost-effectiveness (35). Generally, emulsion sunscreens spread easily and are elegant on the skin, can reach high protection factors, and limit the interaction among different active components (35, 36).

Emulsions are thermodynamically unstable, thus different compounds and specific know-how must be employed to ensure their stability for at least 2-3 years at storage temperatures between the 10-40 °C (33). One way to stabilize sunscreens is to produce microemulsions. If the interfacial area of the two immiscible liquids is increased at its maximum (i.e. the dimension of droplets is decreased by several orders of magnitude), the internal energy of the system becomes strongly dependent on the interfacial tension between oil and water. Particularly, for ultra-low interfacial tensions ($< 10^{-1}$ mNm⁻¹) the internal energy may become negative, thus stabilizing the microemulsion indefinitely. Such ultra-low interfacial tensions are usually achieved by using a combination of lipophilic and hydrophilic surfactants. However, surfactants and other additives (e.g., thickeners, perfumes, preservatives, and vitamins) may cause skin irritation, and must thus be carefully selected (33).

Indeed, the interaction of sunscreens with the skin is the most important aspect of the emulsion. This interaction generally occurs on the stratum corneum (SC, ~30 µm thick), which is the body's barrier against chemical and biological attacks. The SC can be represented as a liquid-crystalline barrier of bilayered lipid structures, generally containing a high water content. The cosmetic formulations must maintain this liquid-like structure of the skin, and especially maintain a high moisture level, otherwise causing a “dry” skin feeling, and the sunscreen transdermal uptake (33).

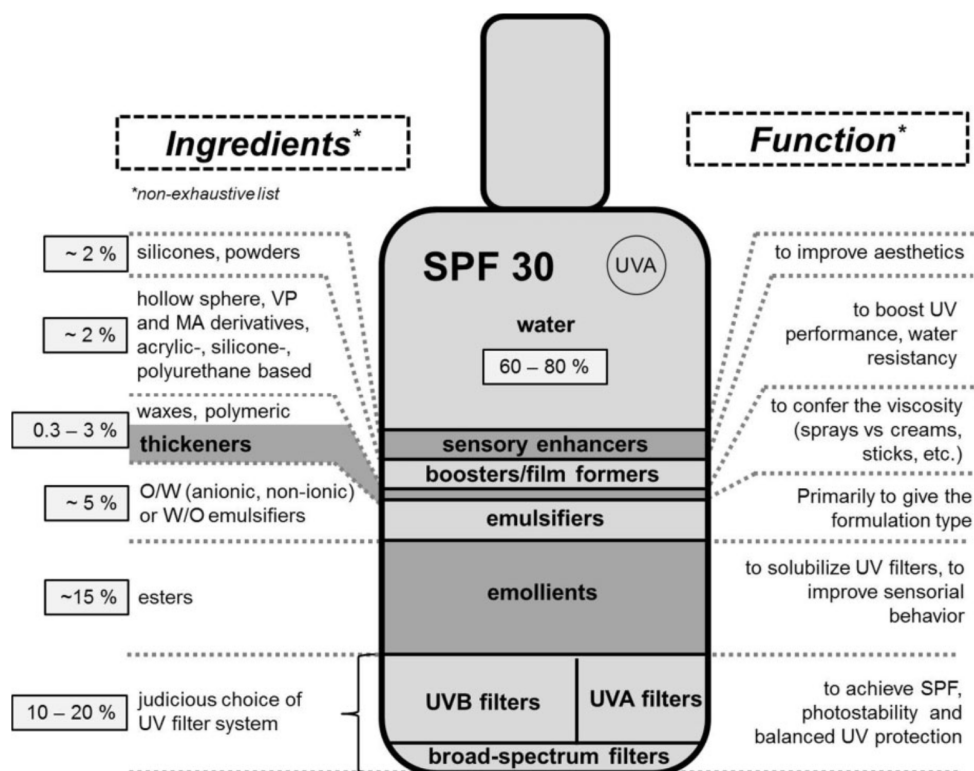


Figure 3-5. Ingredients and their purposes for a typical sunscreen. SPF, sun protection factor; O/W, oil-in-water; W/O, water-in-oil; UV, ultraviolet; VP, vinylpyrrolidone; MA, maleic anhydride. Figure from (10).

3.2 UV filters

UV filters (UVfs) are the active compounds dedicated to UV protection. UVfs are found in many personal-care products but also have become ubiquitous in packaging, plastics, dyes, and many other materials. Indeed, UV rays have a detrimental effect on several goods, promoting products degradation. For example, under UV exposure, wood-plastic composite, epoxy resins, and other plastics tend to lose their color and physical properties, mainly due to photooxidation reactions. Similarly, excessive UV exposure of food may induce unwanted degradation of fats, pigments, and vitamins, see e.g. (14, 37-40).

UVfs are organic or inorganic compounds that should absorb UV photons by jumping to excited states and then dissipating the energy without losing efficacy. Most UVfs have limited absorption ranges and, for these reasons, several filters are combined to obtain broad-spectrum UV protection. UVfs represent 2-20 wt% of sunscreen formulations (14) and many issues are still open regarding their efficacy and stability.

In the following, an overview of inorganic and organic UVfs is provided, also highlighting some aspects related to their safety and stability.

3.2.1 Inorganic UV filters

Inorganic UV filters can block UVR by scattering and/or absorbing UV photons. The main factors affecting their UV absorbance are the reflective index, the particle size, the homogeneity and type of dispersion, and the thickness of the formulation film applied (41).

Indeed, as well described in (42), the processes responsible for incident light attenuation by solid particles may be summarized by the following equation:

$$I_t = I_0 - (I_r + I_s + I_a)$$

Where I_t is the intensity of transmitted radiation through the material, I_0 is the intensity of the incident radiation; I_r , I_s , and I_a are the intensities of the reflected, scattered, and absorbed radiation, respectively.

For submicronic particles, the reflected intensity is negligible, while scattering and absorption prevail. The two latter phenomena depend mostly on particle size and chemistry, respectively.

When the particle size is an order of magnitude smaller than the incident wavelength, their scattering is well described by the Rayleigh equation, while when the two dimensions are of the same magnitude order, Mie scattering prevails. In this latter case, Mie's equation describes the light scattering from particles as follows:

$$I_s \propto \frac{N d^6}{\lambda^4} \left[\frac{m^2 - 1}{m^2 + 2} \right] I_0$$

where N is the number of particles, d is the particle diameter, λ is the incident radiation wavelength, and m is the relative refractive index, i.e. the ratio between the refractive index of the particle and that of the dispersing medium.

The two abovementioned equations and considerations, lead to conclude that particle size is a factor that strongly influences the effectiveness of inorganic UV filters. The refractive index of the dispersant is also important in determining the value of m , given as fixed the refractive index of the particles (42). Moreover, being the intensity of scattered radiation proportional to λ^{-4} , small particles scatter UVRs more than the longer visible light wavelengths (43).

As already mentioned, absorption is strictly linked to the chemical composition and structure of particles. Indeed, the absorption of photons generally relates to the excitation of electrons of the Highest Occupied Molecular Orbital (HOMO) to the Lowest Unoccupied Molecular Orbital (LUMO). These transitions are allowed if the photons are in the UV-Vis energy range (200 – 800 nm). If a metal atom in octahedral coordination has partially occupied d orbitals, the photoexcitation often promotes an electron from a lower energy d orbital (t_{2g}) to a higher energy d orbital (e_g) (Figure 3-6).

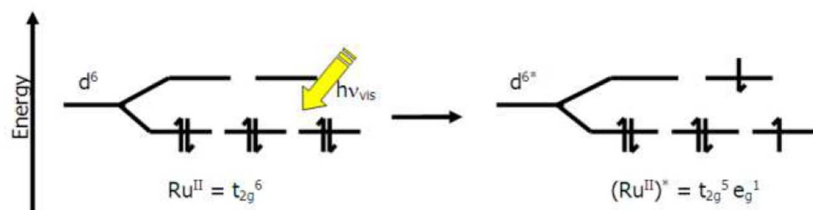


Figure 3-6. Photoabsorption of visible light inducing a d-d transition in Ru(II) explaining the visible color of some Ru-bearing organic molecules (44).

Introduction

When the compound has no d electrons (d^0 compounds such as TiO_2) a d-d transition is not possible and the excitation is possible by transferring an electron from the ligand atom (e.g. O) to the metal empty d orbitals (ligand-metal charge transfer, LMCT). While d-d transitions may be induced by visible photons, LMCT requires higher energy radiation in the UV interval. Thus TiO_2 absorbs in the UV while it appears white in its bulk form (44).

Particle size may secondarily affect absorption efficacy by increasing the number of photon-particle interactions with decreasing particle size. In this sense, all interactions and scattering/absorption processes are even more intricate due to the likely formation of aggregates, that may control the resulting light-matter interaction (42). During the first decades after their appearance in 1952, the absorption capacity of inorganic UVfs was underestimated and they were often referred to as “physical filters” (43).

The two most employed inorganic filters are ZnO and TiO_2 , the latter being used in cosmetics since 1952 (43). Inorganic filters have the advantage of being photostable under UV exposure and having a broad absorption band in the UVB and UVA region (for TiO_2 and ZnO , respectively). However, in cosmetics, a thick layer of oxides is required to effectively cut UVR, and the first formulations with inorganic filters were characterized by a white tone and low spreadability. The whitening was even more marked for TiO_2 particles due to their higher refractive index. Many efforts were made to improve the aesthetical acceptability of inorganic filters, mainly by the reduction of particle size and the use of pigments. The particle size underwent a progressive reduction during the last decades (down to 20-50 nm, (43) reducing skin whitening but shifting the absorption band toward higher energy (42, 45). Moreover, smaller oxide particles display a reduced scattering (linked to whitening reduction) and an enhanced absorbency with a consequent improved catalytic activity that may compromise sunscreen safety, as will be further discussed in section 3.3 (41, 43).

Iron oxide particles were sometimes added to other inorganic filters to mediate, via their reddish tone, the whitening of ZnO and TiO_2 (43, 46). Some iron oxide nanocomposites demonstrated their potential in replacing the commonly employed ZnO and TiO_2 in sunscreens, also thanks to their lower photocatalytic activity and natural skin color (47), but still are poorly found on the market compared to traditional filters.

Inorganic UV filters are of interest also in industrial fields other than cosmetics and are employed as nanosized particles also in polymers, consumer goods, and surface treatments (48, 49).

3.2.2 Organic UV filters

Compounds such as salicylates, benzophenones, cinnamates, and camphor derivatives are the most common organic UV filters. Their molecular structure allows these compounds to pass to an excited state upon the absorption of UV photons of proper wavelength (42). The absorbed energy is dissipated through three main relaxation processes: i) the emission of new photons (radiative decay, i.e. fluorescence and phosphorescence); ii) heat transfer via collisions with surrounding molecules (non-radiative decay); iii) and photoisomerization and photodegradation (photochemical reaction) (43, 50). The higher is the efficiency of the energy dissipation to the ground state, the higher the UV filter molecule stability (51). The ideal lifetime of a UV filter excited state is of few picoseconds. In fact, the excited state is highly reactive and longer lifetime (e.g. a nanosecond) may cause reaction pathways breaking down the molecule and forming reactive oxygen species (ROS) or other toxic byproducts (50, 52).

Jablonski Diagrams (**Figure 3-7**) are visual representations to understand the physical processes taking place during molecule photoabsorption and the fate of the excited state. In the following, a brief description of the main processes is reported.

3.2.2.1 Jablonski Diagrams

Aleksander Jablonski (1898 – 1980) was a Polish academic who devoted his life to the study of molecular absorbance and emission of light.

A Jablonski diagram is an illustration of the different electronic states of a molecule and the possible transitions between them, elucidating the basic principles of organic molecular photophysics (53).

Typically, the diagram represents different energy levels on the Y-axis and grouped in columns on the X-axis, with changing total spin quantum numbers. The numbering of levels just refers to their order in the energy ladder, without implying any other property (e.g. it is not linked to orbital geometry).

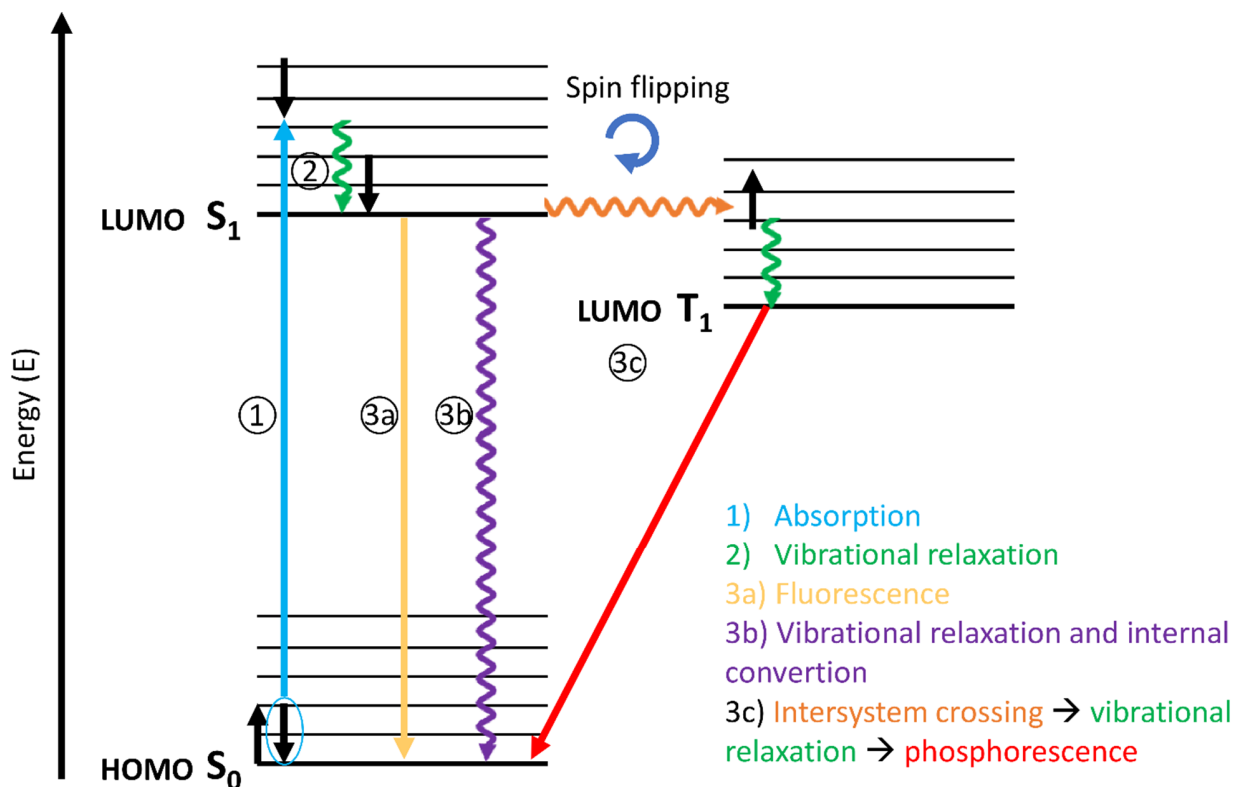


Figure 3-7. Jablonski Diagram showing the interactions between light and matter. Straight arrows indicate radiative processes (i.e. photoabsorption or photoemission), while wavy arrows indicate non-radiative transitions (i.e. vibrational relaxation and intersystem crossing). Different paths are explained in the legend.

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Figure 3-7 shows an example of Jablonski Diagram. S_0 and S_1 are the ground and excited electronic singlet states, respectively. The singlet states contain electrons (black short arrows) with spin $+1/2$ and $-1/2$ so that the total spin is equal to zero. If one of the electron's spin flips, then the electrical level is called triplet state (T, e.g. T_1), and is still an excited state but with non-zero total spin. S_0 is also referred to as the highest occupied molecular orbital (HOMO), while S_1 and T_1 are both lower unoccupied molecular orbitals (LUMO), differing only on electrons' spin. All thin black solid horizontal lines on the top of S_0 , S_1 , and T_1 represent molecular vibrational states of the corresponding electronic state. The lower line of each electronic state, is a ground vibrational state, while higher lines are excited vibrational states. As an example, a molecule in the ground electronic state S_0 may vibrate weakly so being also in the ground vibrational state, or it may vibrate intensively thus being at the highest S_0 excited vibrational state, or in one of the intermediate S_0 excited vibrational states.

Through the Jablonski Diagram, it is possible to represent the excitation and relaxation processes pertaining to the molecule-light interaction. The example in **Figure 3-7** starts from a molecule in the ground state with two electrons of opposite spin in its HOMO S_0 . A photon of proper energy (in the UV-Vis spectrum) hits the molecule and is absorbed, promoting an electron to the excited state, without affecting its spin, so that the electron is now in the LUMO S_1 (path 1). Upon photoabsorption, the molecule also vibrates, so that the excited electron will be on one of the high vibrational levels of the S_1 . The first process, occurring after photon absorption, is vibrational relaxation, which is often represented by a wavy arrow, indicating a non-radiative process (path 2). This process takes the excited electron to the ground vibrational state of the excited electronic state (S_1) via heat transfer to the surrounding molecules. Then, the relaxation process may take three different paths:

1- Fluorescence is the first process that may take the electron from the S_1 bottom straight to the ground electronic and vibrational state S_0 by emitting a light photon (path 3a). It is noteworthy that the fluorescence photon will be of lower energy compared to the absorbed light photon since some energy was dissipated through vibrational relaxation at the excited state. In other words, the wavelength of the emitted photon will be longer, thus explaining why many materials emit visible light under UV exposure.

2- The second process that may occur after vibrational relaxation, is another vibrational relaxation coupled with internal conversion (path 3b). In this case, the process is a non-radiative recombination since no emission occurs and energy is dissipated as heat (vibrational relaxation) causing also a change in the electronic state (internal conversion). Internal conversion is favored if the higher vibrational levels of the lower electronic state are close to, or overlap, the lower vibrational levels of the higher electronic state (54). For molecules that easily undergo photoisomerizations at the excited state (e.g. displaying intramolecular H-transfer), internal conversion is favored compared to other relaxation processes (51).

3- The third fate of the excited state may be the intersystem crossing (path 3c). The spin of the electron flips after the vibrational relaxation at the S_1 , taking the electron to the triplet excited state T_1 , since the total spin is no longer zero. The ground vibrational state of T_1 is energetically lower than that of S_1 since the electronic repulsion is always lower in the triplet than in the singlet state. Therefore, the flipped electron will be at a high vibrational state of T_1 , at about the same energy as S_1 bottom. The electron will now undergo vibrational relaxation to the ground vibrational state of T_1 and, subsequently, it will go back to the unexcited singlet state by emitting a photon (phosphorescence) and flipping its spin. Also, the phosphorescence photon is of lower energy compared to both the absorbed light and the fluorescence photon, since even more thermal energy is dissipated. Spin flipping is a more time-consuming process, thus the intersystem crossing (and hence phosphorescence) is slower (from 1 ms up to several minutes) compared to fluorescence (from 1 ns to 1 μ s) (55).

As already mentioned, the excited state is highly reactive, and multiple photoabsorption events may bring electrons to excited states higher than S_1 (not shown in **Figure 3-7**). In this case, the usual process is vibrational relaxation and internal conversion down to S_1 , followed by the abovementioned relaxation paths down to the ground S_0 states. Indeed, at energy levels higher than S_1 , vibrational and electronic excited levels strongly overlap,

and vibrational relaxation and internal conversion occur simultaneously. Conversely, the major energy gap between S_1 and S_0 makes fluorescence and phosphorescence compete in this transition (54, 56).

Spectroscopic techniques are the main methods to investigate spectral features of a given system (liquid or solid), by showing how efficiently each wavelength, in a given interval, is absorbed or transmitted. The interesting interval for this thesis is mainly that of UV and visible light, and data will thus be reported and discussed referring to UV-Vis spectroscopy (hereafter UV-Vis).

3.2.2.2 Avobenzene (AVO)

Avobenzene (i.e. 1-(4-*tert*-butylphenyl)-3-(4-methoxyphenyl)propane-1,3-dione, or Butyl methoxydibenzoylmethane, or BM-DBM, or Parsol 1789, hereafter AVO) is the most commonly employed UVA filter in cosmetics.

AVO is a white crystalline powder at room temperature, with melting point at 83.5 °C, boiling point at 400-450 °C at 1 atm, molecular mass of 310.4 g/mol, and density of 1.221 g/cm³ (57).

Avobenzene has an equilibrium mixture of keto (K, i.e. diketo) and chelated-enol (CE, i.e. chelated keto-enol) forms, but also non-chelated enol forms (NCE, i.e. non-chelated keto-enol) are possible (**Figure 3-8**). All these forms are more or less persistent at the ground or excited state. The crystalline structure of K AVO was reported by (58) and is shown in **Figure 3-9**.

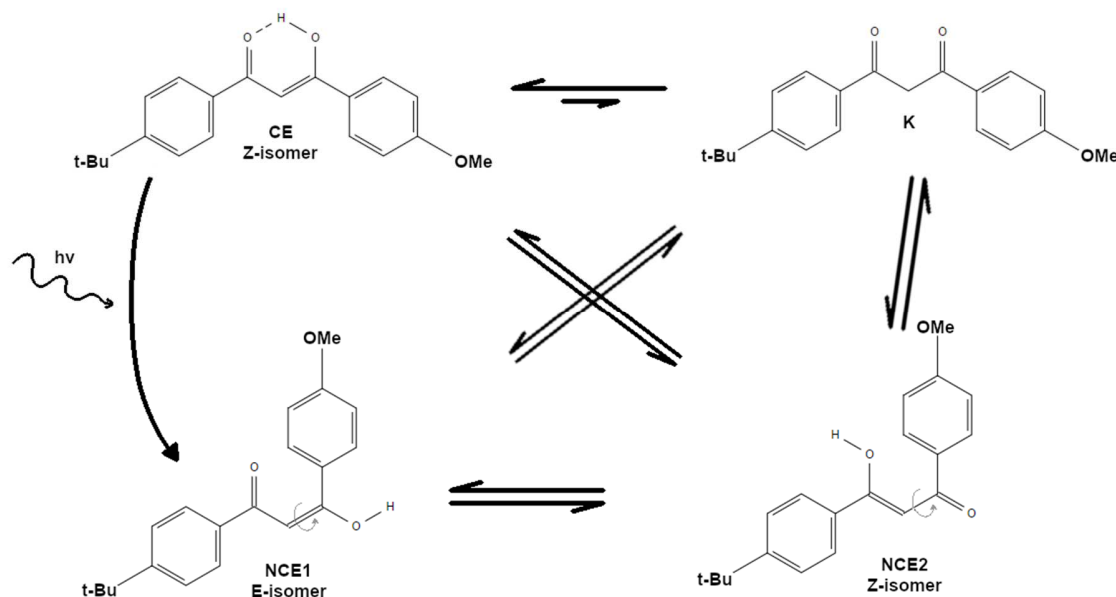


Figure 3-8. Avobenzene conformations: chelated keto-enol (CE), diketo (K), and two non-chelated keto-enol isomers (E-isomer NCE1, Z-isomer NCE2). The bond rotating during CE-NCE1 and CE-NCE2 conversions is shown.

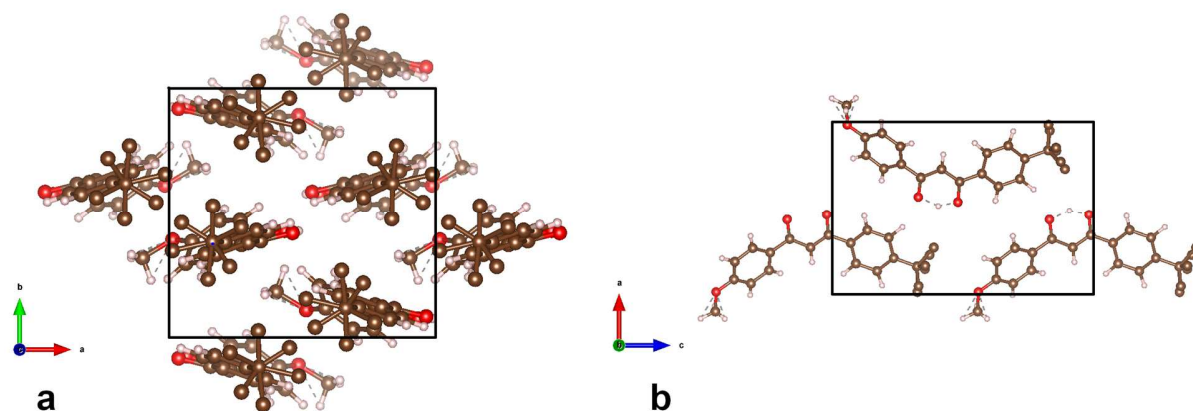


Figure 3-9. Crystal structure of diketo avobenzone (K AVO) as refined by (58). Space group $Pna2_1$, $a = 10.6819(9)$, $b = 9.9640(10)$, $c = 16.2694(9)$. Projections are along the (001) and (010) directions in (a) and (b) panels, respectively. In (b) only some equivalent positions of AVO are shown.

Providing a clear and comprehensive description of the photochemical behavior of AVO is challenging. However, the previously reported Jablonski diagram (section 3.2.2.1) might help in visualizing the relationship between different AVO forms.

The CE AVO (Z isomer) may be considered as the S_0 ground state of the molecule and is generally favored (up to 90% of the total) thanks to its intramolecular hydrogen bond (**Figure 3-8**, (59-63)). By absorbing a UV photon, the CE form jumps from the S_0 to a photoexcited enol state S_1 (in this discussion, all vibrational relaxation processes will be omitted). The typical fate of S_1 is now the internal conversion down to the ground state S_0 mediated by the rotations of the hydroxyl group or of the single (remaining a Z isomer) or double (becoming an E isomer) C-C bonds (61-63). Whatever the rotation occurring, the intermediate species are non-chelated enol forms (NCE1, NCE2, **Figure 3-8**) that finally reconvert quickly (milliseconds lifetimes) to the starting, more stable, CE form (60, 63, 64). This process explains why the CE form of AVO does not display fluorescence under UV exposure. Indeed, the path back from S_1 to S_0 is a non-radiative internal conversion (path 3b of **Figure 3-7**). Less frequently (i.e. with a low quantum yield), the S_1 enol state, once excited, may lead to the formation of the keto (K) form (59, 60). An energy barrier separates the K from the ground CE form, thus making K more persistent (up to hours, **Figure 3-10**) (63). This persistent K form can be photoexcited to singlet or triplet states, which may induce photodegradation of AVO by alpha cleavages (Norrish Type I process) of carbonyl groups (61, 62, 64, 65). Indeed, for example, if AVO is selectively irradiated by a 266 nm laser (i.e. at the excitation wavelength of the K form) in acetonitrile, an irreversible lowering of the 355 CE signal occurs, but with no evidence of an emerging K formation, indicating AVO degradation (60). This observation underlines the connection between the photodegradation of AVO and the excited triplet state of its K form.

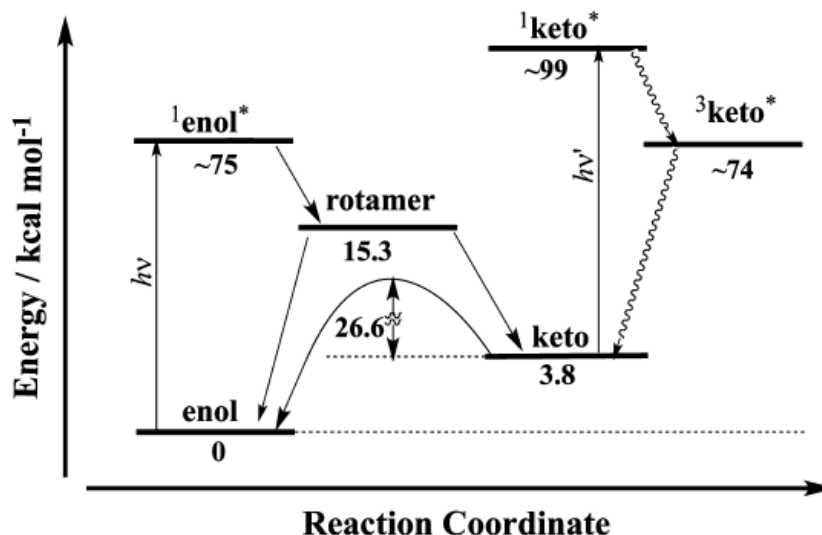


Figure 3-10. Energy diagram of avobenzone in solvent. The energy barrier is visible between the keto (i.e. diketo) and the unexcited enol (i.e. chelated keto-enol) forms of AVO. Other excited states are also shown. Figure from (63).

The polarity of the environment, together with the availability of protons (protic vs non-protic solvents) and the presence of other chemical species, affects the keto-enolic equilibrium and thus the stability and the spectral features of AVO. The behavior of AVO during UV exposure is also strongly dependent on the experimental conditions, such as sample thickness, light power, and timing of exposure (59-61, 63). The larger availability of protons in polar protic solvents makes AVO more stable in this kind of environment, by favoring the S_1 - S_0 internal conversion in the enol forms (64).

As regards its spectral features, AVO displays a large absorption band at 350-370 nm with a shoulder at 380 nm and a weaker band at 260-270 nm in different solvents (**Figure 3-11**) (59, 60). The shoulder and the weaker band are attributed to the K form (n - π^* and π - π^* transitions, respectively) (59), while the wide 355 nm band is characteristic of the CE one and lowers during ketonization (59, 63). The absorption of the K form also displays a tail in the UVB interval, leading to its activity under solar light exposure (64).

The complexity of AVO photochemistry is evidenced by its behavior in different environments. Cantrell et al. (2001) (60) report that the CE signal at 355 nm lowers upon continuous UVA irradiation of AVO in acetonitrile (a polar solvent), but recovers almost totally after resting in the dark for some hours. Conversely, Huong and coworkers showed that the AVO CE form is completely stable in diluted polar solutions (included acetonitrile), while the K form is favored in non-polar solvents: absorbance changes, as low as 1-2%, were observed irradiating diluted solutions of AVO in polar solvents (66). In the same work, the authors investigated also the behavior of AVO in non-polar solvents, aqueous solutions, concentrated solutions, and some commercial sunscreens. AVO showed a reversible ketonization under UV exposure in diluted non-polar solutions. Indeed, the K form totally reconverts to the keto-enol by storing the solution in the dark (**Figure 3-11**).

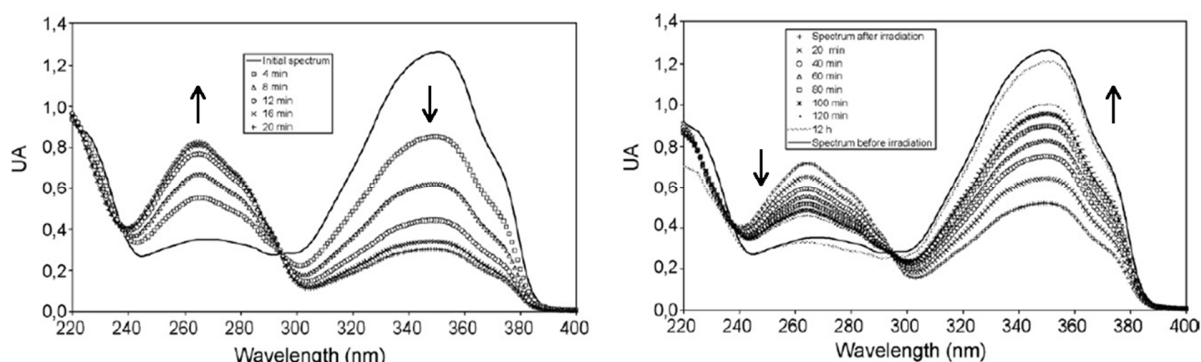


Figure 3-11. Absorption UV-Vis spectra of AVO in heptane. a) data collected before irradiation (solid line) and during UV irradiation, each 4 minutes up to 20 minutes; b) spectra of the non-irradiated solution (solid line), and of the irradiated solution during storing in the dark, each 20 minutes up to 2 hours and finally after 12 hours. Arrows indicate the direction of absorption variations. Figure from (66), arrows added.

By adding 1% polar solvent in a non-polar solution, the keto-enol form of AVO is again stabilized, hindering its transient K form. As regards aqueous solutions, AVO in isopropanol (polar) was found stable up to 75% of water. If the water content is increased by over 90%, an irreversible degradation of AVO is observed. Indeed, the characteristic 355 nm band lowers and a large number of products were detected in HPLC chromatograms. AVO in concentrated (2-4% of AVO), non-volatile, solutions (mineral oil, isostearyl isostearate, capric caprylic triglyceride, alkyltartarate, alkyl lactate) degrades losing up to 80% of its absorption due to the exposure of a thin film to a solar simulator (550 W/m² for 15 min). Similar behavior of AVO was detected in 11 commercial sunscreen products under the same exposure conditions. However, high SPF (50+) products, after the addition of proper stabilizers, demonstrated higher stability of AVO (see (66)). By other authors, emulsions containing AVO as the only UV filter were found to lose up to 90% of UV filtering power after 4 hours of UV exposure. Photodegradation of AVO can be reduced by adding other UV filters to the emulsion (e.g. octocrylene, oxybenzone, or a mixture of octisalate and homosalate). However, a formulation containing both AVO and octinoxate (OMC) rapidly degrades under UV exposure, with a total loss of UV protection in less than 4 hours. The degradation of AVO and OMC mixtures is linked to photochemical reactions between their excited states, which lead to the formation of unstable photoproducts (67).

Toxicological tests were performed on AVO, revealing cutaneous and ocular irritation, together with phototoxicity and subcutaneous toxicity (59). The triplet state of the K form, indeed, was found to be responsible for the formation of singlet oxygen species (¹O₂, a toxic reactive oxygen species, ROS) (60, 64). The addition of triplet state quenchers can inhibit the formation of ¹O₂ species (60).

3.2.2.3 Octinoxate (OMC)

Octinoxate (octyl methoxycinnamate or Parsol MCX or, hereafter, OMC) is one of the most commonly employed UVB filters. Particularly, OMC is used together with other UVfs to reach high SPF values of the final formulations (32, 68). During the last decade, OMC has been progressively substituted by other UVfs due to concerns about its potentially harmful effects on the environment (see section 3.3). As for AVO, a brief description of OMC features and response to UV exposure is reported in the following.

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Pure OMC is, at room condition, a clear, almost colorless liquid, with melting point at $-68.3\text{ }^{\circ}\text{C}$, boiling point at about $380\text{--}400\text{ }^{\circ}\text{C}$, molecular mass of 290.40 g/mol , and density of 1.01 g/cm^3 (69).

OMC displays its main absorption in the UVB range with a low-energy tail in the UVA interval. At the ground state trans (E) and cis (Z) isomers coexist in OMC solutions, with the E isomer prevailing, and the E/Z ratio being solvent-dependent (**Figure 3-12**) (70).

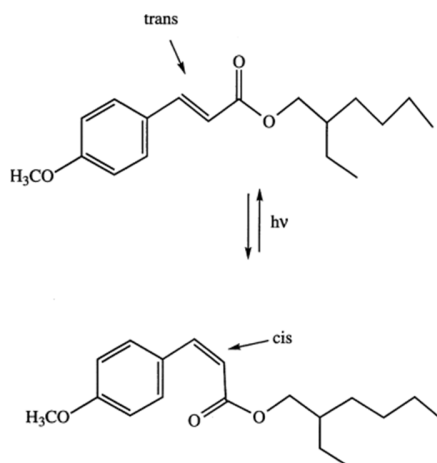


Figure 3-12. Octinoxate trans (E) and cis (Z) isomers. Figure from (71).

Under UV exposure, at the excited S_1 state, photoisomerization occurs about the propenyl double bond, favoring the formation of cis-OMC, which remains then stable also after relaxation (70-73). OMC suspensions move quickly ($<50\text{ s}$) to a new trans-cis equilibrium, also losing up to 30-40% of their original absorbance. Indeed, the absorption efficacy (i.e. the extinction coefficient, ϵ) of trans-OMC is almost double that of cis-OMC (70, 73). The deactivation of excited OMC in solution mainly occurs by isomerization and internal conversion (path 3b of **Figure 3-7**), as evident by the low fluorescence yield (70, 73). Thus, the two isomers, in organic solutions, are very stable and do not induce the formation of other species absorbing in the UV range. Hence, the primary consequence of UV exposure is a change in the trans/cis ratio and a consequent lowering of UV absorption capacity (70, 71, 74).

Generally, the trans-OMC displays its absorption maximum (λ_{max}) at 310 nm, while the cis-OMC at 305 nm (70). However, as was shown for AVO, also the behavior of OMC varies by changing the experimental conditions. OMC displays different behaviors in organic or aqueous environments, in polar or apolar solvents, in diluted or concentrated solutions, and bulky or thin layers.

As an example, λ_{max} of trans-OMC shifts from 291 to 310 nm by changing solvent polarity from the apolar cyclohexane to the polar ethanol. This redshift makes OMC absorption better overlapping the solar spectrum (70), and the same redshift was observed for OMC fluorescence spectra in polar solvents (73). Conversely, cis-OMC λ_{max} (305 nm) is not affected by solvent polarity.

The solvent polarity affects the OMC photoisomerization, by modulating the energy gap between charge transfer and π - π^* energy levels, consecutively affecting the deactivation path of OMC S_1 (73). Also, trans-OMC is more hydrophobic than cis OMC, thus the trans-cis equilibrium moves towards the cis form with increasing polarity (74). UV irradiation of OMC can cause the formation of ROS, and $^1\text{O}_2$ in particular, depending on solvent

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polarity. As the short lifetime of OMC S_1 should not allow the formation of $^1O_2$ strictly from S_1 , the observed formation of $^1O_2$ indicates that, under some conditions, an excited triplet state of OMC is formed, even if the deactivation of S_1 by internal conversion and photoisomerization (path 3b) is generally very effective. Polar solvents may explain the observed ROS production by stabilizing the S_1 state, thus allowing, albeit minorly, the production of excited, longer-living, triplet states (73). In polar, aqueous solutions, the triplet excited OMC may interact with H_2O molecules producing hydroxyl derivatives upon direct photolysis (66, 68). The presence of oxygen causes degradation of OMC: in air-saturated solutions in polar solvents, OMC undergoes irreversible transformations under UV exposure, in addition to reversible trans-cis isomerization. Indeed, the absorption of OMC in polar oxygenated solutions decreases also after the reaching of the new photostationary trans-cis equilibrium. This behavior is not reported in deoxygenated polar solvents or oxygenated apolar solvents (73).

The aggregation of OMC molecules in colloidal aqueous suspensions (also at low μM concentrations), or in thin neat OMC films, favors the degradation process, inducing the formation of various species. Some of those photoproducts absorb in the UVA range and induce the production of $^1O_2$ (68, 70). In these conditions, OMC displays a red-shift of the absorption band toward the UVA (λ_{max} at 328 nm), and a marked tail in the red visible light, together with three absorption bands at about 280, 310, and 400 nm, and a high background due to particle-like scattering. Moreover, aggregated OMC molecules have a strong yellow tone which, in similar cinnamate derivatives, was attributed to photo-Fries rearrangement; intriguingly, such processes should be impossible in OMC for the absence of phenolic linkages. Alternative pathways may involve the reaction of molecular fragments with whole OMC molecules, leading to dimerization and photocyclization. Indeed, the appearance of the 280 and 400 nm bands indicates the formation of photoproducts with lowered and enhanced conjugation (i.e. with shorter or longer alternation of single and double C-C bonds), respectively. The overall red-shift can be a direct effect of both these intermolecular interactions, and the formation of larger molecules (70). Also, some neo-formed peaks disappear under protracted UV exposure, indicating further degradation of OMC byproducts. The long lifetime of the excited states of these byproducts may explain such reactions, which were not observed for monomeric OMC in dilute solutions. Indeed, the excited 400 nm absorber, formed in aggregated OMC molecules, displays a long lifetime that may result in further reactions at the excited state. The aggregation of OMC must be prevented, as the excitation of these 400 nm species was also demonstrated to cause $^1O_2$ production under UVA exposure (70, 75).

The behavior of OMC in an aqueous environment is particularly interesting for the implications on the environmental fate of such sunscreen in nature. Indeed, as was shown, the photochemistry of OMC in a water-based environment is complex (**Figure 3-13**). Fortunately, in nature, OMC photochemistry mainly involves direct photolysis reactions, while reactions among the decayed products are in general negligible for the low concentration of dispersed OMC (generally ppb-ppt). Despite this, in some specific settings such as surface waters and sediments, a higher concentration (ppm) of OMC may occur with potentially harmful effects (66, 68).

A deeper discussion of UV filters' impact on the environment will be discussed in section 3.3.

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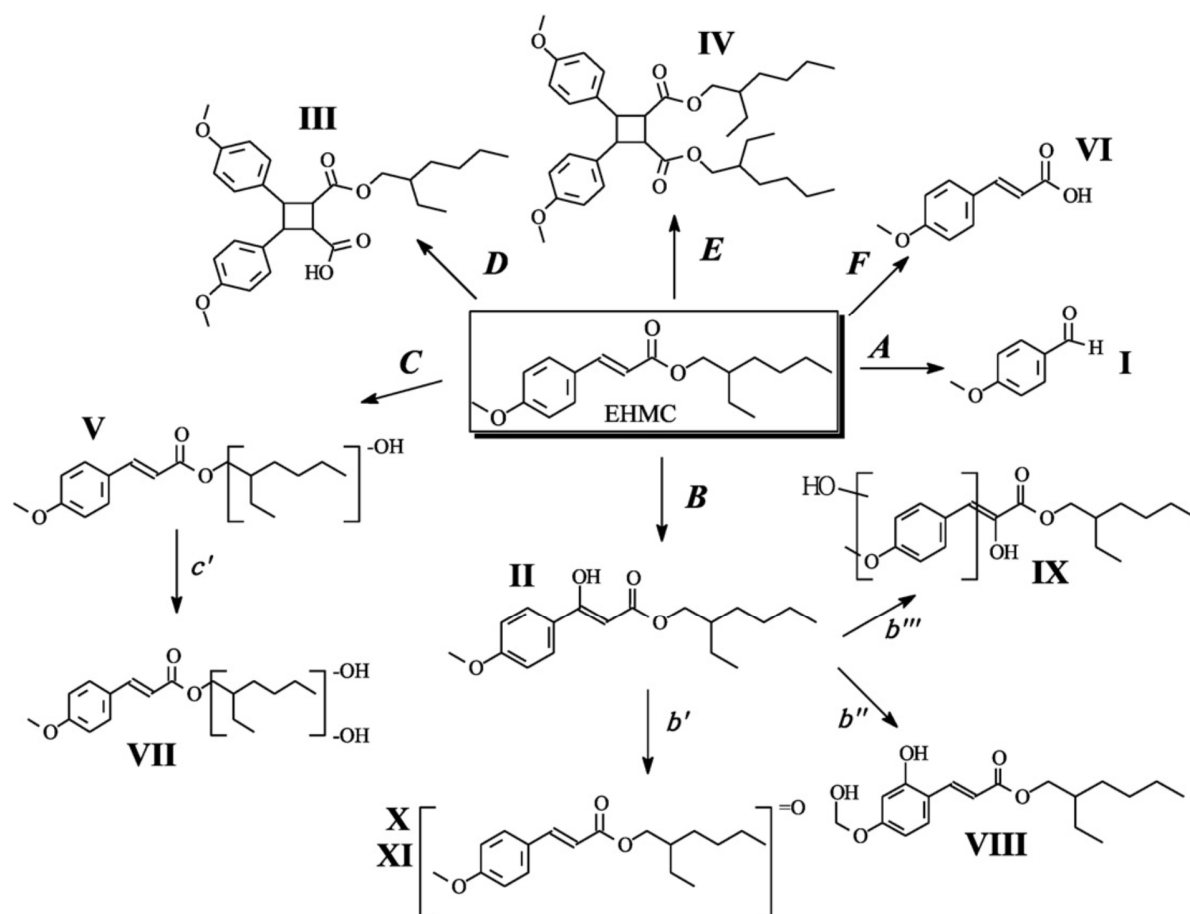


Figure 3-13. Possible pathways of photodegradation pathways of OMC in an aqueous environment. EHMC is pristine OMC. Routes A and F involve OMC dealkylation, while paths B, C, D, and E occur only through direct photolysis and follow mono- or di-hydroxylation, possibly involving the dimerization of OMC; path F involves dealkylation processes leading to the formation of 4-methoxycinnamic acid. The figure is from (68).

3.3 UV filters' ambiguity: benefits and issues for human health and environment

As discussed previously, UV filters are of paramount importance in protecting humans from UVR. However, despite the ubiquity of UVfs, e.g. in personal-care products, their effects on health and the environment are ambiguous. The behaviors of AVO and OMC molecules summarized in section 3.2.2, highlight the complexity of the photochemistry of UVfs. In this scenario, the interaction of UVfs and their degradation products with the environment is even more complicated and thus researched in-depth, with various stability and safety issues that deserve to be understood and hopefully solved.

The UVfs efficiency in energy dissipation under UV exposure is of paramount importance. As was shown (section 3.2.2.1), internal conversion is one of the fastest and most effective deactivation paths of UVfs excited states. The internal conversion rate is strongly enhanced when excited molecules can undergo trans-cis photoisomerization or keto-enol tautomerization. If this kind of “safe” reaction is not efficient, UVfs' bonds may break and recombine, forming new chemical species. These structural changes may be reversible or irreversible,

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leading in the latter case to photoinstability. The photodegradation of UVfs causes a lowering of UV protection. All photoproducts are of difficult characterization, and many of them were found to induce ROS production, with potentially harmful effects on living organisms (51).

The combination of multiple UVfs and additives is often adopted to obtain broad-spectrum sunscreen products, *e.g.*, (76, 77). This may preserve the protective effect against UVR but might also cause the build-up of degradation products on the skin or inside organisms (66). In some conditions, the interaction between different compounds may foster the photodegradation process: the co-presence of OMC and AVO in the same formulation, for example, induces the complete photodegradation of both UVfs after 4 h of UV exposure (67). Repeated application of sunscreens is needed to compensate for the loss of efficacy due to the UV filter decay but may cause the accumulation of photoproducts in the skin (66). It is worth noting that complex formulations enable many different reaction paths between their components, increasing the risk of allergic reactions (70, 78). The stability of sunscreen is not easily predicted, since all these complex interactions between co-formulants may radically change the reactivity/stability of individual components (51, 52).

The behavior of UVfs is also affected by the surrounding environment. After dispersion in the aquatic environment, UVfs can undergo direct photolysis or indirect photochemistry. Direct photolysis refers to all UV filters transformations directly induced by the absorption of UV photons. Conversely, the indirect photochemistry implicates the absorption of light by other species (*e.g.* chromophoric dissolved organic matter, CDOM) with the consequent formation of reactive species (*e.g.* ROS) that further react with UVfs causing their degradation (68).

The problems are not only linked to organic UVfs. Inorganic filters (see section 3.2.1) are excellent photocatalysts and induce the formation of ROS if irradiated in an aqueous environment (**Figure 3-14**) (43, 79, 80). Moreover, inorganic UVfs were found to enhance the degradation of organic filters (79).

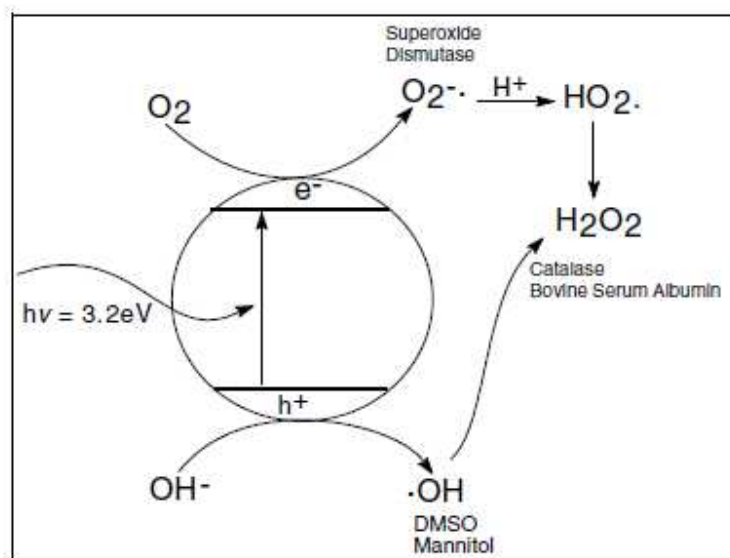


Figure 3-14. A simple scheme of photoinduced ROS production from uncoated TiO_2 particles in oxygenated aqueous suspensions. Figure from (43).

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As an example, the degradation rate of OMC was sensibly accelerated when it was exposed to UVR in the presence of TiO₂, with a half-life of fewer than 40 minutes (68). Inorganic UVfs are thus often coated with organic or inorganic compounds to deactivate their external surface, thus inhibiting photocatalytic reactions and reducing their interactions with other components (76, 80).

Organic and inorganic UVfs are gaining more and more attention during the last decades as emerging contaminants, being detected in many natural matrices (e.g. rivers, lakes, seawater, wastewater, sludge, soils, crops, and biota (14, 68, 81-85)). The occurrence of organic UVfs was also reported in biota and seawater in polar regions (Arctic and Antarctic) confirming their global diffusion, highlighting the risk that these contaminants pose to vulnerable ecosystems (83). The behavior of UV filters is mainly linked to their high lipophilicity and low biodegradability. The aquatic environment is the most affected by the accumulation of UVfs, which were detected in ppb to ppt levels in surface waters (68). UVfs enter the water cycle directly from aquatic recreational activities, or indirectly from urban wastewaters. The latter path is particularly relevant for organic UVfs (14, 83, 86-88). Indeed, organic UVfs escape wastewater treatment plants thus entering the natural water cycle (87). Interestingly, the amount of UVfs measured in seawaters was often found to follow a seasonal trend, with higher levels in summer (up to 4.4 times higher) compared to the other seasons. However, quite high levels were detected throughout the year, especially in surface waters near wastewater effluents (83). These data stress the role of both direct and indirect release of UVfs in seawater, with the former being shorter in time but higher in levels compared to the latter. Once UVfs are in the aquatic environment, they can accumulate in sediments and biota, e.g., (81, 85, 86, 90, 91). UVfs bioaccumulate at different trophic levels and were detected, e.g., in mussels, crustaceans, eels, fishes, marine mammals, and aquatic birds (86, 92-95). Indeed, especially organic UVfs tend to accumulate in fatty tissues of all exposed organisms, due to their high lipophilicity (14, 68). During the last decades, the impact of UVfs on corals is of particular scientific interest. Danovaro and coworkers (96) showed that different sunscreen products can cause almost complete coral bleaching within 48 hours, even at concentrations lower than 10 ppm. The same team reported the effect of inorganic UVfs on stony corals, showing, e.g., that uncoated ZnO particles cause faster coral bleaching compared to coated TiO₂ particles (95). Based on this evidence, various States (e.g. Hawaii, Palau, US Virgin Island and Key West, and Mexico) have restricted the use of some organic UVfs, and the EU reduced their concentration limit in sunscreens (European commission, 2017) (14, 96).

The increasing awareness of the impact of UVfs on aquatic organisms has brought attention to their possible effects on human beings (14). A high concentration of UVfs can expose organisms to oxidative stress due to the formation of ROS (see **Box 3-1**, (17-19, 87)) and was proven to act as endocrine disruptors by in-vitro and in-vivo tests (14, 68). The high persistence of UVfs and their byproducts in the aquatic environment rise also concerns about their presence in drinking water supplies (91, 92), with even more severe implications for human health.

The toxicity of AVO and OMC has been thoroughly investigated in the literature, being the two among the most (if not truly the most) employed UVfs in cosmetics.

OMC is typically considered safe for humans, and very few photosensitization reactions are reported (32, 72). However, as it was discussed previously (section 3.2.2.3), OMC was found to induce ROS production, especially when it aggregates (68, 70). Moreover, OMC was found to penetrate the human skin, with evidence that in the lower epidermis the aggregation of OMC may occur, possibly inducing ROS production underneath the skin (70). Some concerns arise on high-dosage exposure of humans to OMC. Indeed, in vivo and in vitro experiments showed estrogenic effects of OMC in rats, with reproductive and neurological consequences on their offspring (68). OMC, as was stated by in vitro tests, can induce DNA damage to cells, and demonstrated a high hazard index in human liver stem cells and lymphoblastoid cells (14).

OMC occurrence in the environment has been assessed in waters, soils, and biota, e.g., (68, 83, 96). The phototransformations of OMC in the marine environment depend on the water depth and the DOC (dissolved organic carbon). The presence of CDOM may compete with OMC in light absorption, thus reducing OMC

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degradation (68). Under UV exposure, aqueous OMC solutions form several different products, some of which were predicted to be highly toxic for marine species. Danovaro and coworkers showed that OMC is one of the most threatening UVfs for corals, possibly promoting viral infections (96).

AVO is also considered safe and quite stable if pure. However, many studies revealed a strong dependence of its behavior on the presence of other compounds and UVfs (97). Many UVfs, added to AVO-containing formulations, were found to stabilize AVO in its active form. Conversely, formulations containing both AVO and OMC displayed an enhanced photodegradation of the two UVfs during thin films UVR exposure. Indeed, the photolysis process of OMC and AVO prevails on the photoisomerization, leading to the production of ROS. The lifetime of free radicals derived from AVO in these conditions is extended up to several minutes by the semi-condensed lotion matrix. AVO fragments may then interact with the OMC molecule inducing its degradation. Further processes may subsequently involve the highly reactive triplet states of all previously formed products. During the last decades, many efforts were spent in studying OMC and AVO decay products, trying also to investigate their potential toxic properties, e.g., (52).

Accordingly to Bonda (98), the behavior of UVfs in formulations may change considerably moving from laboratory conditions to actual practice. It is worth noticing that the photoinstability of UVfs does not necessarily coincide with a toxicity towards organisms (70). Moreover, despite the potential toxicity of UVfs and their byproducts, sunscreens are generally not dangerous in the amounts normally applied to the skin (99), and they are an essential defense against UV rays. However, the issues linked to their use, diffusion, and stability call for an exhaustive study for the elucidation of their behavior. Similarly, the development of safer sunscreens is urgent on the ground of environmental concerns.

Various strategies to improve UVfs stability, or at least prevent loss of efficacy, were investigated and will be discussed in the next section.

3.4 UV filters' engineering

The research on UVfs and sunscreens aims to overcome all issues linked to the stability of UVfs and to enhance the protective efficacy of the final sunscreen product. These requirements are pursued by several strategies, focusing both on the stability of UVfs, and on the sunscreen formulation.

To obtain safer formulations, stabilizers (e.g. single-single (S-S) and triplet-triplet (T-T) quenchers) are typically added to sunscreens to prevent the degradation of UVfs by making more efficient the deactivation process of the UVf's excited states. These compounds (e.g., Octocrylene, 4-Methyl benzylidene camphor, Diethylhexyl naphthalate, Polyester-8) act by favoring internal conversion of energy, thus reducing the probability of intersystem crossing and, thus, of photochemical reactions at the triplet excited state. Most excited state quenchers absorb in the UVR interval, and many of them are also approved UV filters. Of note, new quenchers are sometimes added as inactive ingredients (i.e. non UVfs) before their use as UVf is authorized by competing authorities (13, 51, 98, 100). Antioxidants are also added to sunscreens as ROS quenchers (100), capable of preventing the toxic effects of UVfs byproducts. Moreover, the fast deactivation of free radicals and ROS inhibit the radical chain reactions, which are one of the main causes of UVf degradation. As an example, AVO stability may be improved by adding emollients (10) or other UVfs to the formulation but excluding OMC that degrades quickly if combined with AVO. Other UVfs may extend AVO lifetime by competing in UV absorption. AVO can also be stabilized by triplet-triplet energy transfer to the excited state of the other filter, which may be then degraded itself. The other UVfs added to AVO can also act as antioxidants, deactivating ROS by chemical or physical processes (64).

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As for stabilization strategies of UVfs, attempts are made to either obtain new UVfs or to modify the existent UVfs to improve their properties.

Inorganic UVfs were already shown to be photocatalytically active (section 3.2.1 and 3.3), with a consequent ROS production and accelerated degradation of organic filters. Thus, metal oxide filters in cosmetics are often coated with inorganic (e.g. alumina, silica, zirconia) or organic (e.g., dimethicone, and plastics) layers, to reduce the release of ROS, or scavenge them before they interact with other compounds or the skin itself (43, 95). In a recent review, Adler and DeLeo (2020) underlined that published data on coated and uncoated TiO₂ and ZnO nanoparticles are not entirely clear, and in some cases coated and uncoated forms showed similar results, especially on skin permeation tests (101). Furthermore, composite inorganic UVfs were reported, mainly aiming at the inhibition of the catalytical properties of traditional metal oxide particles. For example, nanocomposites of TiO₂ dispersed on micro-sized ZnO particles were demonstrated to lead to high sun protection factors (SPF, **Box 3-2**) (102).

The behavior of organic UVfs is even more complicated due to the several reactions possible at the excited state. However, some structural features (e.g. isomerism, tautomerism, a hydroxyphenyl group ortho to a carbonyl or ring-bound nitrogen) seem to correlate to a higher photostability. The main effect of these features is that of favoring a fast internal conversion (path 3b of **Figure 3-7**), rather than intersystem crossing (path 3c). Conversely, compounds with vinylic moieties (e.g. OMC) or amine substituents seem to be less photostable, even if the formulation components can still affect their fate (98). All these aspects must be considered while searching for new effective UVfs.

The encapsulation of organic UVfs is another option to improve their stability. A summary of this topic is presented in the next section, due to its particular relevance to this thesis.

3.4.1 Encapsulated filters

During the last decades, the need to obtain safer UVfs prompted a strong interest in the development of encapsulated organic UVfs. Carriers, and particularly nanocarriers, are used to transport drugs or active ingredients to a targeted location. In pharmacology, these carriers generally do not have any active biological role but work only as transporters. In cosmetics, the use of carriers (e.g. nanoclays and mesoporous silica) is reported in various cases (e.g. UVfs, antioxidants, vitamins) (42).

In the literature, several studies reported the encapsulation of organic UV filters in both inorganic and organic capsules, stressing the interest in these systems (for a review (34)). The encapsulated filters prevent the interaction of UVfs (and of their possible byproducts) with the skin, thus preventing skin sensitization. Moreover, photodegradation of encapsulated UVf may be reduced, skin protection may be improved by the capsule absorption/scattering contribution, and the formulation can be more evenly spread, inhibiting filter aggregation. Moreover, the encapsulated active compound is isolated from possible incompatible components of the formulation (34, 42, 103).

Among inorganic matrices, hydrotalcites (104), amorphous silica (105, 106), mesoporous materials (107, 108), and metal-organic frameworks (MOFs) (109) were reported as encapsulating agents, along with organic capsules such as, e.g., polymers (110), ethylcellulose (111), lipid particles, nanoemulsions, and liposomes (34).

The encapsulation of OMC into poly-dil-lactide-coglycolide organic nanoparticles enhanced the stability of the filter by about 20% (32). Similarly, the encapsulation of AVO was reported in β -cyclodextrin. In this case, the degradation of AVO was not prevented, but it was demonstrated that the photoproducts were retained inside the capsules, thus reducing toxic effects and sensitizing reactions (59).

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Mesoporous silica materials (i.e. amorphous solids bearing hexagonal arrays of nanosized pores) have been used as inorganic shielding. The pore dimension enables the encapsulation of medium-small molecules, which can be adsorbed and released. Encapsulation of OMC, benzophenone-3, and of few other UVfs into mesoporous silica was reported (42, 107, 108), with some promising results such as an enhancement of UV filtering properties. Of note, the interaction of UVfs with mesoporous materials was found to be weak, and the molecules are readily released. To overcome this issue, in some cases, the pore openings were plugged with other compounds. However, the resulting materials were suitable only for water-based sunscreen formulations (Section 3.1.2), due to the lipophilicity of plugs that would be released in oil-based formulations (42, 107, 108).

The effectiveness of UVfs' encapsulation is highlighted in several patent applications. For example, the use of amorphous-silica spheres as encapsulating agent of UVfs was patented, demonstrating their stabilization by preventing the interaction between different active components in the formulation (112). Similarly, zeolite imidazolate frameworks (ZIFs), a particular group of metal-organic frameworks (MOFs) were used for the encapsulation of OMC and other UVfs. MOFs are microporous crystalline materials composed of regular complexes of organic molecules coordinated to metal cations, forming channels and cages of molecular sizes (**Figure 3-15**). ZIFs are MOFs in which the organic compound is imidazolate and the metal ion is zinc. Despite the good efficacy of UVfs encapsulation in ZIFs, the stability of MOFs in aqueous environments is known to be limited (113), especially when compared to that of their inorganic counterparts, zeolites (see below).

Zeolites (section 3.5) were also evaluated as an inorganic host for organic UVfs; however, a thorough investigation of their use as scaffolds for the stabilization of photolabile molecules is still lacking. In the literature, three papers published by Chretien and coworkers (114-116) presented preliminary results on the encapsulation of oxybenzone (OXB) and para-aminobenzoic acid (PABA) UVfs into sodium Y zeolite (NaY). The authors showed that PABA encapsulation into NaY zeolite enhances the absorption power of the filter, also broadening its absorption in the UVA interval. Moreover, the encapsulation was found to reduce to about one-third the oxidative stress on a target protein when compared to the pristine UVf, indicating a reduction of ROS production. Authors also suggested that the zeolite-encapsulation of PABA would also inhibit the electron-exchange energy transfer, which causes DNA damage (114). Similarly, OXB retained (or slightly improved) its spectral features after encapsulation into NaY zeolite, again showing absorption broadening in the UVA interval. Furthermore, the encapsulated OXB displays a very low sensitizing activity, which is high for the pristine filter. OXB is known to be photounstable in the presence of TiO₂, but Chretien and coworkers demonstrated that when OXB is encapsulated in the zeolite the degradation is significantly decreased.

Most of the literature on encapsulated UVfs focuses on their stability in a medium-short timescale (in the range of hours) since this is the most important to study the properties of sunscreens on human skin in their practical use. The leaching of the UV filter from its capsule in a longer time has never been studied, and pertaining the end-of-life disposal into the environment, encapsulated UVfs will probably behave as pristine filters. A deeper understanding of the long-term properties of encapsulated filters is thus needed before they can be safely formulated into commercial sunscreens.

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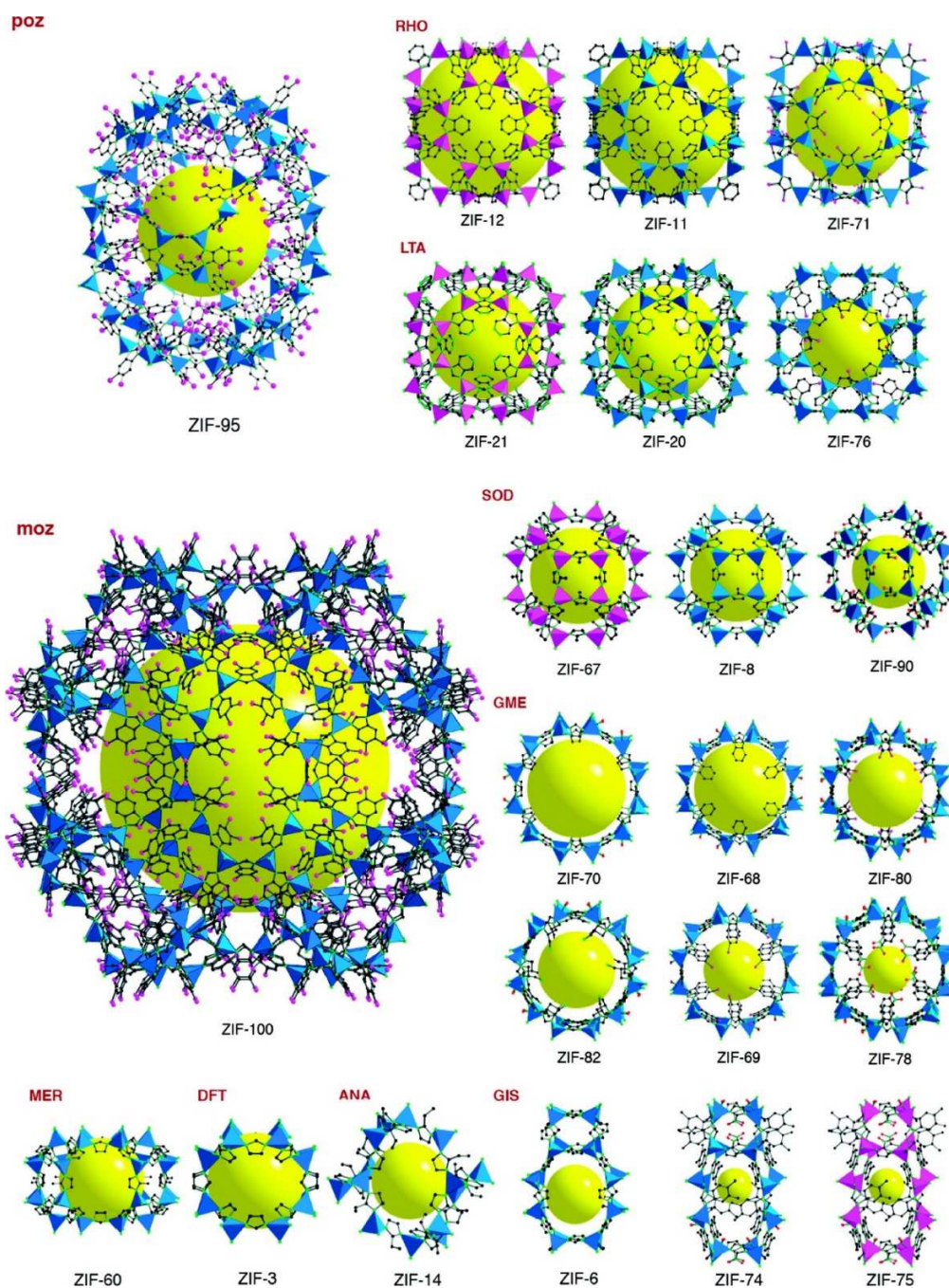


Figure 3-15. Examples of zeolite imidazolate framework (ZIF) crystal structures grouped according to their zeolite-equivalent topology (three-letter symbol, see section 3.5.1). Topologies poz and moz are reported using the RCSR (Reticular Chemistry Structure Resource (117)) structure symbols. For each ZIF the largest cage is shown. Tetrahedra of ZnN_4 are in blue and CoN_4 in pink, linked by a ball-and-stick representation of organic molecules. Spaces inside cages are given as yellow balls. H atoms are omitted, while C (black), N (green), O (red), and Cl (pink) are reported as small spheres. Figure from (118).

3.5 Zeolites

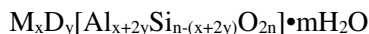
3.5.1 General features of zeolites

Zeolites (from the Greek “zeo” = to boil and “lithos” = stone, i.e. “boiling stone”) are a wide group of mineral and synthetic materials characterized by an open crystalline microporous structure. Starting from the natural, aluminosilicate phases, the term has progressively broadened to include various synthetic zeolites and other zeolite-like materials. The latest official zeolite mineral definition is as follows (119):

“A zeolite mineral is a crystalline substance with a structure characterized by a framework of linked tetrahedra, each consisting of four O atoms surrounding a cation. This framework contains open cavities in the form of channels and cages. These are usually occupied by H₂O molecules and extra-framework cations that are commonly exchangeable. The channels are large enough to allow the passage of guest species. In the hydrated phases, dehydration occurs at temperatures mostly below about 400 °C and is largely reversible. The framework may be interrupted by (OH, F) groups; these occupy a tetrahedron apex that is not shared with adjacent tetrahedra”.

As it was stated by Baerlocher and coworkers (2007, (120)), an all-inclusive definition of zeolite and zeolite-like material is challenging. The number of tetrahedral atoms (T) per 1000 Å³ should be used to discriminate zeolite and zeolite-like materials (T < 21) from other denser, fully crosslinked frameworks (T > 20) (120, 121).

A general chemical formula for aluminosilicate zeolites is:



Where M are monovalent and D divalent cations; the square brackets include the framework tetrahedral cations and oxygen atoms. The extraframework content is usually represented, in natural phases, by the exchangeable cations Ca, Na, Mg, K, H, Ba, Sr, and by H₂O molecules (122). Nowadays, almost any extraframework atom has been reported in synthetic zeolites, e.g. Li, Be, Cs, Cu, Pb, REE, and organic molecules, as well.

Besides specifying that tetrahedral trivalent cations may be represented by Al, Fe, B, Ga, Ti, and Ge, Paillaud and Patarin (123) differentiate zeolites, with Si/T < 500, from zeosils, with Si/T > 500. Aluminophosphates are a very important group of materials among other zeolite-related microporous solids, (123).

Zeolites frameworks are often classified by their channel system, which can be 1-, 2-, or 3-dimensional, indicating in how many directions the extraframework species are allowed to diffuse (**Figure 3-16**) (120).

Zeolite frameworks are designated by three capital letters generally referring to the Type Material (i.e. the first species used to describe that framework structure) (120, 124). A hyphen or a star precedes the 3-letters code if the framework is interrupted or disordered, respectively (123). The International Zeolite Association (IZA), in its Database of Zeolite Structures (www.iza-structure.org), counts up to 244 different frameworks and provides detailed descriptions for each of them.

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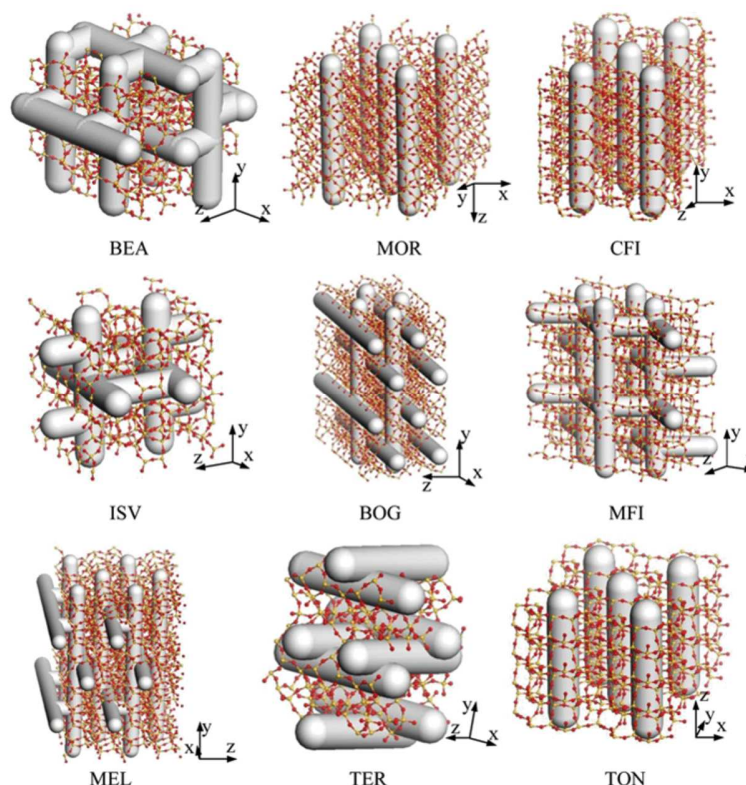


Figure 3-16. Schematic drawing of selected zeolite structures. The gray cylinders represent the channels, and the ball and stick represent zeolite frameworks. Figure from (125).

Zeolite properties are strongly influenced by the ratio between tetravalent and trivalent cations in the tetrahedral sites, which is reported as R:

$$R = \text{Si}/(\text{Si} + \text{Al} + \text{T}^{3+})$$

where T^{3+} are other trivalent framework cations. Zeolites are hence defined “silica-rich” ($R > 0.80$) or “silica-poor” ($0.50 < R < 0.60$), while “medium-silica” are those with intermediate R values.

The Si/Al ratio is often used instead of the R parameter, and hereafter it will be used in this thesis since all studied zeolites are aluminosilicates.

Low Si/Al ratios indicate a high Al content and thus a high number of extraframework cations. These zeolites are generally highly hydrophilic and with a high cation exchange capacity. Conversely, zeolites with a high Si/Al ratio have less demand for charge balancing cations and are more hydrophobic and organophilic. Zeosils represent somehow the endmembers with the highest Si/Al ratios and are thus sometimes referred to as all- or high-silica (HS-) zeolites. Zeosil frameworks contain almost only tetravalent cations (commonly Si) and are usually obtained by dealumination processes. These post-synthesis treatments usually cause the formation of structural defects and mesoporosity (123).

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Thanks to their features, zeolites display unique properties of industrial relevance. Among the most relevant are:

- High and selective cation exchange capacity
- Reversible dehydration
- Molecular adsorption and sieving
- Surface activity and catalytic properties

Zeolites display an effective and selective cation exchange capacity. Indeed, once a cationic zeolite is put in contact with a solution containing cations, the extraframework species in the channels can be exchanged with the surrounding medium, preserving the charge balancing in the structure. The term “selective” indicates that zeolites preferably absorb, or retain, certain atoms/molecules due to their dimension, charge density, abundance, and hydration capacity (126-128).

Similarly, zeolites are also capable of absorbing organic molecules. The size and shape of the entry rings of channels and cages, typically ranging between 4 and 12 tetrahedral atoms (i.e. 3 to 10 Å of free diameter), is the first parameter to be considered in evaluating the capacity of a molecule to diffuse in the structure. Indeed, the guest kinetic radius must be smaller than the zeolite opening. In this sense, zeolites may also act as shape-selective molecular sieves (129), discriminating molecules of different dimensions or conformation (e.g. branched vs linear molecules). Zeolites are hence exploited as selective absorbers and molecular sieves in the petrochemical industry, for wastewater treatment, in fertilizers, and for freshwater softening (i.e. removal of exceeding Ca and Mg in “hard” water for detergency), e.g., (126, 130).

Recently, extra-large-pore zeolites (e.g. with channels of 24 tetrahedral atoms, **Figure 3-17**) were synthesized by adding germanium atoms in the synthesis media, shading light on new and always wider applications (123, 131, 132).

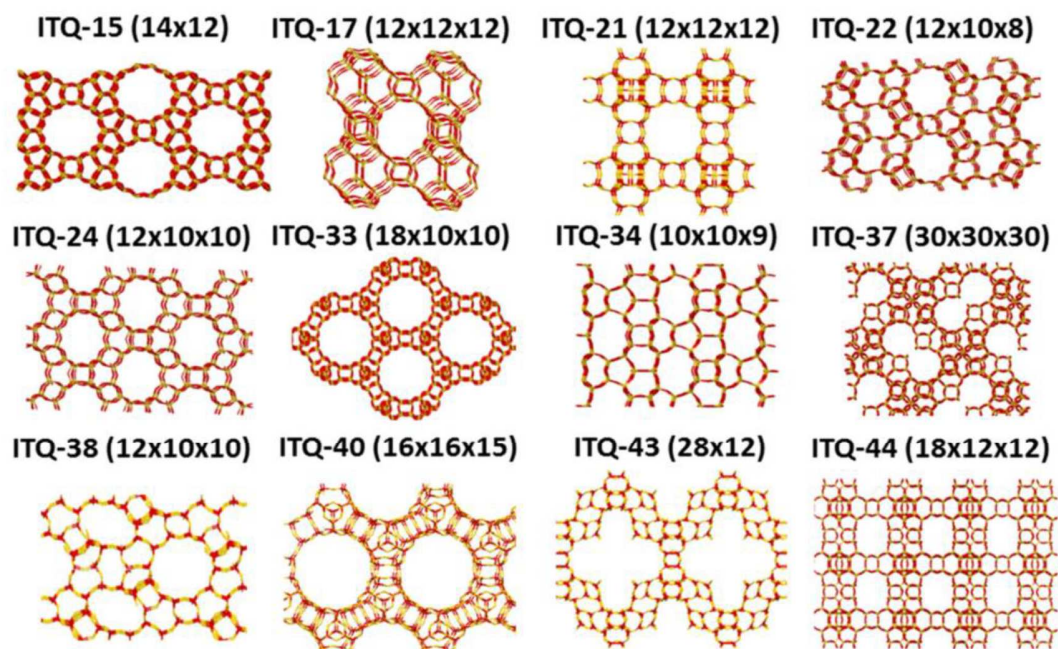


Figure 3-17. New germanosilicate zeolites with large and extra-large pores. Figure from (131).

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Thanks to their reversible dehydration, zeolites find application in energy storage, gas dehydration, and heat storage, e.g., (133-135).

Zeolites display a huge specific surface area (up to $800 \text{ m}^2 \text{ g}^{-1}$) and the possibility of fine-tuning the structure acidity by changing the Si/Al ratio. These properties make zeolites very interesting materials for hydrocarbon cracking and many other catalytic processes (**Figure 3-18**). In fact, catalysis is the second most important industrial application of zeolites, just after detergency. The field of catalysis prompts continuous scientific research on new zeolites and zeolite-like materials and has led to interesting developments such as e.g. the synthesis of single-layered zeolite nanosheets and complex multi-scale designed zeolite composites (136), up to 3D-printed zeolite monoliths, e.g., (137-139).

Synthetic zeolites are employed also for photosensitive materials, fuel cell membranes, new ceramic materials, and technological surfaces. Some cutting-edge applications of synthetic zeolites for organics removal, encapsulation, or stabilization will be presented in the next section.

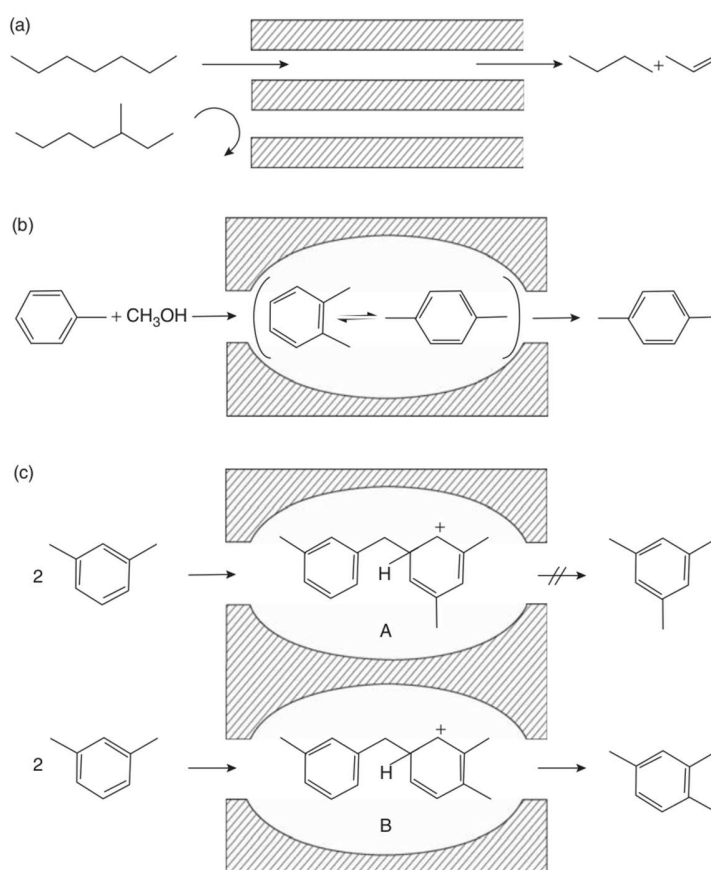


Figure 3-18. Shape selectivity in zeolites. (a) Reactant selectivity; (b) Product selectivity; (c) Restricted transition state selectivity (129).

Synthetic zeolites can be obtained from pure chemicals but recently much effort has been devoted to the use of natural-source materials (e.g. clay minerals, diatomaceous earth) and even waste materials (140-144). The use

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of secondary raw materials and wastes for the production of zeolites is in agreement with a “Circular Economy” approach, aiming to reduce the environmental impact of industry (145).

Zeolitites (i.e. rocks deriving from alteration of volcanic tuff and composed of at least 50% of zeolites) can be employed for several applications. Indeed, zeolitites show zeolitic properties empowered by the characteristics of the original rock (high water-retention capacity, mechanical strength, high permeability, and low density). These materials find applications in natural gas treatment, paper industry, sewage plants, feedingstuffs, farming, and floriculture, e.g., (146-148). Natural zeolitites are also applied for the remediation of water and soils polluted by radioactive nuclides; these nuclides are indeed strongly retained by the zeolitic structure after insertion. Radionuclides result thus inert and fixed in the soil, avoiding the contamination of vegetables and animals (130).

During the last decades, new high-tech applications of synthetic and natural zeolites are arising in different fields ranging from the cosmetic and biomedical industry to gas sensing (for reviews see (149-152)).

3.5.2 Zeolites-organic composites: from waste purification to drug delivery

Thanks to the properties described in section 3.5.1, zeolites are used for several applications, in which trapping/hosting organics of various kinds is required (e.g. removal from wastewaters, separation from complex mixtures, encapsulation). Once the molecules are hosted in the cavities, the obtained “hybrid” may merely act as a carrier (e.g. drug delivery) or be itself a technological device (e.g. sensors). Moreover, zeolites are promising for the supramolecular ordering of many different compounds, with the perspective of developing a new class of hierarchically organized multifunctional hybrid materials (153). Some examples are briefly reported in the following.

3.5.2.1 *Ethanol-Water separation*

Effective recovery strategies of target molecules are mandatory for the development of biofuels from natural sources, in which the starting feedstocks are often very dilute aqueous solutions. One example is the purification of ethanol from water. In this case, the distillation process is usually adopted, but it can become too energy-consuming if azeotrope solutions are formed. Indeed in azeotropes, solute and solvent evaporate at the same concentration rate as the liquid form, making distillation ineffective. Ethanol 96% is a typical example of an azeotrope. A more energy-saving option to obtain pure ethanol is distillation followed by pervaporation systems. Pervaporation implies the use of molecular sieves to selectively absorb one of the two components. Among molecular sieves, zeolite membranes have been successfully used and were found to save up to 52.4% of energy compared to the traditional azeotropic distillation (154, 155). The economic and environmental impact of such a difference cannot be ignored, since the global production of ethanol has been higher than 25 billion gallons (i.e. about 100 million m³) per year since 2015 (156).

The selective adsorption of ethanol-water mixtures by different zeolite frameworks has been investigated to understand how the zeolite topology and acidity, together with environmental parameters (e.g. temperature and pressure) affect the process (157, 158). As an example, Confalonieri and coworkers report the penetration of azeotrope in all-silica chabasite zeolite (Si-CHA) under compression. At ambient pressure, water and ethanol penetrate Si-CHA in a ratio similar to that of the original azeotrope. Conversely, under pressure the Si-CHA is enriched by H₂O molecules, thus dehydrating the external solution (157). Water and ethanol were found to penetrate also into the hydrophobic all-silica ferrierite zeolite, upon pressure. The pressure induces the two compounds of the azeotrope solution to organize separately into different channels of the structure, thus constructing a 2D supramolecular architecture. This peculiar organization is retained after pressure release, foreseeing future exploitation of similar ordering properties of zeolites for new functional materials (154, 159).

3.5.2.2 Zeolite-based drug delivery systems

Much effort has been spent in developing new drug delivery systems, able to trap a biologically active substance, transport it to a target site in the organism, and release it there in a controlled way. In this setting, zeolites have attracted increasing attention for their potential use in medicine. Natural clinoptilolite, e.g., was found to be safe and non-toxic for both humans and animals (160). Moreover, in vitro tests showed that zeolites have a beneficial impact on bone cell production, display antibacterial activity, and help the regulation of the immune system. From a pharmacological perspective, the possibility to realize delayed-release composites is the main appeal of zeolite delivery systems. Zeolite X and a physical mixture of zeolites X and A, e.g., were demonstrated capable of encapsulating ketoprofen. This hybrid increased the half-life and bioavailability of the drug at various pH conditions mimicking gastrointestinal fluids. Moreover, the hybrid reduced the undesired release of ketoprofen at the gastric level, thus reducing the occurrence of side effects (161).

More recently, nanosized Na-FAU zeolite was suggested to be effective in reducing hypoxia (i.e. oxygen depletion) in glioblastoma brain tumors (162). Hypoxia is typical of tumoral areas and stimulates tumor development and resistance. Thus, finding efficient methods to oxygenate tumors is of paramount importance for the development of effective therapies, particularly for better glioblastoma prognosis. In that study, zeolites were loaded with a hyperoxic/hypercapnic gas mixture (carbogen, 95% O₂ + 5% CO₂), and the gas release was measured in aqueous solutions at different oxygen saturation levels of physiological interest. Fascinatingly, the nano-zeolite released larger amounts of oxygen in solutions of lower oxygen saturation. The intravenous injection of carbogen-carrying nano-zeolites can then release oxygen selectively in areas of severe hypoxia, thus targeting tumors such as glioblastoma, without inducing exceeding oxygenation of healthy tissues. The authors also confirmed the non-toxic profile of nano-zeolites through a wide number of in vitro and in vivo tests (162).

3.5.2.3 Organic contaminants removal from wastewaters

Zeolites are commonly employed for the removal of pollutants from contaminated natural matrices. As an example, zeolites, especially natural ones, were successfully employed for the fixation or removal of radionuclides in soil and water after nuclear plant accidents, e.g., (163-165). In general, zeolites find wide applications in wastewaters treatment plants to remove heavy metal ions contaminants and organic compounds thanks to their cation exchange and molecular sieving properties, e.g., (166-172).

Various persistent and mobile organic compounds (PMOCs and VOCs) are produced and released from industrial activities, and finally accumulate persistently in the water system. Recently, researchers from the University of Ferrara (Italy) and the Italian National Research Council reported the case study of a contaminated site in the Tito Scalo area (Potenza province, Italy) (168, 169, 171). The Tito Scalo site is characterized by diffuse contamination of groundwater and is classified as a “contaminated Sites of National Interest” (SIN). Three main categories of pollutants are present, namely, heavy metals (As, Fe, and Mn), chlorinated solvents (trichlorethylene, 1,2-dichloroethylene, 1,1-dichloroethylene, and vinyl chloride), and sulfates. Two zeolites with different Si/Al ratios and topologies were employed to account for different pollutants with different chemical behavior, namely high-silica ZSM-5 (MFI topology) and low-silica 13X zeolite (FAU topology). The absorption of contaminants was performed at the pilot scale, using the batch method. High-silica ZSM-5 turned out to be more effective in chlorinated solvents removal, while 13X was more selective for heavy metal ions. The results confirm the exploitability of zeolites in permeable reactive barriers for the in situ decontamination of wastewaters (168).

3.5.2.4 Supramolecular dyes

Zeolites have been studied as hosts for the stabilization of degradable dye molecules. As an example, flavylum derivatives are dyes that can exhibit yellow, magenta, and cyan colors. Although more ecofriendly

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compared to other dyes, flavylum is quite unstable in a basic environment or upon heating, and the industrial application of its derivatives is thus unfeasible. The encapsulation of flavylum into protonated Y (FAU) and mordenite (MOR) zeolites afford materials with improved thermal and chemical stability. Notably, the authors revealed a stronger stabilization of the dye in the smaller channels of mordenite compared to the supercage of Y, indicating an active role of the zeolite topology on the properties of the hybrid material (173).

In addition to dye stabilization, zeolites are of interest for the development of photoactive hybrid materials by the encapsulation of active organic compounds. Particularly, the organization of photoactive molecules into one-dimensional channel systems may exhibit unusual properties such as optical anisotropy, efficient energy transfer, high stability, and photoactivity (174-176). Such materials may find application in solar power devices, electronics, and nanosensors (153, 177, 178). For this reason, dye-zeolite composites were thoroughly investigated. Previous studies, e.g., (174-176, 179-181), have shown that the photoactivity of organic-zeolite composites strongly depends on host-guest and guest-guest interactions, the number of loaded molecules, and the zeolites topology. For example, Gigli and coworkers studied an assembly of close-packed fluorenone dye molecules inside the one-dimensional channel of L zeolite (180). Fluorenone architecture inside L zeolite is formed by a single, continuous nanostructure of dye molecules formed by pairs of π -stacked molecules connected by another single fluorenone molecule, somehow resembling the solid structure of the dye (**Figure 3-19**). Thanks to experimental and computational studies, the confined molecules revealed strong interactions with the zeolite extraframework K^+ by the carbonyl group of fluorenone, and weaker van der Waals interactions between dye molecules (153, 180). The system is even more stabilized by a hydrogen bond network of coadsorbed H_2O molecules. The authors also suggest that the carbonyl interaction with extraframework cations may be the key to the stabilization of many other organic compounds inside cationic zeolites. Indeed, organics that are not capable of strongly interacting with the zeolite are easily released in humid environments, favoring the penetration of H_2O molecules.

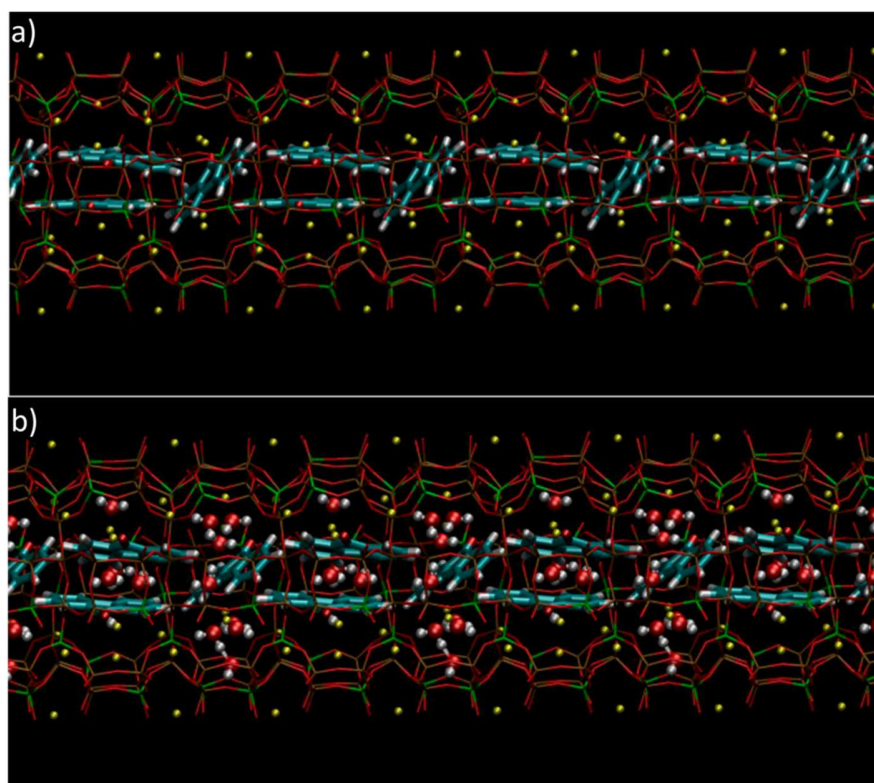


Figure 3-19. Computational structure of (a) dry zeolite L-fluorenone; (b) hydrated zeolite L-fluorenone. Zeolite structure - brown: Si, green: Al, red: O, K^+ as yellow spheres. FL atoms - cyan: C, red: O, white: H. Figure from (180).

3.5.2.5 Zeolite-based cosmetic ingredients

The use of zeolite-based hybrid UV filters is scantily reported in the scientific literature, and just slightly more in industrial patents. However, the variability of zeolite topologies and the possibility of fine-tuning their hydrophobicity/hydrophilicity (i.e. their Si/Al ratio) make zeolites adaptable to be used in different hybrid zeolite/filter composite, and different cosmetic vehicles (e.g. water-in-oil or oil-in-water formulations). Three papers that were published by Chretien and coworkers are particularly relevant and were already discussed in section 3.4.1 (114-116).

Here some advanced zeolite-based materials are presented that were reported in patent applications as potential cosmetic ingredients. The majority of the published material focuses on the effects of different charge-balancing cations more than on the topology of zeolite frameworks. For instance, several products exploit the excellent chelating properties of Zn cation to trap organic species. Zeolite/UVf compounds were evaluated for the prolonged and controlled release of organic UVfs. In this case, UVfs were not adsorbed inside zeolite porosities, but just on the external grain surface. The slow-release was expected to extend UV protection by continuously replacing the UVf absorbed through the skin (182). However, this approach may cause an undesired uptake of UVf as discussed in section 3.3.

Zn-exchanged zeolites were proposed for the encapsulation of UVfs and other non-antibiotic organics for the topical treatment of skin rash and sunburns, also exploiting the slow release of the actives from the zeolite (183, 184). Zn- and Ti-containing zeolites were proposed for use as physical UV filters thanks to their enhanced filtering power and low ROS production compared to original TiO₂ and ZnO metal oxides (185). Finally, silver exchanged zeolites were investigated as antiseptic and antimicrobial agents, e.g., (186).

3.6 Aim of the thesis

This thesis investigates the encapsulation of organic UVf into zeolites of different topology and chemical compositions. In fact, the inspiring and promising scenario reported by Chretien and coworkers (114-116) deserves to be further explored by testing the effects of different zeolite/UVf combinations on the final spectral features of the hybrid systems. Moreover, the environmental aspects must be evaluated as a response to the negative impact of organic UVfs that was recently reported.

The objects of this study are two of the most commonly employed UVfs, the UVA filter avobenzone (AVO), and the UVB filter octinoxate (OMC) - section 3.2.2. As previously highlighted, these two UVfs are probably the most effective organic filter available on the market, especially when they are combined. However, their use in the current form presents concerns about their increasingly evident environmental toxicity (OMC is currently banned in Hawaii and many other localities) and reciprocal instability. Thus, it is of economical and technological interest to find a sustainable, effective and cheap way to stabilize each of the two compounds and possibly their mixtures.

With this aim, zeolites with LTL, MOR, FAU, and MFI topologies (a detailed description of the investigated phases will be provided in section 4.1.2) and variable Si/Al ratios were selected for the encapsulation of OMC and AVO. These phases were selected based on:

- i) their main channel size, to be large enough to allow the penetration of OMC and AVO molecules.
- ii) their easy availability on the market, in bulk quantities.

The hybrid UVfs here presented (hereafter ZEOfilters) are expected to overcome the issues linked to both the bare organic UVfs and the filters encapsulated in matrixes other than zeolites. Particularly, ZEOfilters will:

- i) improve the stability and efficacy of the UVf (e.g. hindering photoisomerization reactions)

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- ii) avoid allergic reactions (e.g. limiting the interactions between the filters and the skin)
- iii) limit the pollution (e.g. limiting the dispersion of the bare UVf in the environment)

The encapsulation of UVfs into zeolites is expected to prevent the degradation of the UVf thanks to the spatial confinement exerted by the zeolite on the molecule, and by limiting interactions among formulation compounds. These two protective effects were already observed in other zeolite/dye composites (e.g. (173)), and encapsulated UVf (e.g. (34)), respectively. The same sheltering effect and the consequent reduction of UVf degradation products will prevent (or at least reduce) allergic reactions. The impact of UVfs on the environment will be possibly mitigated by two mechanisms. Firstly, UVfs entering the environment from wastewater treatment plants will be greatly reduced since ZEOfilters will be more easily retained by the sewage plants. Secondly, ZEOfilters entering the environment (e.g. by direct bathing) will retain UVfs, thus reducing their biological uptake and bioaccumulation.

The majority of encapsulating materials employed up to now has demonstrated to be unstable in environments with chemical or physical stress and to easily release the encapsulated actives (section 3.4.1). Conversely, zeolites are highly resistant in a wide range of environments, especially those resembling seawater.

This thesis aims to study the encapsulation effects on the molecule photostability and to unveil the fate of the UVf once the ZEOfilters will be dispersed in the final cosmetic formulation and the natural environment. Going into detail, the objectives of this thesis can be outlined as follows:

- Optimize a loading procedure of organic UVfs into zeolites (ZEOfilters' synthesis)
- Test the stability and efficacy of the realized ZEOfilters
- Test the efficacy and safety of ZEOfilters in simulated field conditions (i.e. in simple formulations and simulated seawater)
- Investigate the zeolite-UVf interaction through structural investigation to unravel the correlations among structure and the observed properties

4 Materials and methods

In this chapter, the employed materials and the applied analytical techniques will be presented. All materials were purchased from industrial suppliers to favor reproducibility.

4.1 Materials

4.1.1 Selected Organic UV filters

Octinoxate (OMC) and avobenzone (AVO) were selected for this study since are two of the most commonly employed organic UVB and UVA filters, respectively (**Figure 4-1**). Both these molecules are known to be highly photolabile, thus their stabilization is of primary importance. A detailed description of the two molecules and their spectral characteristics are reported in section 3.2.2.

Octinoxate ($C_{18}H_{26}O_3$, colorless liquid, MW 290.40 g/mol, SG 1.01 g/ml, purity >96,0%) and avobenzone ($C_{20}H_{22}O_3$, white powder, MW 310.39 g/mol, purity >98,0%) were purchased from TCI (Tokyo Chemical Industry Co., Ltd.).

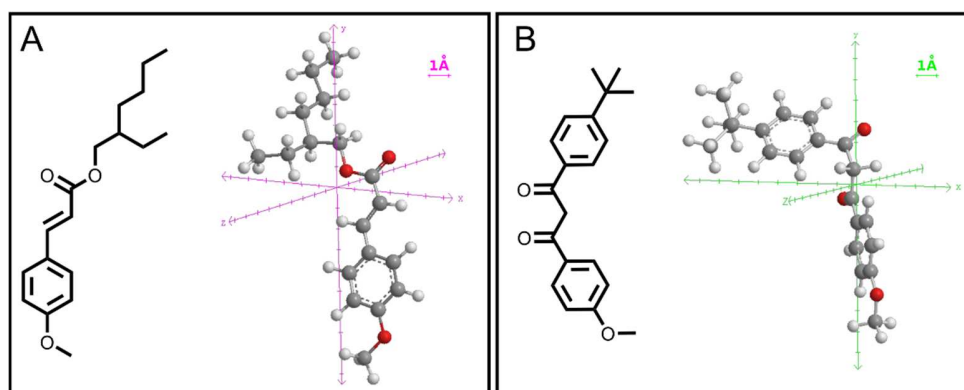


Figure 4-1. Molecular models and structures of octinoxate (OMC, Panel A) and avobenzone (AVO, Panel B). Molecular axes are in Å, 1 tick= 1 Å.

4.1.2 Selected Zeolites

In this thesis, different zeolites with at least one 10MR (10-membered ring) or a 12MR channel were selected, to allow the insertion of OMC and AVO molecules. The chosen framework topologies are MOR, LTL, FAU, and MFI (187) and are shown in **Figure 4-2** (188). Moreover, a high-silica and a low-silica form of MOR (HS-MOR, Na-MOR, respectively), FAU (HS-FAU, 13X-FAU, respectively), and MFI (ZSM5-398, ZSM5-30, respectively) topologies were tested to investigate how the Si/Al ratio could affect the encapsulation and the properties of the final material. **Table 4-1** reports all the main characteristics of the different zeolites and the labels that will be used hereafter. In the following, a brief description of each zeolite framework will be provided.

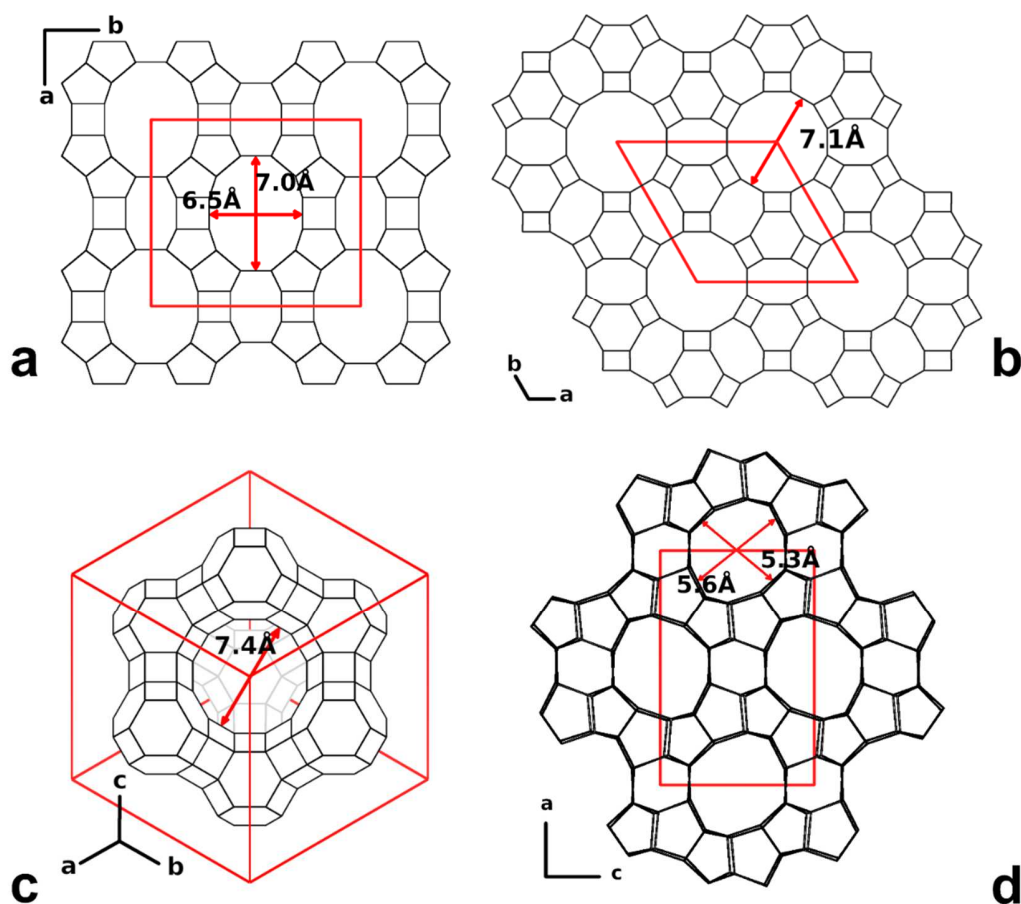


Figure 4-2. Topology of the employed zeolites: a) MOR, b) LTL, c) FAU, d) MFI.

Mordenite framework (MOR (187), **Figure 4-2a**) displays a 1D channel system with two parallel channels of different sizes running along the *c* axis: a large 12-membered-ring channel (12MR, maximum diameter of a sphere that can diffuse along it: 6.45 Å), and a strongly elliptical 8MR channel. Two MOR samples have been tested: a high silica sample and a Na sample. HS-MOR has already been investigated as a suitable host for organic molecules under different conditions (172, 194, 195). The temperature-induced structural changes of HS-MOR were investigated and published during the first period of this project. HS-MOR was revealed to be highly stable, but also structurally defective, as a consequence of the post-synthesis dealumination process, showing some degree of acidity (189). Weak interactions of H₂O molecules with the framework and the presence of hydroxyl groups with different condensation responses were evidenced. Infrared characterization also highlighted that the desorption of H₂O molecules under degassing is complete already at room temperature. The full paper on the thermal behavior of HS-MOR is reported in **Appendix I**.

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Table 4-1. Main features of employed zeolites. Informal labels, framework topology code, Si/Al molar ratio, chemical formula, space group and unit cell parameters (references in brackets, # G. Cruciani personal communication), average grain size, and channel system (by International Zeolite Association shorthand notation, the number of asterisks indicates one-, two- or three-dimensional channel systems) (187). Si/Al ratios and chemical formulas are from X-ray fluorescence, the grain size was measured by laser diffraction particle analysis.

Label	Framework topology	Unit cell		Channel system	Si/Al	Chemical formula	Average grain size	Producer (Product code)
		(s.g. a, b, c, V) [Å, Å, Å, Å ³]		(IZA shorthand notation)	Mol. Rat.		(Dv 50)	
HS-MOR	MOR	<i>Cmc2₁</i>	(189)	[001] 12 6.5 x 7.0* <-> [001] 8 2.6 x 5.7**	110	-Si ₄₈ O ₉₆	10 µm	Tosoh Corp. (HSZ-690HOA)
		<i>a</i> 18.0609(2)						
		<i>b</i> 20.2095(2)						
		<i>c</i> 7.4546(1)						
		<i>V</i> 2720.9(1)						
Na-MOR	MOR	<i>Cmcm</i>	(190)	[001] 12 6.5 x 7.0* <-> [001] 8 2.6 x 5.7**	9.2	Na _{5.47} Mg _{0.07} (Al _{4.97} Si _{42.84})O ₉₆ x 22.7H ₂ O	11 µm	Tosoh Corp. (HSZ-642NAA)
		<i>a</i> 18.097						
		<i>b</i> 20.381						
		<i>c</i> 7.493						
		<i>V</i> 2763.7						
LTL	LTL	<i>P6/mmm</i>	(180)	[001] 12 7.1 x 7.1*	2.9	Na _{0.41} K _{0.03} (Al _{9.14} Si _{26.79})O ₇₂ x 17.1H ₂ O	2 µm	Tosoh Corp. (HSZ-500KOA)
		<i>a</i> 18.3795(4)						
		<i>c</i> 7.5281(2)						
		<i>V</i> 2202.4(1)						
HS-FAU	FAU	<i>Fd-3m</i>	(191)	<111> 12 7.4 x 7.4***	280	-Si ₁₉₂ O ₃₈₄	38 µm	Tosoh Corp. (HSZ-390HUA)
		<i>a</i> 24.259(4)						
		<i>V</i> 14277.1(4)						
13X-FAU	FAU	<i>Fd-3m</i>	(192)	<111> 12 7.4 x 7.4***	1.2	Na ₉₉ Mg _{0.3} K _{0.2} (Al _{86.07} Si _{102.40})O ₃₈₄ x 236.6H ₂ O	5 µm	BDH Chem. Prod. 54017 (out of stock)
		<i>a</i> 25.099(5)						
		<i>V</i> 15811						
ZSM5-398	MFI	<i>P2₁/n</i>	(193)	{[100] 10 5.1 x 5.5 <-> [010] 10 5.3 x 5.6}***	237	Mg _{0.22} Ca _{0.05} (Al _{0.40} Si _{95.50})O ₁₉₂ x 4.9H ₂ O	6 µm	China Catalyst (CCG05Z4001)
		<i>a</i> 19.8999(5)						
		<i>b</i> 20.1174(6)						
		<i>c</i> 13.3892(4)						
		β 90.546(3)°						
		<i>V</i> 5359.9(3)						
ZSM5-30	MFI	<i>P2₁/n</i>	#	{[100] 10 5.1 x 5.5 <-> [010] 10 5.3 x 5.6}***	14	H _n Mg _{0.16} (Al _{6.40} Si _{91.08})O ₁₉₂ x 31.8H ₂ O	3 µm	China Catalyst (CCG05Z301)
		<i>a</i> 19.9019(3)						
		<i>b</i> 20.1230(3)						
		<i>c</i> 13.3869(2)						
		β 90.501(2)°						
		<i>V</i> 5361.1						

Zeolite L framework (LTL (187), **Figure 4-2b**) has a 1D channel system constituted by a circular 12MR channel (maximum diameter of a sphere that can diffuse along it: 7.5 Å) and a smaller elliptical 8MR channel, both running along the *c* axis. The extraframework K cations are present over three distinct crystallographic sites (196). Zeolite L (hereafter LTL) has been deeply characterized (196, 197), and employed for example for the absorption of dye molecules (175, 198-201).

Faujasite framework (FAU (187), **Figure 4-2c**) is constituted by a tridimensional 12MR channel system (maximum diameter of a sphere that can diffuse along them: 7.35 Å). The interconnecting channels form 8 supercages (maximum diameter of a sphere that can be included: 11.24 Å) for each unit cell. Also in this case a silica sample and a NaX sodic sample were tested. While HS-FAU has almost no extraframework cations, 13X-FAU has Na cations located at different crystallographic sites, for a total of about 100 Na per unit cell (p.u.c.) (192, 202).

ZSM-5 framework (MFI (187), **Figure 4-2d**) consists of straight 10MR channels running along *b* direction intersecting a sinusoidal 10MR channel running along *a* axis (maximum diameter of a sphere that can diffuse along them: 4.46 Å and 4.7 Å respectively). MFI has been deeply tested for the removal of organic compounds from aqueous media (203-205). A protonated low-silica form (ZSM5-30) and a high-silica form (ZSM5-398) were both tested.

4.2 Methods

4.2.1 Particle size analysis of zeolites

The particle size distribution of each zeolite was determined before UVf loading. Indeed, the dimension of grains may affect factors such as the diffusion path of the guest molecules inside the zeolite or the stability of cosmetic formulations.

The particle size distribution of pristine zeolites was obtained by laser diffraction particle size analysis using a Mastersizer 3000 laser grain-size analyzer. The instrument works in the range from 0.01 to 3500 µm, employing a read He-Ne (632.8 nm, < 4mW) and a blue LED (470 nm, 10 mW) lasers. Hydro EV dispersion unit was used according to the reference standard ISO 13320: 2009 "Particle size analysis - Laser diffraction methods". The optical model used was the Mie model with a zeolite refractive index of 1.48. Zeolite-water suspensions were sonicated for 15 minutes before all measurements. **Table 4-2** defines the main particle size parameters.

LTL particle size was partially optimized by wet grinding to reduce the particle size distribution interval.

Table 4-2. Main parameters describing particle size distributions.

Parameter	Definition	
D [4;3] [μm]	$\Sigma d_i^4 / \Sigma d_i^3$	De Brouckere mean diameter: mean diameter of particles considered as spheres with equivalent volume; d_i is the diameter of particle i
Dv (10) [μm] Dv (50) [μm] Dv (90) [μm]		Size of particle below which 10, 50, 90 % of the sample lies. Dv50 is the median.
Span	$(Dv90 - Dv10) / Dv50$	Measurement of the width of the distribution. The narrower the distribution, the smaller the span becomes.
Uniformity	$\Sigma V_i Dv50 - D_i / Dv50 \Sigma V_i$	Measure of the absolute deviation from the median. V_i is the volume % of size class i with D_i mean diameter
Volume Above 2000 μm [%] Volume 63-2000 μm [%] Volume 2-63 μm [%] Volume Below 2 μm [%] Volume Below 1 μm [%]		Volume percentage of particles in each size range

4.2.2 Synthesis of ZEOfilters

A loading procedure of the organic UVf into different zeolites must be simple, replicable, and must produce a hybrid material with the maximum loading of UVf inside the zeolite and without molecules on the outside of the zeolite grains.

The employed procedure can be pointed out into four main steps (**Figure 4-3**):

- Zeolite dehydration
- Zeolite loading with UVfs
- Hybrid Washing
- Hybrid Drying

After UVf loading the samples were kept in the dark as much as possible, to prevent undesired photoreactions. For each stage of the process, different parameters, materials, and techniques were tested, particularly focusing on the HS-MOR/OMC and LTL/OMC systems. Finally, an optimized loading procedure was obtained and demonstrated to be highly reproducible, also permitting quick investigation of new zeolite-UVfs systems.

In the following, an overview of each step will be provided, while a more detailed description of all different trials will be provided in the Results section, indicating strengths and weaknesses of each test.

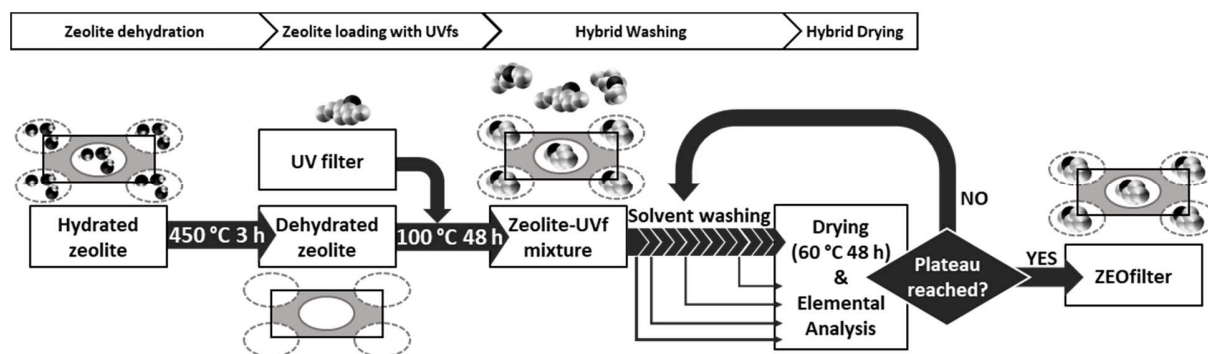


Figure 4-3. Schematic representation of the synthesis procedure of ZEOfilters.

4.2.2.1 Zeolite dehydration

As already stated zeolite structures contain a variable, but generally high, number of H₂O molecules. Low silica zeolites, with a high number of extraframework cations, are generally more hydrophilic and display quite strong H₂O-metal interactions. On the contrary, high silica zeolites are more hydrophobic, with fewer H₂O molecules that mainly interact with residual cations or structural Si-OH defects (i.e. silanols). Thus, both high- and low-silica zeolites must be dehydrated before loading the UVf. Dehydration was performed at 450 °C for 3 h in open porcelain crucibles. Dehydrated zeolites were then covered and stored in desiccators. The dehydration was preferably performed on the same day of UVf loading, since zeolite rehydration can easily occur even under proper storage conditions.

4.2.2.2 Zeolite loading with UVfs

After the dehydration, zeolites were loaded with the organic UVf. Different strategies may be adopted to load organic compounds into zeolites, e.g. direct loading from vapor or liquid phase, or ship-in-a-bottle synthesis in the case of molecules larger than zeolite apertures. Also, a thermal treatment is often adopted to favor the diffusion of the guest molecules inside zeolite porosities (115).

In this thesis, the soaking method was adopted, contacting the zeolite directly with the pure UVf. During the loading process, solvents were not employed to simplify the interpretation of chemical data (see section 4.3.1), and to prevent solvent-solute competition during absorption.

The dehydrated zeolite was mixed with OMC, which is liquid at room temperature, or AVO, which is solid, in glass tubes. After homogenizing by stirring, the tubes were sealed with Teflon plugs, and the mixture was heated using an oil bath at 100 °C for 48 h. The procedure can be described as soaking since at 100 °C both OMC and AVO are liquid. The samples were frequently checked and stirred during the thermal treatment, to improve UVf homogenization. During all loading-steps glass tubes with the samples were covered with aluminum foil to minimize light exposure.

Different loading parameters such as zeolite/UVf weight ratio, loading temperature, and time were varied to optimize the loading procedure. The zeolite/UVf ratio, e.g., was varied significantly during the development of the project, as it is shown in **Figure 4-4**. During the first exploring tests, the amount of UVf used was largely exceeding the maximum that could have been hosted in the channels of the zeolites (loading expected on the base of steric hindrance). The large excess should have ensured reaching the maximum loading. The maximum loading was then experimentally determined, and loadings were performed using just a small amount of exceeding UVf. Other considerations about loading parameters will be discussed in the Results chapter.

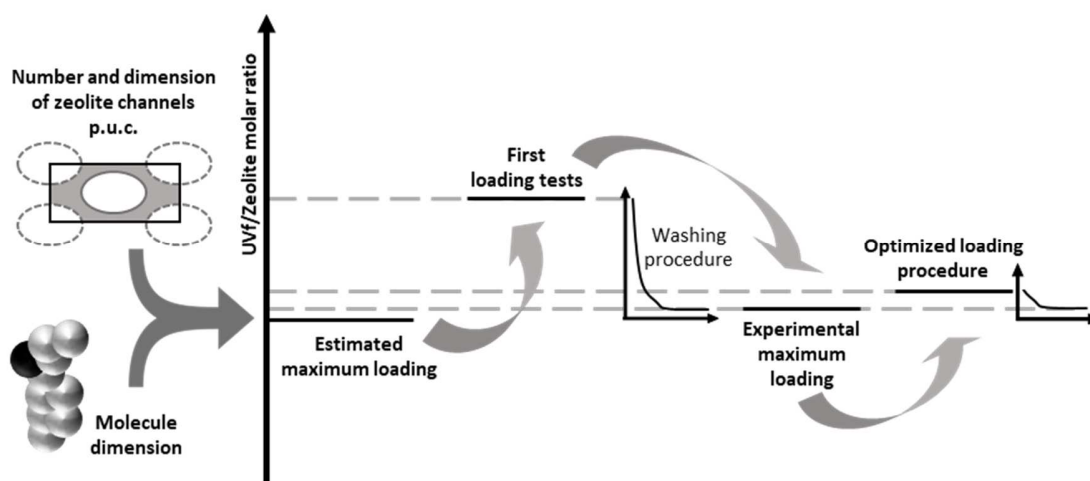


Figure 4-4. Schematic representation of the optimization of loading procedures for a given zeolite/UVf composite.

4.2.2.3 Hybrid Washing

The loading step provided a mixture of zeolite and UVf where organic molecules are supposed to be inside zeolite porosities, on the grain surface, and in the intergranular spaces, as well. Thus a washing step was required to remove all the unencapsulated UVf molecules, possibly without removing those inside the zeolite porosities. Indeed, the presence of free UVf molecules - behaving as the pristine UVf- may influence the performance of the hybrid material.

Two diverse washing procedures were employed, namely the Soxhlet Extraction (SE) and the Ultrasound-Assisted Extraction (UAE). In both cases, the sample was contacted with an organic solvent aiming at the solubilization of the unencapsulated molecules.

The SE was performed with a 70 ml Soxhlet extractor using acetone as solvent. Ethanol, isopropyl alcohol, and water were also tested as solvents but then were discarded as less effective (section 5.2). A small amount of hybrid powder was sampled at regular time intervals during the washing procedure, dried in an oven at 60 °C for 48 h to remove the solvent, and analyzed with elemental analysis (EA) to determine the carbon content evolution of the hybrid over washing. The hybrid amount washed in the soxhlet was variable depending on different samples, while the volume of the Soxhlet was fixed. Thus, to plot the chemical data obtained by EA as a function of the degree of washing – without being influenced by the amount of powder washed – the parameter l/s (i.e. liquid/solid ratio) was introduced. l/s is defined as:

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$$l/s = (\text{number of washing cycles}) * (\text{solvent volume}) / (\text{hybrid sample weight}) = [\text{ml/mg}]$$

The l/s parameter allows the trend comparison between different samples upon washing.

UAE was also performed using acetone as solvent. Samples to be washed by UAE were divided into various aliquots and inserted in proper centrifuge tubes. The solvent was added up to a 0.03 ml/mg ratio. The samples were then entered into an ultrasonic bath, repeating 3-7 cycles of 20 min each. At each cycle, the sample was centrifuged at 5000 rpm for 10-20 minutes and the hybrid separated from the solvent, which was then replaced. Different aliquots were stopped after a different number of washing cycles, entered in an oven at 60 °C for 48 h for solvent removal, and analyzed by EA. The same l/s parameter employed for SE was used to plot the carbon content of each aliquot to monitor the washing process.

4.2.2.4 Hybrid Drying

At the end of the washing process, all samples were heated in oven at 60 °C for 48 h, thus allowing the removal of the employed solvent. The drying step was performed also for each aliquot collected for EA measurements.

The zeolite/UVf hybrid obtained after the final drying is referred to as ZEOfilter, a term that will be thus subsequently used in this thesis.

4.3 Chemical characterization of ZEOfilters

ZEOfilters were characterized using a multi-techniques approach. Here below the analytical methods employed to determine the ZEOfilters' chemical composition are reported.

4.3.1 Elemental Analysis (EA)

The Elemental Analyses (EA) identify and quantify carbon, hydrogen, nitrogen, and sulfur (CHNS EA) in liquid or solid samples, providing results as weight percent of the element. EA were performed using a Thermo-Fisher CHNS FLASH 2000 analyzer at the University of Modena and Reggio Emilia. The measurement is performed through flash combustion of the sample at 1800 °C. This process decomposes any compound releasing reduced elementary gases. The gases are finally injected into a gas chromatography column (GC) where a thermal conductivity detector (TCD) determines the amount of each element.

In the case of the ZEOfilters, from 0.7 mg to a few mg of sample was employed for each measurement, and the analyzed elements were C and H.

4.3.2 Thermogravimetric Analysis

Thermogravimetric Analyses (TGA) measure weight changes of a given, generally solid, sample upon heating. Heat-induced weight variations of the sample are measured and plotted against temperature (TG, [weight %]), together with the weight-variation rate (DTG, [weight %/°C]). Moreover, TGA can be coupled with a mass spectrometer to analyze the gas evolved during the heating (TGA-MSEGA), thus identifying the released

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volatiles. TGA, compared to EA, provides more detailed information on the processes occurring inside the sample. Indeed, the release temperature of a given volatile (e.g. H₂O or organic compounds) is higher for compounds stronger interacting with the sample matrix.

TG analyses were performed using a Seiko SSC/5200 thermal analyzer at the University of Modena and Reggio Emilia. TGA was performed on about 20 mg of hybrid in an open Pt crucible from room temperature to 1050 °C, at the heating rate of 10 °C/min. TGA of samples containing organics (i.e. ZEOfilters and pristine UVfs) were performed under an inert, helium stream, to prevent oxidation reactions. TGA measurements of pristine zeolites were performed in an air stream.

TGA were performed on representative samples of each ZEOfilter type. Samples at different washing stages were analyzed by TGA to compare the filter release at different temperatures. The only LTL/OMC ZEOfilter was analyzed by TGA-MSEGA, as a proof of concept, to confirm the temperature of the release of UVf. TGA-MSEGA was performed using a quadrupole mass spectrometer (ESS, GeneSys Quadstar 422), in He stream with a flux of 100 ml/min. Several masses compatible with H₂O and OMC fragments were analyzed in multiple ion detection mode (MID), providing a qualitative determination of the evolved masses as a function of temperature.

4.4 Structural characterization of ZEOfilters

Most promising ZEOfilters were investigated by Fourier Transform Infrared (FT-IR) spectroscopy and Synchrotron-Radiation X-Ray Powder Diffraction (SR-XRPD) trying to unravel their structural features beyond their physical and chemical properties.

4.4.1 Fourier Transform Infrared Spectroscopy (FT-IR)

The FT-IR exploits the interaction of an infrared beam with the sample to unravel the vibrational features and the chemical bonds of the target compound, also allowing for discrimination between different isomers. Moreover, the analysis of vibrational features of UVf molecules encapsulated in the zeolite pores will help in understanding their interactions with the hosting framework and the other guest molecules. The coupling of vibrational and electronic spectroscopies will possibly elucidate the impact of such interactions on the optical properties of ZEOfilters.

For this thesis, FT-IR spectroscopy measurements were preliminarily performed on HS-MOR/OMC and more deeply on the LTL/OMC ZEOfilter.

HS-MOR/OMC FT-IR spectra were collected on a Bruker IFS66 spectrophotometer equipped with a La-DTGS detector and a KBr beamsplitter. Each spectrum is the average between 128 scans in the 4000-400 cm⁻¹ range with a resolution of 4 cm⁻¹. The spectra of OMC were collected by the thin film method by putting a drop of liquid between two KBr windows, while the ZEOfilter spectra were obtained by making a self-supporting pellet of powder with an optical thickness of about 10 mg/cm² and by evacuating it (residual pressure 10⁻⁴ mbar) into a traditional infrared cell equipped with KBr windows. Moreover, some measurements were performed after 180 minutes of *in situ* UV exposure, by focalizing a solar simulator lamp on the sample (**Figure 4-5**). The lamp was kept on during the data collection.

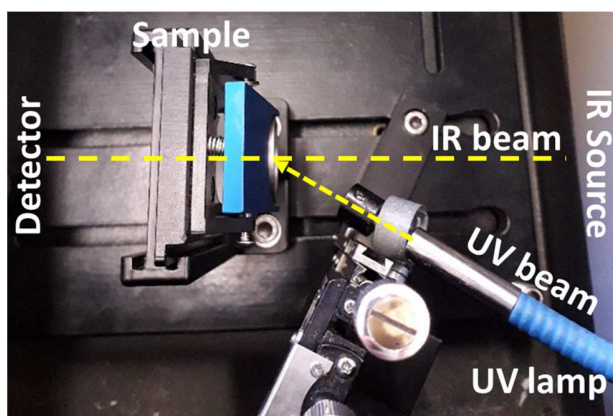


Figure 4-5. Experimental setup of FT-IR measurements with *in situ* UV exposure.

Concerning LTL/OMC, three samples were prepared: i) unoptimized LTL/OMC loaded with exceeding OMC, and without washing step; ii) optimized LTL/OMC, i.e. loaded with excess and washed with acetone until the plateau was reached; iii) ad hoc LTL/OMC, i.e. directly loaded with an amount of filter to obtain a UVf/zeolite molar ratio of 0.5. An aliquot of each type of ZEOfilter was pressed in self-supporting pellets (“optical density” of ca. 10 mg·cm²) and placed in quartz cells equipped with KBr windows designed to carry out spectroscopic measurements in controlled atmosphere. The cells were connected to a conventional vacuum line (residual pressure < 1×10⁻⁴ mbar) allowing *in situ* data acquisition during thermal treatments and adsorption-desorption experiments. A Bruker Equinox 55 spectrometer (resolution: 2 cm⁻¹; detector: MCT) was employed, averaging 128 interferograms for each spectrum.

All the IR spectra have been normalized by the “optical density” of the pellets to allow quantitative comparison of spectra acquired on different pellets.

4.4.2 Synchrotron-Radiation X-Ray Powder Diffraction (SR-XRPD)

X-Ray Diffraction is the most powerful technique to investigate the structure of crystalline materials. The study of hybrids zeolite/organics requires the employment of highly-brilliant sources to have the highest possible resolution and intensity, especially in the high-2theta-angle region, where most structural information is retained. Synchrotron facilities offer the required instrumental features, such as the possibility to choose the proper X-ray wavelength, and a high signal-over-noise detector.

SR-XRPD patterns of LTL/OMC were collected preliminary at the beamline XRD1 of the ELETTRA Synchrotron in Trieste (Italy). Data collection was performed in Debye Scherrer geometry using borosilicate capillaries (ø 0.8 mm), and a 2D detector (Dectris Pilatus 2M, pixel size 172 µm × 172 µm). Detector distance, orientation, and beam center were calibrated with Fit2D software on LaB₆ data. The integration of diffraction images was performed using Dioptas software (206). Some measurements were performed with *in situ* heating at 120 °C using an Oxford Cryostem 700 (available temperature range from -193 to 125 °C). These data mainly enabled a qualitative evaluation of ZEOfilters loading (see section 5.6.2).

The most promising ZEOfilters, obtained with LTL and 13X zeolites, were analyzed by SR-XRPD at the high-resolution beamline ID22 of ESRF-EBS (Extremely Brilliant Source) synchrotron. Notably, the experiment took place in December 2020, a few months after the upgrade of the facility. Data collection was performed using a wavelength (λ) of 0.3544016 Å in Debye-Scherrer geometry. The detecting apparatus is a multianalyser stage of nine detectors, each preceded by a Si(111) crystal analyzer. The samples were placed in quartz glass capillaries ($\varnothing$ 0.5 mm), open on the holding side to enable proper dehydration of the sample upon heating. Indeed, data collections were performed at room conditions, at 45 °C, 110 °C, and -193 °C, by using an Oxford Cryosystems Cryostream cold-nitrogen-gas blower. Isothermal heating of 30 minutes was performed before each data acquisition. The measuring spot on the capillary varied during measurements to avoid radiation damage. Data collections upon heating were performed to follow ZEOfilter dehydration up to 110 °C, where most weakly adsorbed H₂O molecules should have been removed. Then, the XRPD pattern at -193 °C was collected to minimize the thermal motion of extraframework species, thus reducing data noise and possibly simplifying structural refinement.

Structural refinement was performed only on LTL/OMC hybrid at -193 °C. the Rietveld refinement was made using Topas software in launch mode with Jedit as the input editor (207). The starting model of LTL was from (208). A Chebyshev polynomial was implemented to refine the background, while the profile was fitted with a Thomson pseudo-Voigt function (209). Soft constraints were applied to the Si-O bonding distances (1.65 Å). The OMC molecule was inserted as a rigid body. The initial location of the molecule was obtained through Simulating Annealing, its position was then refined imposing anti-bumping restrains as well as the torsion of rotatable angles, the occupancy factor (unique for all the atoms of the molecule), and the thermal parameter (unique for all the atoms of the molecule). Hydrogen atoms were also present in the refined model (overall 26 positive charges are not negligible) but they were not considered during structural interpretation.

4.5 Characterization of ZEOfilters' properties

The ZEOfilters' effectiveness and stability were deeply investigated in terms of absorption of UV radiation. Moreover, the release of UVfs from ZEOfilters in sunscreen formulations was evaluated under storing and operating conditions.

4.5.1 UV-Visible Spectroscopy

UV-Visible Spectroscopy (UV-Vis) allows the study of the interactions of ultraviolet and visible light with a solid or liquid sample. The sample is irradiated with a monochromatic beam and the transmitted or diffused light is measured and compared to a reference beam, to evaluate sample absorption at different wavelengths. As already mentioned in section 3.2, absorption phenomena in the UV-Vis range are due to electronic transitions from the ground to the excited state of atoms or molecules and are strongly dependent on the surrounding environment. UV-Vis spectroscopy may be performed in transmission or diffused reflection mode (**Figure 4-6**).

Concerning the transmission experiments, the samples are generally clear liquids held in completely transparent cuvettes of pure silica glass for UV measurements. A beam of monochromatic light is split into two parallel beams, one passing through a reference material (reference beam), and the other passing through the sample (**Figure 4-6a**). The intensity ratio between the sample-transmitted light and the reference beam is called transmittance (%T) and indicates the percentage of photons passing through the sample in the incident-beam direction. Transmission data are often provided as absorbance (*A*), which is calculated from transmittance as:

$$A = 2 - \log(\%T)$$

The advantages of absorbance use, in diluted solutions, are mainly linked to its linear correlation with analyte concentration and the optical path of the sample, known as the Lambert-Beer law:

$$A = \varepsilon l c$$

where ε is the molar extinction coefficient of the analyte, l is the optical path length, and c is the analyte concentration. Thus, given fixed the optical path, it is possible to calculate the analyte concentration knowing ε , or vice-versa.

UV-Vis spectroscopy in reflection mode is similarly obtained using monochromatic light but, in this case, the sample is generally solid and opaque. The sample is placed into an integrating sphere, facing the light source. The light beam hits the sample and is partially absorbed and back-diffused. The integrating sphere collects all light diffused from the sample and directs them to the detector (**Figure 4-6b**). The sample reflectance (%R) is a parameter defined as the ratio between the light diffused from the sample and that diffused from a reference white standard (often barium sulfate). The diffuse reflectance is then often converted into a pseudo-absorbance parameter through the Kubelka–Munk transformation, providing data similar to the absorbance of transmission UV-Vis spectroscopy (210, 211).

Transmission and reflection methods have both advantages and disadvantages. Transmission measurements are performed with a well-known optical path but generally focus only on directly transmitted beam losing all the diffused radiation. Conversely, the reflection method collects all the radiation diffused by the sample but with a more complex light-sample interaction, e.g. the optical path inside the sample is strongly sample-dependent, and thus almost unknown. The advantages of both methods may be somehow combined by total-transmission UV-Vis spectroscopy, in which the sample, which must be clear, is placed in front of the integrating sphere facing the incoming beam. In this way, all the directly transmitted and diffused light is collected by the sphere and directed to the detector (**Figure 4-6c**) (212).

In this thesis, UV-Vis measurements aim to determine the UVfs filtering properties once they are encapsulated in the zeolite.

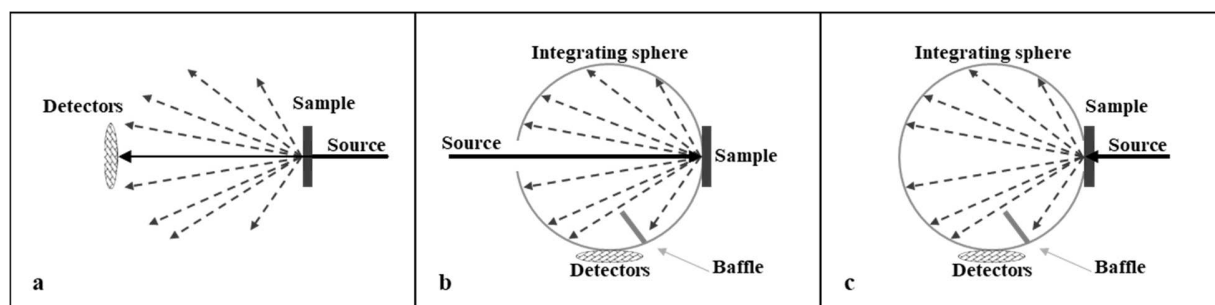


Figure 4-6. UV-Visible spectroscopy in (a) transmission, (b) reflection, and (c) total-transmission setups.

Materials and methods

For this project UV-Vis measurements were performed in transmission mode with different instruments:

- V-570 Jasco spectrophotometer (University of Modena and Reggio Emilia) in the 200–800 nm interval with 1 nm resolution, at ambient temperature.
- Cary 5000 UV-Vis-NIR, double beam spectrophotometer by Varian (now Agilent), (ICGM -Université de Montpellier, CNRS, ENSCM, France) equipped with a tungsten-halogen visible and deuterium arc UV lamps and PbS NIR detector.

The spectra of octinoxate and avobenzone in ethanol, acetone, and ethyl-acetate solutions ($1 \text{ ppm} < c < 200 \text{ ppm}$) were collected employing a 1 cm optical-path QuartzSil cuvette. UV-Vis spectra of pure filters in vaseline oil (v.o.), zeolites in v.o., and ZEOfilters in v.o. were collected using a quartz-slide sandwich (213).

4.5.2 Solar radiation exposure test

In view of ZEOfilters' employment in sunscreens, the evaluation of the material stability under UV exposure and its filtering power is of paramount importance. The ZEOfilters were irradiated with a solar simulator lamp and analyzed by UV-Vis spectroscopy after irradiation.

The employed solar simulator is an ATLAS SunTest/CPS+ apparatus at the ICGM (Université de Montpellier, CNRS, ENSCM, France). All the samples for irradiations tests were placed in spectroscopic 1-cm quartz cuvettes sealed by Teflon® plugs. The cuvettes were kept horizontally during exposure, with the transparent face pointing to the light source. ZEOfilters were irradiated as neat powders spread on the internal face of the cuvette, while pure UVfs were dispersed at 1 wt.% in vaseline oil (v.o.).

The experiments were performed two times:

- 1- setting the lamp power at 500 W/m^2 for 130 minutes at the temperature of 43°C .
- 2- setting the lamp at 750 W/m^2 for 4 hours at 43°C .

After UV exposure, ZEOfilters were mixed with vaseline to reach a composition of 1 wt% of UVf in the mixture, i.e. UVf (in ZEOfilter): (zeolite + v.o.) = 1:99. Subsequently, UV-Vis spectra were acquired using the quartz-slide sandwich setup, about 25 and 2 hours after the first and second exposure test, respectively. Spectra of blank samples (i.e. unexposed samples) were also acquired for comparison.

4.5.3 Development of an emulsion formulation for the delivery of ZEOfilters

Sunscreen formulations are the most common products employing UVfs. Thus, it is important to assess the behavior of these new UVfs into formulations for their possible industrial exploitation.

The feasibility to formulate a topical product using ZEOfilters was evaluated. In this case, the development and characterization of ZEOfilters' formulations are very important for the possible interactions of the ZEOfilters with other components of the formulations, that could lead to UVfs degradation or their release in the formulations themselves.

Preliminary very simple oil-in-water formulations were realized at the ICGM (Université de Montpellier, CNRS, ENSCM, France) for the delivery of LTL- and 13X-FAU-based ZEOfilters, while more optimized formulations were realized at the University of Turin (Italy) using LTL-based ZEOfilters.

4.5.3.1 Preliminary formulation tests

A distilled water and vaseline oil (v.o.) emulsion was prepared as a starting matrix for ZEOfilters. Hydrophilic (Eumulgin-SMO-20, BASF, Germany) and lipophilic (Dehymuls-SMS, BASF, Germany) surfactants were employed together with a thickener (Simulgel-600, SEPPIC, France) to stabilize and provide viscosity to the formulation. The formulation was prepared with 20 wt.% v.o., 2 wt.% Eumulgin-SMO-20, 3 wt.% Dehymuls-SMS, and 25 wt.% distilled water. Finally, 2 wt.% of thickener was added.

The preparation was performed with a standard procedure (**Figure 4-7**): water and oil phase (vaseline and both surfactants) were heated and stirred at 70 °C for 10 minutes separately; heating was stopped, the two phases were blended for 10 minutes by a rotor-stator homogenizer, obtaining a homogeneous emulsion. Then the pristine zeolites (LTL or 13X-FAU) or the respective ZEOfilters were added at 20 wt.%. Finally, SIMULGEL-600 thickener was added as 2 wt.% of the emulsion (i.e. zeolite excluded), and the product was further blended for 10 min. The thickener completely changes the rheology of the formulation improving its viscosity.

The structure of the so obtained formulations (i.e. droplets dimension and powder dispersion) was investigated by optical microscopy in transmitted light, immediately after the preparation and after 4 days. For this purpose, one drop of each emulsion was placed on a microscope slide and flattened using a coverslip, forming a thin transparent film.

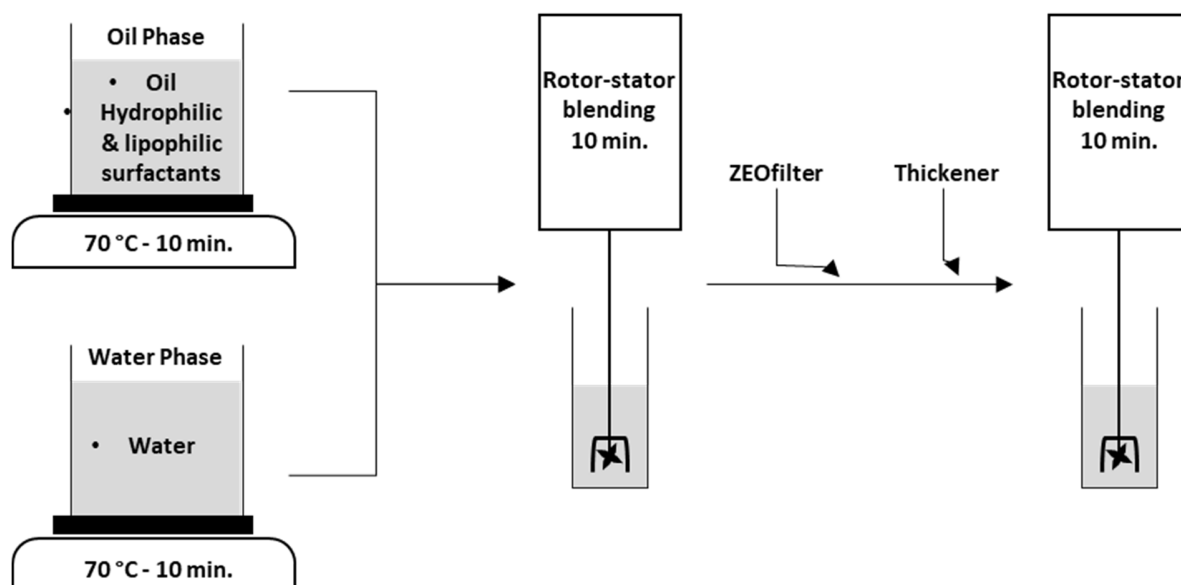


Figure 4-7. Production scheme of preliminary formulations.

4.5.3.2 Optimized formulation

An oil-in-water (O/W) emulsion was developed using the components reported in **Table 4-3**. An aqueous phase and an oil phase were prepared independently (**Figure 4-8**). The aqueous phase contained deionized water, PEG 400, Disodium EDTA, carbomer 341, and methyl paraben. The oil phase consisted of glycerin, mineral oil, cetyl alcohol, and dimethicone. Aminomethylpropanol was added at the end of the process to increase the viscosity of the formulation.

Materials and methods

The ZEOfilters were dispersed in the aqueous phase to reach the avobenzone or octinoxate concentration of 1 mg/ml in the final formulation, and sonicated for 15 minutes. The lipid phase was then added to the aqueous one and the mixture was homogenized using a high shear homogenizer (Ultraturrax®, IKA, Königswinter, Germany) for 5 min at 24,000 rpm, obtaining the O/W emulsion. Considering the emulsions containing the free UV filters, each filter was dispersed in the aqueous phase to reach the avobenzone or octinoxate concentration of 1 mg/ml in the final formulation, and sonicated for 15 minutes before the addition of the lipid phase. With this procedure, formulations were prepared to contain ZEOfilters or unencapsulated UV filters, as reported in **Table 4-4**.

Table 4-3. O/W formulation composition

Component	Wt. %	Function
Deionized water	87	main phase
Glycerin	4.9	humectant
PEG 400	0.6	emulsifier
Disodium EDTA	0.1	stabilizer
Carbomer 341	0.4	surfactant
Mineral oil	3.8	oil phase
Cetyl alcohol	0.2	emulsifier and thickening agent
Dimethicone	0.5	emulsifier
Aminomethylpropanol	0.3	neutralizing agent
Methyl paraben	0.2	preservative
ZEOfilter	2	UV filter

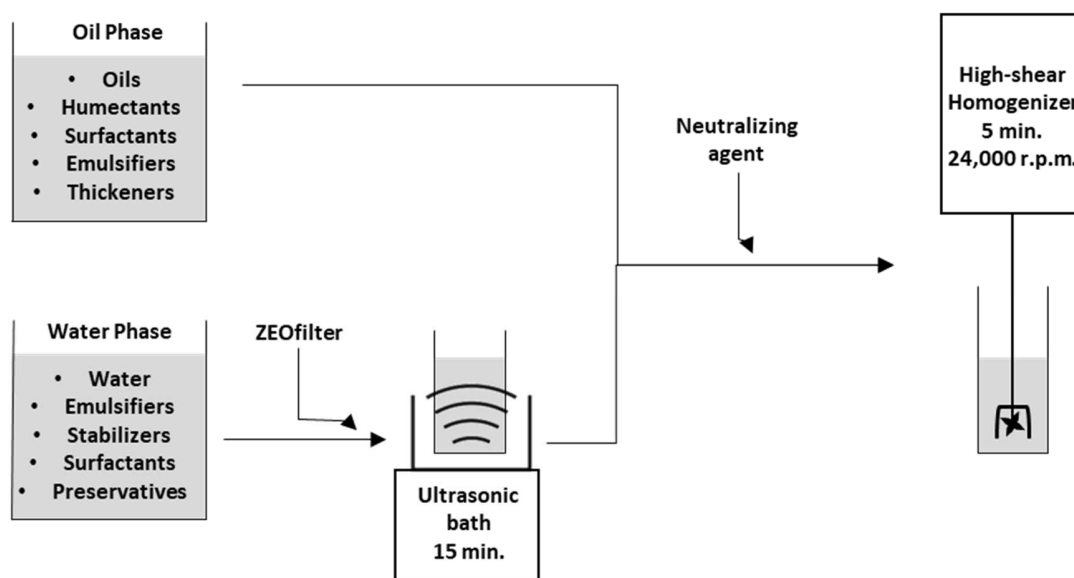


Figure 4-8. Scheme of optimized formulations preparation.

Materials and methods

The emulsions formulations were characterized in vitro by optical microscopy analysis to evaluate the size distribution of the dispersed oil droplets. Thanks to optical images, the stability over time of the emulsions was checked after 3 months. The viscosity and the rheological properties were determined using a rotational viscosimeter (Brookfield DV III+ Rheometer). The pH was measured at room temperature using a pHmeter Orion model 420A.

Table 4-4. Prepared oil-in-water formulations. c = active compound concentration.

Formulation	Active compound 1		Active compound 2		OMC in formulation [mg/ml]	AVO in formulation [mg/ml]
		c [mg/ml]		c [mg/ml]		
F1	LTL/OMC	19.4	-	-	1	-
F2	LTL/AVO	18.6	-	-	-	1
F3	LTL/OMC	19.4	LTL/AVO	18.6	1	1
F4	LTL/OMC	9.7	LTL/AVO	9.3	0.5	0.5
F5	AVO	1	-	-	-	1
F6	OMC	1	-	-	1	-
F7	OMC	1	AVO	1	1	1

4.5.4 In vitro permeation studies

In vitro permeation tests (PTs) aim to evaluate the permeation of a target compound through a membrane. Studying cosmetics and drugs, the membrane often resembles human skin, and PTs provide the intake amount and rate of the target compound topically applied on the skin. In the case of sunscreens, it is important to assay the percutaneous absorption of UVfs since their intake in the dermis or the organism may cause undesired reactions (section 3.3).

PTs conducted on ZEOfilters and ZEOfilters-based formulations aim to verify the release of UVf from the zeolite, possibly leading to the subsequent intake of the UVf. Moreover, the penetration of the hybrid particles through the skin was evaluated, being of potential health concern.

Materials and methods

PTs were carried out using a static vertical diffusion Franz cell to evaluate AVO or OMC permeation. The Franz cell consists of a donor compartment (DC), in which the sample to be tested is placed, and a receiving compartment (RC) containing the receiving phase, separated by a membrane (Figure 4-9). The target molecule or compound (pure UVfs, ZEOfilters, or formulations) is added in DC and, subsequently, it is quantified in RC by HPLC measurements. This indicates the capability of the target to permeate the membrane. Moreover, the use of skin membranes enables the measurement of the accumulation of the target species in the different skin layers. In the case of ZEOfilters, the experiment was first performed using a synthetic membrane (Spectra/Por cellulose dialysis membrane, Spectrum Laboratories, Rancho Dominguez, California) with a molecular weight cut-off of 14,000 Da (minimum radius of about 1.5 nm). In this way, the release of UVf from ZEOfilters was evaluated in aqueous suspensions and O/W formulations. Moreover, tests were also performed using purposely prepared slices of pig ear skin as the membrane. The pigskin was purchased from a local slaughterhouse. Skin slices with a thickness of 1 mm were isolated with a dermatome from the inner side of pig ears and then were frozen at -18°C . Before the experiments, the skin was equilibrated in saline solution (NaCl 0.9 % w/w) added with sodium azide (0.01% w/v) at 25°C for 30 min to preserve its integrity. After washing with saline solution, the skin layer was inserted between the two compartments of the vertical Franz cell, with the stratum corneum side facing toward the DC. Both experiments with synthetic and skin membranes were performed as follows. The receptor phase in the RC was a phosphate-buffered saline (PBS) 0.05M (pH 5.5) containing sodium dodecyl sulfate (SDS) 0.1% as the solubilizer. PBS is commonly employed in biological research to simulate human physiological conditions. Into the DC was placed 1 ml of ZEOfilter aqueous suspension at the AVO or OMC concentration of 1 mg/ml, or 1 g of O/W formulation containing ZEOfilters at the concentration of 1 mg/g of UVfs. The donors were applied for 26 h at an infinite dose (Box 4-1). The receiving phase was withdrawn at regular times and replaced with the same amount of fresh receiving medium. UVf permeation was evaluated by determining the cumulative amount of drug reaching the receiving phase over time by HPLC analysis (see below). Table 4-5 reports all the performed permeation tests.

Box 4-1. *Permeation tests at infinite dose.*

Permeation tests are performed with infinite dosing when the permeant concentration within the formulation in the donor compartment may be assumed to be fixed throughout the experiment. In this case, indeed, the thermodynamic activity of the permeant would not change. Generally, to reach such a condition, the donor phase is renovated regularly, or a small amount of exceeding permeant is added so that molecules permeating in the receiving compartment are readily replaced (214).

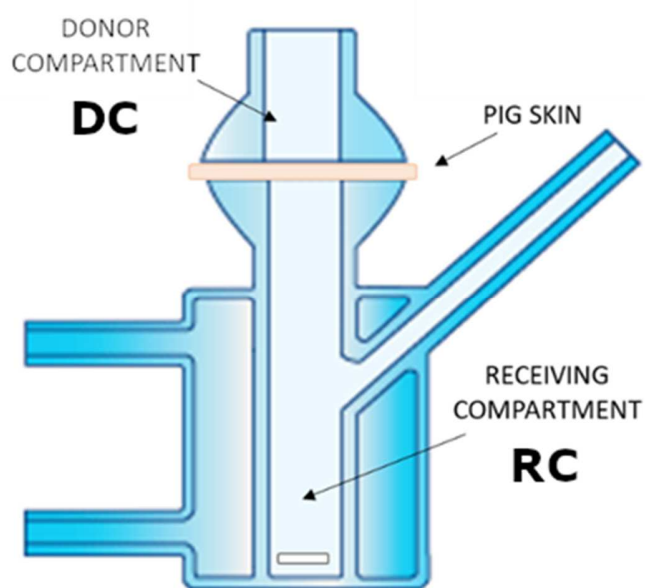


Figure 4-9. Static vertical diffusion Franz cell.

Table 4-5. Performed skin permeation tests. DM: donor medium; AS: aqueous suspension; O/W: oil-in-water emulsion; PS: pigskin; SM: synthetic membrane.

ZEOfilter	UVf wt.% in ZEOfilter	Donor Medium (DM)	UVf concentration in DM	Membrane
13X-FAU/OMC	6.60	AS	1 mg/ml	PS
	12.15	AS	1 mg/ml	PS
13X-FAU/AVO	9.83	AS	1 mg/ml	PS
HS-FAU/OMC	15.74	AS	1 mg/ml	PS
LTL/AVO	5.74	AS	1 mg/ml	PS
	4.9	AS	1 mg/ml	PS
	4.9	O/W	1 mg/g	PS
	4.9	O/W	1 mg/g	SM
LTL/OMC	4.44	AS	1 mg/ml	PS
	5.15	AS	1 mg/ml	PS
	5.15	O/W	1 mg/g	PS
	5.15	O/W	1 mg/g	SM
HS-MOR/AVO	5.94	AS	1 mg/ml	PS
HS-MOR/OMC	11.03	AS	1 mg/ml	PS

4.5.4.1 Quantification of UVfs in pigskin

Accumulated OMC and AVO were quantified in pigskin by solvent extraction at the end of the *in vitro* PTs, separating different skin layers. At the end of PTs, skin membranes were washed with saline to remove the exceeding donor phase on the surface and dried using cotton wool. Then the stratum corneum (SC) was separated by the tape-stripping method, using an adhesive film (Scotch Booktape, 3M, USA), and repeating the procedure 25 times. After removing the SC, the stripping tapes were transferred into glass vials and extracted by methanol or isopropanol for OMC or AVO recovery, respectively. Considering epidermis (E) and dermis (D), the two layers were either analyzed together (E+D) or separated using the thermal-shock technique. To separate E and D, skin samples were soaked in 1.8 mL of water at 60 °C for 30 s and immediately cooled in ice at 0 °C for 5 minutes. The two parts were cut with a scalpel into small pieces and added with 5 mL of methanol or isopropanol for solvent extraction of OMC and AVO, respectively. Each extraction (i.e. whatever if SC, E+D, or E and D separately) was carried out in an ultrasonic bath at 40 °C for 15 minutes and repeated three times.

4.5.4.2 Quantitative determination of UV filters by HPLC analysis

The quantitative determination of OMC and AVO was carried out by High-Performance Liquid Chromatography (HPLC) analysis using a binary pump (Shimadzu Model LC-6A), a 100- μ L injection loop, and a UV-Vis detector (Shimadzu Model SPD-10AV). The analytical column was a 5- μ m pore size, 4.6 $\times$ 150 mm C18 column (Agilent). For the quantification of AVO, the detection wavelength was 358 nm, the mobile phase was methanol:water (92:8 v/v) and the flow rate was 1 mL/min. The retention time was approximately 4 min. Considering OMC, the detection wavelength was 310 nm, the mobile phase was a mixture of acidic water (pH 3) and acetonitrile (20:80 v/v) and the flow rate was 1 mL/min. The retention time was approximately 6.8 min.

To obtain the calibration curve a stock standard solution was prepared dissolving a weighed amount of AVO and OMC in methanol or isopropanol, respectively. Then, each solution was diluted with the respective mobile phase, providing a series of standard solutions over the concentration range of 0-10 μ g/mL. A linear calibration curve was obtained for each UVf over the respective concentration range, with a regression coefficient of 0.999. Calibration curves are represented in **Figure 4-10**.

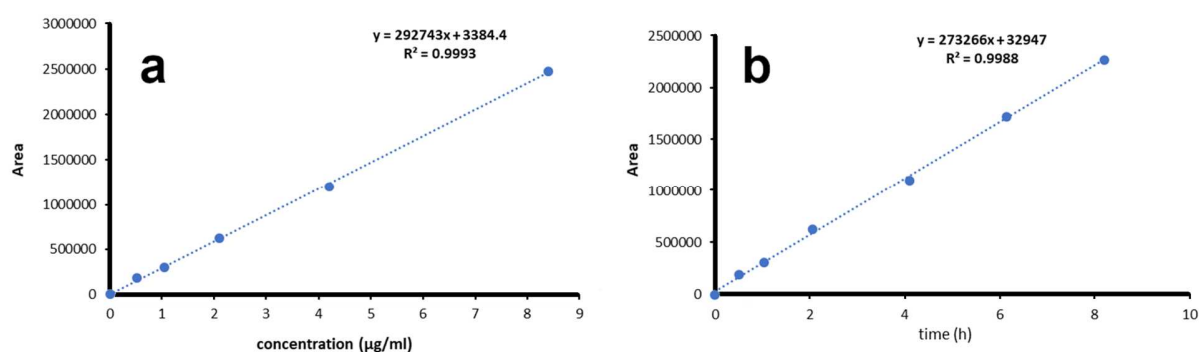


Figure 4-10. Calibration curve of AVO (a) and OMC (b) used for HPLC measurements.

4.5.5 Leaching tests of ZEOfilters into simulated seawater

LTL-based and 13X-FAU-based ZEOfilters were dispersed into simulated seawater to evaluate the leaching of UVfs from the zeolite pores. This investigation is necessary to predict what the behavior of ZEOfilters would be after their release into the environment.

Leaching tests were performed using the static batch method at the constant liquid/solid rate of 10 ml/g. Simulated seawater was obtained using Kent Reef Salt Mix (California, USA) at 38‰ salt in MilliQ water. 0.6 g of ZEOfilters were dispersed in 6 ml of seawater inside 15 ml Falcon tubes, and the samples were kept shaking in the dark at room temperature. Leaching water was withdrawn at different times by centrifuging and replaced with the same amount of fresh seawater. The collected water samples were analyzed to quantify leached UVfs. The measurements were performed by UV-Vis spectroscopy or HPLC. Concerning UV-Vis, water samples were extracted in ethyl acetate, and UVfs were quantified using a reference scale of the pristine OMC and AVO in ethyl acetate, in the concentration range of 0-50 ppm and 0-25 ppm, respectively (**Figure 4-11**). Concerning HPLC, measurements were performed directly on the seawater.

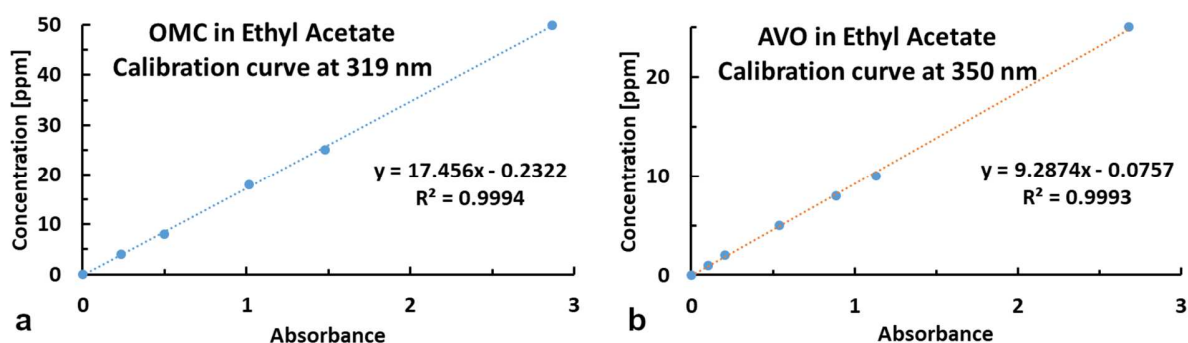


Figure 4-11. UV-Vis spectroscopy calibration curves of OMC (a) and AVO (b) in ethyl acetate.

4.6 Synopsis of ZEOfilter systems and characterization

During the thesis, overall, 87 ZEOfilters samples were produced. **Table 4-6** summarizes for each zeolite/UVf combination the number of samples produced, the main synthesis parameters, and the analyses (s.l.) performed. It is noteworthy that for HS-MOR/OMC and LTL/OMC samples the number of prepared samples is higher compared to other systems. Indeed, these ZEOfilters were employed to optimize the loading procedure, while other systems were explored more efficiently with a lower number of trials, also according to the scheme in **Figure 4-4**. Similarly, LTL and 13X-FAU ZEOfilters are those with a more complete analytical investigation, due to their more promising features. On the contrary, Na-MOR with both UVfs and HS-FAU/AVO were not further investigated after elemental analysis (EA) due to the too-low carbon content obtained after loading.

Materials and methods

Table 4-6. Synopsis of ZEOfilters. ZEOfilters are indicated specifying zeolites (using labels of this thesis) and UVfs, and for each combination, the number n° of independent synthesis performed is provided. In the synthesis conditions section, the higher and lower value of loading UVf/Zeolite ratio [mol/mol] and duration (t [h]) is reported, while all investigated temperatures are specified; the highest explored l/s parameter is also reported for each system ($l/s_{\max}$). In the “Analyses” section, crosses indicate whether the test was performed or not for each system.

ZEOfilter			Synthesis conditions				Analyses						
Zeolite	UVf	n° samples	UVf/Zeolite [mol/mol]	T [°C]	t [h]	$l/s_{\max}$ [ml/mg]	EA	TG	UV	IR	PS	FORM	UV exp.
HS-MOR	OMC	22	0.1-33.1	25; 100; 150	10-168	4.8	X	X	X	X	X		
	AVO	3	1.3	90; 100	28-64	1.2	X	X	X		X		
Na-MOR	OMC	5	1.5-25.9	25	48-335	4.8	X						
	AVO	2	1.4-1.5	90	28-64	1.1	X						
LTL	OMC	17	0.5-21.6	25; 100	48-359	4.8	X	X	X	X	X	X	X
	AVO	8	0.5-2.1	90; 100	28-158	0.5	X	X	X		X	X	X
HS-FAU	OMC	2	79.5	100	47-72	0.8	X	X	X		X		
	AVO	2	11.3-14.9	100	70-190	1.6	X						
13X-FAU	OMC	6	7.5-58.7	100	47-188	0.5	X	X	X		X	X	X
	AVO	8	6.1-15.2	100	47-168	1.7	X	X	X		X	X	X
ZSM5-398	OMC	2	39.8-49.7	100	48	1.7	X	X	X				
	AVO	2	5.6-5.8	100	48	1.6	X	X	X				
ZSM5-30	OMC	4	2.4-50.0	100	48-64	1.7	X	X	X				
	AVO	4	1.3-8.5	100	48-64	1.6	X	X	X				

5 Results and discussion

Some of the results reported in this chapter have already been published. The full paper (215) is available in **Appendix II**.

5.1 Particle-size characterization of pristine zeolites

The knowledge of zeolite particle-size distribution is essential since it may affect important parameters such as the UVf loading efficacy, skin permeation, and the final stability of sunscreen formulations.

Figure 5-1 shows the grain size curves of pristine zeolites measured by laser diffraction particle size analyzer, while **Table 5-1** reports the most important parameters. HS-MOR and Na-MOR display an almost perfect unimodal distribution, with a Dv_{50} (i.e. the diameter below which 50% of the sample by volume is) at 12.8 and 10.7 μm , respectively.

13X-FAU and HS-FAU display a bimodal size distribution. 13X-FAU has a small component, accounting for about 10% by volume, centered at around 0.7 μm , while the second, main component is centered at about 5 μm , which represent also the Dv_{50} value (4.9 μm). HS-FAU sample grain size curve shows two main size components, the first (40% by volume) is centered at about 6 μm , and the second at about 90 μm , leading to a Dv_{50} of 37.6 μm .

ZSM5-30 displays, similarly to FAU samples, a bimodal distribution, with values centered at about 0.5 and 4 μm , accounting for 30 and 70% by volume, respectively. The Dv_{50} is 3.11 μm , and the Dv_{90} is 8.59 μm . ZSM5-398 displays a more uniform distribution, which is almost unimodal and centered at about 8 μm . The corresponding Dv_{50} and Dv_{90} are 6.22 and 13.9 μm , respectively.

Different from other samples, LTL zeolite has a more complex, polymodal size distribution, with at least 3 different components at about 0.5, 3, and 55 μm . The resulting distribution covers a quite wide range of particle sizes, with a Dv_{50} of 1.88 μm and a Dv_{90} of 53.8 μm . Since LTL displayed the most promising features as a host for UVfs (see next sections), its particle size was homogenized by wet grinding, trying to reduce the 55 μm component. Finally, the obtained Dv_{50} and Dv_{90} were 2.57 and 15.8 μm , respectively, with a sensible reduction of the coarser component (**Figure 5-1g**).

Table 5-1. Particle-size distribution parameters. *Span* parameter refers to the amplitude of the whole size distribution interval; *Uniformity* refers to the homogeneity of the distribution, with values <1 for sharp distributions; $D[4:3]$ is the average diameter of particles if considered as spheres of equivalent volume; $Dv(10)$, $Dv(50)$, $Dv(90)$ are the particle diameter below which the 10, 50, or 90% by volume of the sample is, respectively.

	HS-MOR	Na-MOR	LTL	LTL grind.	13X-FAU	HS-FAU	ZSM5-30	ZSM5-398
Span	1.78	1.50	28.46	5.972	1.71	3.33	2.60	1.84
Uniformity	0.55	0.46	7.34	1.868	0.53	1.13	0.82	0.57
$D[4:3]$ [μm]	14.50	11.70	14.40	5.71	5.62	53.00	3.91	7.37
$Dv(10)$ [μm]	4.42	4.45	0.37	0.42	1.85	4.15	0.51	2.52
$Dv(50)$ [μm]	12.80	10.70	1.88	2.57	4.90	37.60	3.11	6.22
$Dv(90)$ [μm]	27.30	20.50	53.80	15.8	10.30	129.00	8.59	13.90
Volume Above 2000 μm [%]	0	0	0	0	0	0	0	0
Volume 63-2000 μm [%]	0	0	6.87	0.03	0.00	37.32	0	0
Volume 2-63 μm [%]	99.23	98.81	42.20	55.39	89.07	62.42	65.38	95.80
Volume Below 2 μm [%]	0.77	1.19	50.93	44.59	10.93	0.26	34.62	4.20

Results and discussion

Volume Below 1 μm [%] 0.00 0.80 42.63 35.96 6.50 0.00 24.46 0.40

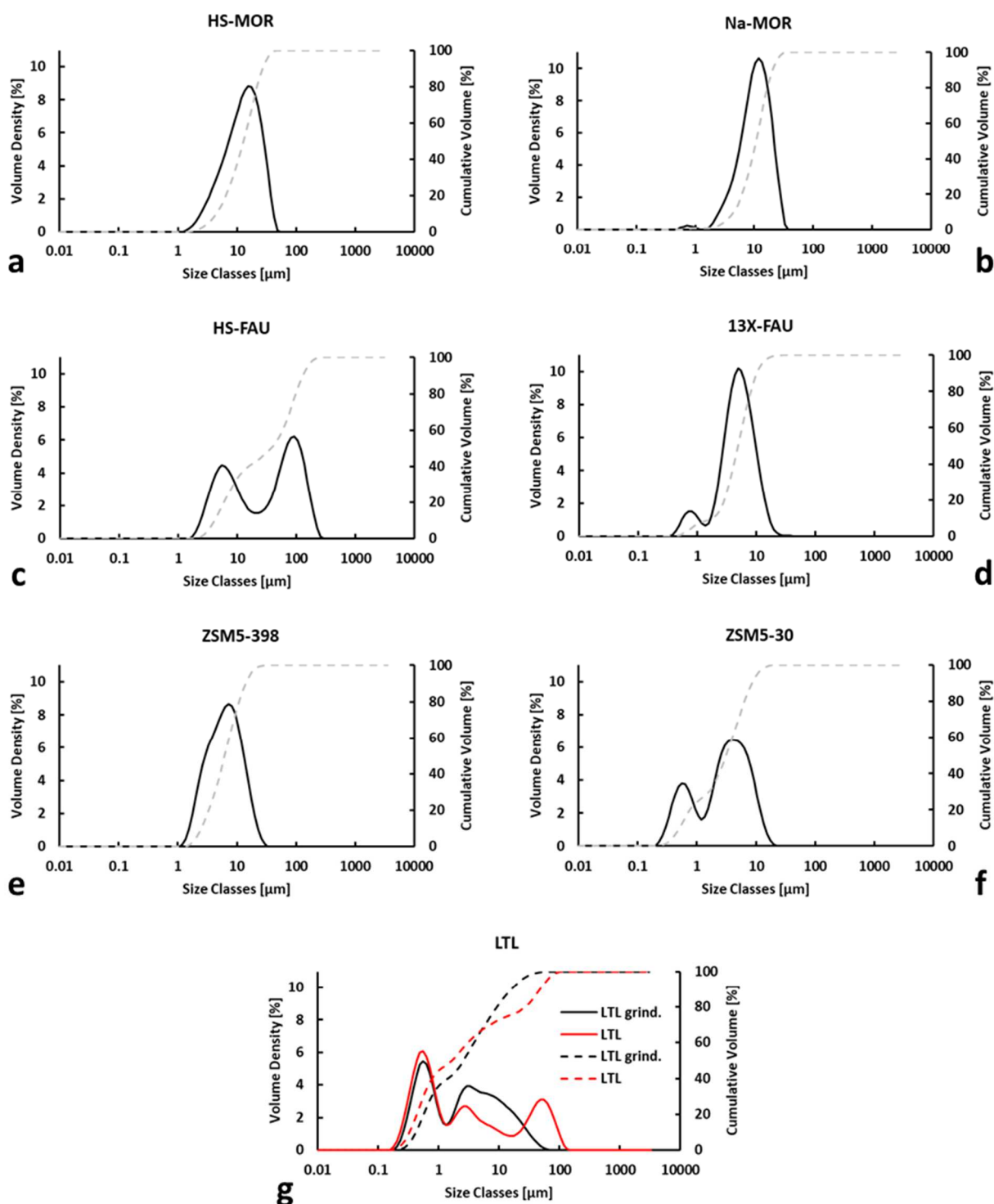


Figure 5-1. Grain size distribution of pristine zeolites. For each particle diameter (i.e. size class) the percentages by volume of the sample with that diameter (volume density, solid curves) or with lower diameter (cumulative volume, dashed lines) are shown. For LTL zeolite, curves are shown before (red) and after (black) wet grinding.

Concerning the cosmetic acceptability of ZEOfilters, two considerations deserve to be done. Firstly, the particle size should not exceed 50 μm , otherwise leading to a sort of “sandpaper effect” on the skin, with possible undesired skin whitening upon topical application. Secondly, too small particles, and especially nanoparticles between 1 and 100 nm, are of particular concern for their potential health hazard, and require safety studies before their approval on the market and, e.g., must be authorized by the European Commission prior to their use in cosmetic products (216). For this reason, the employed zeolites show particle size distribution in the range of 0.5-10 μm . It is worth noting that their particle size distribution could be further refined for a possible future scale-up step of the project.

5.2 Zeolites loading and ZEOfilters characterization

5.2.1 Chemical composition of ZEOfilters

The first aim of this thesis was the optimization of a loading procedure of the organic UVf inside zeolites porosities. Zeolite loading represents a challenge in the preparation of ZEOfilters, especially since the UVf maximum loading in each zeolite was unknown. Moreover, the loading procedure should i) maximize the loading of the UVf and ii) prevent the presence of free UVf on the external grain surface. These two points are crucial for the realization of safe and effective sunscreen hybrid materials.

Briefly recalling the experimental section 4.2.2, the main steps of ZEOfilter syntheses were:

- Zeolite dehydration
- Zeolite loading with UVfs
- Hybrid Washing
- Hybrid Drying

While the dehydration temperature was chosen for each zeolite based on TGA data, the loading temperature of the UVf inside zeolites was set to 100 °C for all the realized hybrids. Indeed, 150 °C was also considered as loading temperature, but then it was discarded due to bare OMC yellowing. Temperatures lower than 100 °C were also discarded to limit the H₂O competition during UVf absorption.

After the loading, the samples were washed with appropriate solvents, so to remove all UVf molecules possibly not encapsulated in the pores and avoid the removal of encapsulated ones. As it was described in the experimental section, Soxhlet extraction (SE) and ultrasound-assisted extraction (UAE) were both evaluated as washing methods, together with acetone and ethanol as the solvent.

To explore the effects of the solvent, a selected zeolite/UVf system (i.e. LTL/OMC) underwent SE by ethanol or acetone. The C% of the system was monitored by elemental analysis (EA) at different washing steps and the results are shown in **Figure 5-2a**. Since the system, before washing, contain a high excess of UVf (i.e. molecules on the surface of grains), the C% considerably drops in the first few washing cycles, and then slowly decreases upon successive cycles for both the solvents. Finally, the C% stabilizes at a certain value, delineating a compositional plateau. The C% at which the system is stabilized using the two solvents is different, i.e. at about 4% and 1% for acetone and ethanol, respectively. Based on these data is possible to hypothesize that in the first and steeper part of the curve, the solvent is solubilizing UVf molecules that are outside the zeolite structure, and the process is highly effective. Subsequently, the achievement of a compositional plateau indicates that no more UVf is extracted from the zeolite. At this stage, the UVf remaining in the system is only that encapsulated within the zeolite. These features of the washing curves were observed for all samples and all washing techniques, however different C% values of the final compositional plateau were observed depending on the zeolite/UVf system, and washing solvent. In some cases, an intermediate trend of C% was observed before the compositional plateau. This observation possibly indicates a certain amount of UVf experiencing a weak interaction with the zeolite, e.g. interacting on the external surface of grains. Finally, too protracted washing procedures lead to a continuous, slow decrease of C%, removing the UVf also from the

zeolite cavities. On the basis of these data, it is clear the paramount importance of stopping the washing process at the right moment and of choosing the right solvent. To do this, it is important to evaluate the obtained final C% in the washed hybrid. In the case of LTL/OMC washed in acetone, it was above mentioned a final content of 4 C%. Considering OMC molecular weight, and the molar weight of the anhydrous LTL (i.e. the weight of one unit cell of the zeolite), this value corresponds to about 0.5 OMC molecules p.u.c. Moreover, in the first instance, it might be estimated that ~ 0.5 OMC molecules p.u.c. could account for the maximum loading in LTL based on its steric hindrance (i.e. c parameter is almost half of OMC molecule length). On the contrary, ethanol seems not appropriate for ZEOfilter washing, as it probably tends to remove immediately the UVfs molecules also from the zeolite pores. On the basis of these results, acetone was employed as the solvent for all the other ZEOfilters.

Figure 5-2b shows the comparison of the washing curves obtained on LTL/OMC system by SE and UAE. Both techniques lead to similar final UVf (i.e. C%) content in the ZEOfilter, even if at different l/s values (see section 4.2.2 for l/s definition). The pros of UAE are the absence of a heating source, and the possibility to work with larger volumes faster, in a more tunable way, while the cons are mainly due to the need for centrifugation at each washing step. The SE was found to be more suited for small-scale operations due to the limited volume of material being processed at once, but it does not require centrifugation of the material, nor handling of the sample between one washing step and the other. It is noteworthy that UAE was found to bring the system to the plateau at lower l/s values, probably due to a more effective solubilization of UVf. Since, as already mentioned, the results are comparable for UAE and SE, the technique was selected on a case-by-case basis, and hereafter the employed method for each sample will not be reported.

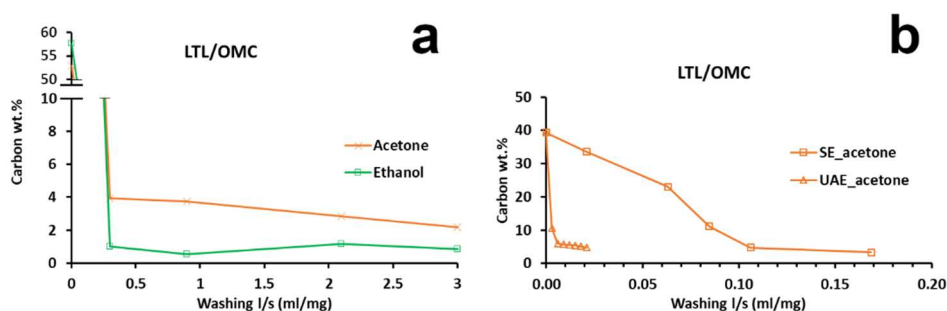


Figure 5-2. Washing curves of LTL/OMC ZEOfilters. a) Comparison between Soxhlet extraction (SE) with ethanol (green curve), which removes OCM almost completely from the Zeofilter, and acetone (orange curve) which stabilizes the system at a higher OCM content for several washing cycles. b) Comparison between UAE and SE washing systems.

After the washing treatment, the samples were dried at 60 °C to remove effectively solvents remaining from the washing step.

The different ZEOfilters were prepared by using different UV filter excess (for different batches of the same system diverse excess were tested), but it is noteworthy that all samples of the same zeolite/UVf system displayed the same final composition and features independently from the amount of filter (in excess) used. Samples obtained at the end of the washing process and laying on the compositional plateau are considered “optimized” after drying.

Table 5-2 reports the synthesis conditions and chemical data (obtained by EA and TGA) for selected samples (one for each zeolite/UVf system). TG data will be further discussed in the next section.

The loading conditions of the different samples reported in **Table 5-2** show a very variable initial UV filter/zeolite molar ratio, ranging from more than ten-fold the amount needed for maximum loading possible (i.e. 13X-FAU/OMC and HS-FAU/OMC) to an almost ad-hoc loading (LTL/AVO). Considering the maximum loading of the various ZEOfilters, it is clear that FAU zeolites can host more molecules p.u.c. compared to MOR or LTL frameworks. Indeed, different framework types have different pores volumes, and FAU accessible volume corresponds to 27.42% of the total cell volume (more than 14000 Å³), compared to 12.27% for MOR (cell volume about 3000 Å³) and 15.37% for LTL framework (cell volumes about 2000 Å³). From the table, it appears that OMC and AVO tend to be trapped differently by different zeolites with the exclusion of LTL and 13X-FAU that can encapsulate about the same number of molecules of both the UVfs. In general, cationic zeolites (i.e. with lower Si/Al ratio) display a quite high loading of AVO, with 13X-FAU showing the highest one, about 10 wt.%, while high-silica zeolites are not suited at all for AVO trapping. Conversely, OMC is more evenly entrapped by all the investigated zeolites, both cationic and high silica. The reason for the different behavior of OMC and AVO should lie in the zeolite-UVf interaction. Both the UVfs are hydrophobic, although AVO behaves as a weak acid due to the β -diketo group. The keto-enol tautomerism is hampered in the solid-state within the zeolite channels, but the proximity to zeolite acid sites may catalyze the interconversion of the keto-enolic form into the diketo one. On the other hand, the presence of metal ions in the zeolite cavities could account for a shifting of the tautomeric equilibrium toward the keto-enol due to its enhanced metal-binding ability (**Figure 5-3**) (217-219). The absence of metal sites to graft in high silica zeolites may explain the less effective encapsulation of AVO.

Table 5-2. Summary table of selected hybrid samples reporting loading conditions and chemical data obtained from elemental and TG analyses (*= optimized washing, i.e. Total UVf wt.% = UVf wt.% in the zeolite pores). All samples were loaded at 100 °C and dried at 60 °C before analyses. TGA was not performed on the HS-FAU/AVO, Na-MOR/OMC, and Na-MOR/AVO systems due to the low UV-filter content (na). l/s = liquid/solid ratio during the washing step (zero value indicates a non-washed sample).

Label	Loading conditions		EA		TG		
	UVf/ Zeolite [mol/mol]	l/s [ml/mg]	C [wt.%]	UVf [wt.%]	Total UVf [wt.%]	UVf in the pores [wt.%]	UVf molecules p.u.c. [mol/mol]
13X-FAU/OMC	55.91	0.10	13.53	18.19	16.0	9.9	6.9
		0.16*	4.91	6.60	6.6	6.6	4.3
13X-FAU/AVO	13.20	0.00	17.29	22.34	20.7	16.1	11.2
		0.06*	7.61	9.83	10.6	10.6	6.6
HS-FAU/OMC	87.46	0.60*	10.29	13.83	13.2	13.2	6.1
HS-FAU/AVO	14.88	0.20*	0.46	0.59	na	na	na
Na-MOR/OMC	24.82	4.8*	0.69	0.93	na	na	na
Na-MOR/AVO	1.37	1.07*	0.75	0.97	na	na	na
HS-MOR/OMC	19.96	0.15	8.21	11.03	7.1	7.1	0.8
HS-MOR/AVO	1.30	0.19*	4.60	5.94	4.9	4.9	0.6
LTL/OMC	17.31	0.84	4.17	5.60	5.9	5.3	0.5
LTL/AVO	0.57	0.22*	4.42	5.71	5.3	5.3	0.5
ZSM5-30/OMC	40.31	1.71*	5.87	7.89	7.6	7.6	1.8
ZSM5-30/AVO	5.44	1.55*	3.15	4.07	4.6	4.6	1.0
ZSM5-398/OMC	40.50	1.71*	1.88	2.53	2.6	2.6	0.5
ZSM5-398/AVO	5.83	0.81*	1.09	1.41	1.4	1.4	0.3

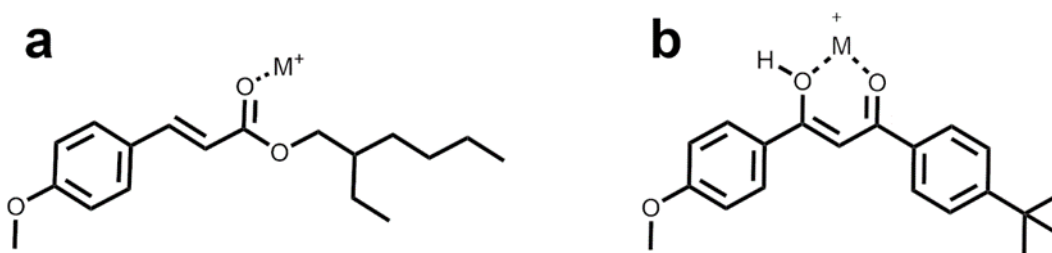


Figure 5-3. Molecular scheme of the possible interaction between OMC (a) and AVO (b) with zeolite extraframework cations.

As discussed in the previous section, the elemental analysis (EA) enabled a first, quick evaluation of UVf content in the ZEOfilter during and after the washing process. However, EA does not indicate whether the UVf is inside zeolite pores or outside. Thus, thermogravimetric analyses (TGA) were performed on selected samples of each ZEOfilter. The bare UVfs OMC and AVO and the pristine zeolites were used as reference systems. **Figure 5-4** shows TGA of bare UVfs, while TGA of pristine zeolites are plotted together with that of the corresponding ZEOfilters. At least two measurements were performed for each ZEOfilter: one on a sample at the beginning of the washing process (i.e. still with UVf on the zeolite grains surface) and another one on the optimized sample (i.e. on the compositional plateau). The comparison between the two TGA enabled to discriminate the contributions of UVf from inside and outside the zeolite pores since differences in the desorption temperatures indicate different interaction strengths between the filter molecules and zeolite atoms. This comparison is shown for the 13X-FAU ZEOfilters in **Figure 5-5**, while for the other ZEOfilters only the data of optimized samples are shown. The bare UVfs decompose over a 100-degrees wide range below ~ 300 °C (OMC) and ~ 350 °C (AVO). These temperature ranges are lower than those reported in the literature for OMC and AVO boiling temperature (i.e. 382 °C and 400 °C at 1 atm for OMC and AVO, respectively (57)), as expected for a TGA carried out in an open crucible setup (220).

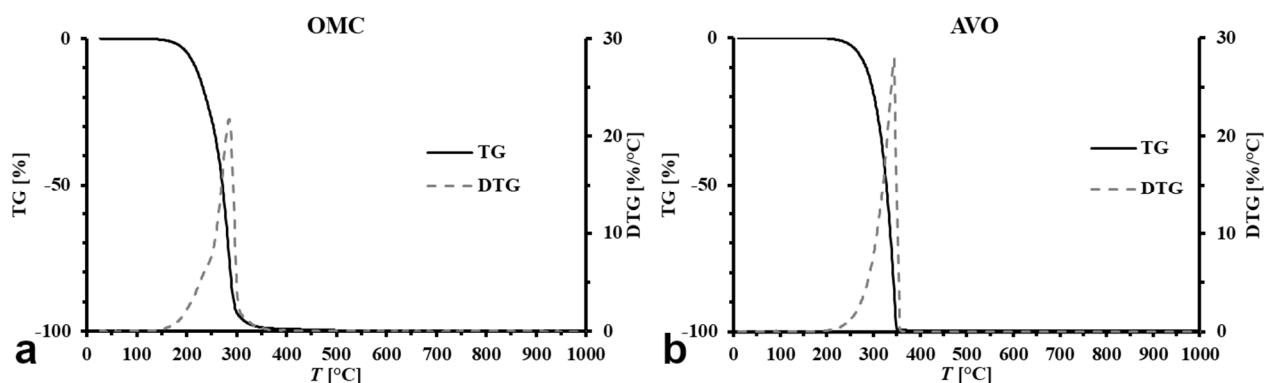


Figure 5-4. Fig. 4. TGA of OMC (a) and AVO (b) in helium atmosphere.

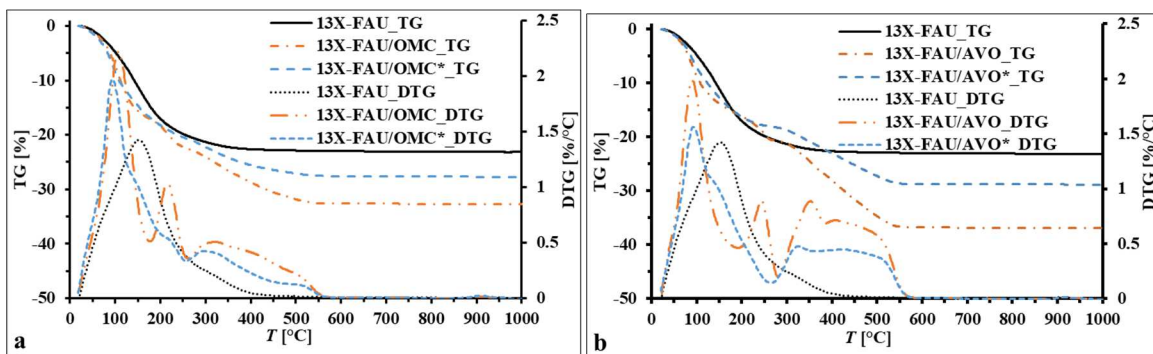


Figure 5-5. TGA of 13X-FAU and derived hybrids with OMC (a) and AVO (b). * Optimized ZEOfilters.

Table 5-2 reports the UVf content for each optimized ZEOfilter, for 13X-FAU/OMC and 13X-FAU/AVO also data relative to unoptimized samples are available. UVf content estimated by EA and TGA may differ due to several factors. Samples have been homogenized after optimization but, at the scale of sampling (1 mg for EA and 20 mg for TGA), some inhomogeneities can occur. Furthermore, elemental analysis is optimal to measure the elemental composition of purely organic compounds, while measuring low C% amounts in silicate matrices such as zeolites is challenging. Finally, the variable H₂O content of zeolites induces weight variation of the samples, with a consequent impact on the C weight percentage. Thus TGA was chosen for the final UVf p.u.c. determination. In this case, given the total weight loss (TG_{tot}), the estimated UVf weight loss (TG_{UVf}), and the molar mass of the bare UVf and anhydrous zeolites (MM_{UVf}, MM_z, respectively), the number of molecules p.u.c. was estimated as follow:

$$UVf \text{ molecules p.u.c.} = \frac{MM_z}{100 - TG_{tot}} * \frac{TG_{UVf}}{MM_{UVf}}$$

The pristine 13X-FAU (**Figure 5-5**, black line plots) displays a single broad weight loss below 400 °C, accounting for 23% weight loss, that can be correlated to the removal of H₂O molecules in the solvation sphere of cations in different sites, consistently with what reported in the literature (202). The two 13X-FAU hybrids shown in **Figure 5-5** (13X-FAU/OMC, 13X-FAU/AVO) show a DTG peak at about 100 °C that can be attributed to H₂O molecules readsorbed during the preparation and/or storing of the ZEOfilters. The lower temperature at which these losses occur suggests that H₂O molecules are more loosely bonded in ZEOfilters than in the pristine zeolites, probably on the surface of the grain or at the channel entrance. This hypothesis is supported by the assumption that the presence of large hydrophobic UVfs in the zeolite channels prevents access to H₂O molecules. The DTG curves of the optimized samples (*) show an H₂O-related shoulder at a slightly higher temperature (about 150 °C), which is not visible in the unoptimized ones. This can be justified by the fact that the excess of UVfs on the surface of grains hinders the access of the H₂O molecules to the zeolite pores. Upon washing the removal of UVfs excess from the grain makes the channels more accessible to H₂O once again and allows the formation of some more stable H₂O-zeolite bonds, similarly to what was observed in the pristine sample. At higher temperatures, the DTG curves of 13X-FAU ZEOfilters show two peaks of different breadth. Unoptimized 13X-FAU/AVO DTG (l/s = 0) displays a noticeable peak at 250 °C (**Figure 5-5b**) that completely disappears in the optimized sample and can be attributed to UVfs loosely bound to the surface of the grains. Similarly, unoptimized 13X-FAU/OMC (**Figure 5-5a**) shows a DTG peak at 220 °C but, in this case, a very small signal remains in the optimized sample, probably indicating a very small amount of UVf molecules on the surface of zeolite grains. The DTG broad bands registered in the range 270–550 °C can be attributed to the decomposition of the UVfs encapsulated into the zeolite porosities, which are calculated as 6.6% and 10.6% wt. for the 13X-FAU/OMC and the 13X-FAU/AVO, respectively. Since the TG losses in this temperature range are higher for the unoptimized samples, we cannot exclude a contribution of molecules more strongly bonded on the surface of zeolite grains. It is worth noting that the decomposition

temperatures observed for the UVf molecules encapsulated into the zeolites are higher than those observed for the pure filters, as a clear consequence of the UVf-zeolite interactions. By applying the above-reported equation to the total UVf loss of the two systems, it can be calculated that 13X-FAU/OMC samples host 4.3 molecules of OMC per unit cell (p.u.c.), while the 13X-FAU/AVO hosts 6.6 molecules of AVO p.u.c. These data are in good agreement with those obtained from elemental analyses (**Table 5-2**). All DTG signals -relative to the organic decomposition- of 13X-FAU/ AVO are shifted toward higher temperatures compared to 13X-FAU/OMC. This shift can be ascribed to the chelating properties of the OO donor group of the β -ketonol moiety of AVO that can form, with the extraframework cations of the zeolite, stronger interactions than the weak coordination bond of the carbonyl oxygen in the ester moiety of OMC (**Figure 5-3**).

Most of the considerations done for 13X-FAU ZEOfilters apply also to the TGA of the other ZEOfilters, which will be thus briefly described and discussed in the following, considering only the optimized samples. TGA of HS-FAU/AVO, Na-MOR/OMC, and Na-MOR/AVO were not performed since the UVf loading, as estimated from EA was too low (**Table 5-2**).

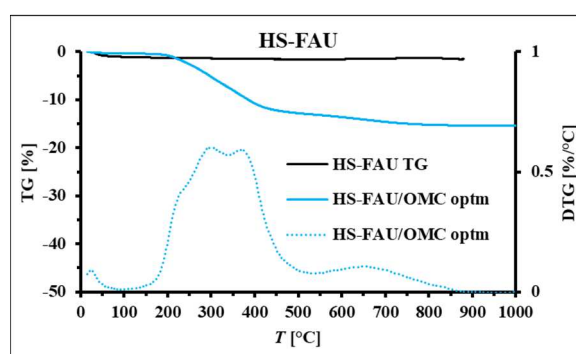


Figure 5-6. TGA of pristine HS-FAU and HS-FAU/OMC ZEOfilter. TGA of the pristine zeolite is from (221). The DTG curve of HS-FAU is not plotted since it is not meaningful for very low TG losses, while TGA was not performed on HS-FAU/AVO due to the too low loading obtained.

Pristine HS-FAU (**Figure 5-6**) displays a total weight loss of about 1.8%, most of which occurs below 100 °C and is thus to be attributed to very weakly physisorbed H₂O molecules. After OMC loading, almost no H₂O loss is observed (0.4% released below 100 °C) and OMC molecules, accounting for 13.2 wt.% are released in the broad interval of 160-600 °C. The value obtained is in good agreement with the UVf content observed by EA (13.83%) and corresponds to 6.1 molecules of OMC p.u.c. (**Table 5-2**).

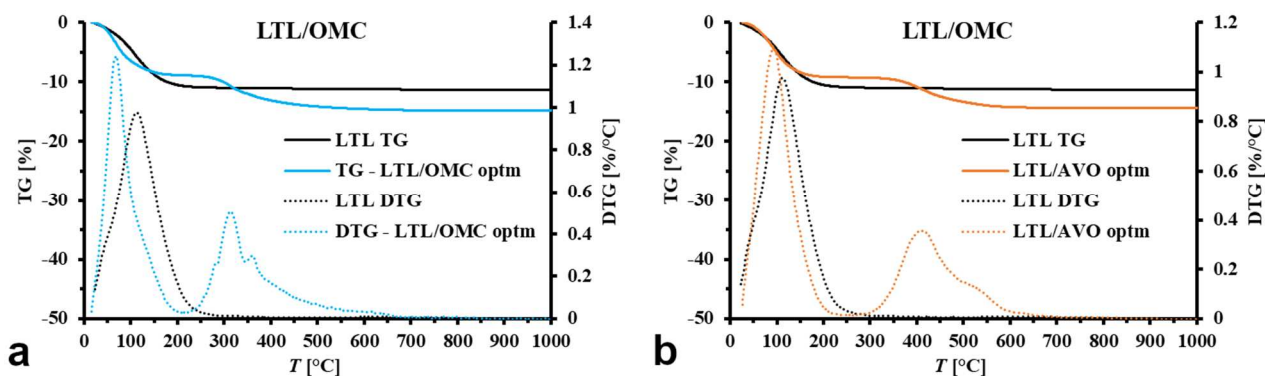


Figure 5-7. TGA of pristine LTL and derived ZEOfilters.

Pristine LTL zeolite (black lines in **Figure 5-7**) loses all H₂O molecules below 250 °C, with a total weight loss of 11.2%. We observe a comparable weight loss of ~9 wt% below 220 °C for both LTL ZEOfilters, possibly due to the fast rehydration of the zeolite after loading. It is difficult to univocally assign this weight loss to structural H₂O or rather to physisorbed surface H₂O, since LTL hosts a large number of weakly bonded H₂O molecules, that can be released below 150 °C (197). Interestingly, the temperature of H₂O release for the hybrids is lower when compared to that of the pristine zeolite, possibly due to the higher amount of physisorbed H₂O molecules. The DTG curve of the LTL/OMC sample (**Figure 5-7a**) shows three peaks at 280, 315, and 360 °C - that can be attributed to OMC molecules differently bonded to the zeolite - accounting for a total weight loss of 5.9%, in good agreement with the value calculated by EA (5.60 wt.%). If we consider only the weight losses above 280 °C the weight loss is 5.3%, a value corresponding to 0.5 OMC molecules p.u.c., nicely matching with the maximum loading predicted by steric hindrance considerations. The remaining 0.6% of OMC may be residual on the external grain surface of LTL particles, thus the LTL/OMC sample in **Table 5-2** is not marked as optimized.

To confirm OMC release upon heating from LTL zeolite, mass analysis of the evolved gasses (TG-MSEGA). Unfortunately, OMC mass is too big to be detected with the employed mass spectrometer, nevertheless, several masses relative to possible fragments of the OMC molecule were qualitatively measured along with H₂O molecule mass. The results reported in **Figure 5-8** show that the mass corresponding to H₂O molecules (17.97 Dalton) was detected only in correspondence with DTG peak below 200 °C, while at higher temperatures only masses possibly derived from OMC fragments (methyl group (15.02 Dalton), acetyl radical (42.99 Dalton), CO₂ (43.97 Dalton), and benzene (52.06 Dalton)) were detected (**Figure 5-8**). It is noteworthy that TG-MSEGA requires a different experimental setup compared to standard TGA, thus the thermal curves obtained in the two setups do not match perfectly. Moreover, it must be noted that the detected masses, even if assigned to specific compounds, may be OMC fragments of equivalent mass.

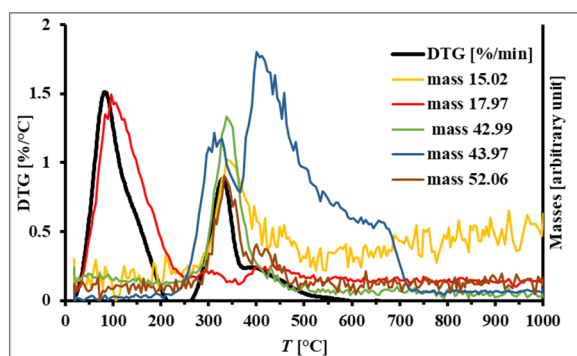


Figure 5-8. Thermogravimetric analysis coupled with mass spectrometry of the evolved gas (TG-MSEGA) of LTL/OMC ZEOfilter. Plotted masses may correspond to: methyl group (15.02 Dalton), H₂O (17.97 Dalton), acetyl radical (42.99 Dalton), CO₂ (43.97 Dalton), and benzene (52.06 Dalton). It must be noted that the detected masses, even if assigned to specific compounds, may be OMC fragments of equivalent mass.

The LTL/AVO hybrid DTG curve shows a broad peak, with a shoulder, between 300 and 650 °C, accounting for a total weight loss of 5.3 wt%, in good agreement with the 5.71 wt% of AVO measured by EA. The value obtained by TGA corresponds to 0.5 AVO molecules p.u.c. Also in the case of AVO, this value may correspond to the highest possible loading in LTL.

For LTL ZEOfilters, the shift in temperature between weight losses of OMC and AVO is even more marked compared to 13X-FAU ZEOfilters. This could indicate a stronger interaction between the UVfs and the extraframework cations in LTL, which presents more accessible cation sites compared to FAU.

The broader DTG peak widths of the 13X-FAU ZEOfilters compared to LTL can be ascribed to their different structure (**Figure 5-9**). In the case of faujasite, not all Na sites can be populated simultaneously, but Na is statistically distributed among them, giving rise to several different configurations in the different unit cells. Conversely, K sites in L zeolite are more regularly distributed along the 12MR channel (c direction). Thus, different Na atoms in the large Y cage of 13X-FAU can interact with UVf molecules with different bond strengths, inducing different release temperatures of the UVf. Conversely, UVf molecules in LTL have all the same surrounding cations to graft, thus leading to sharper DTG.

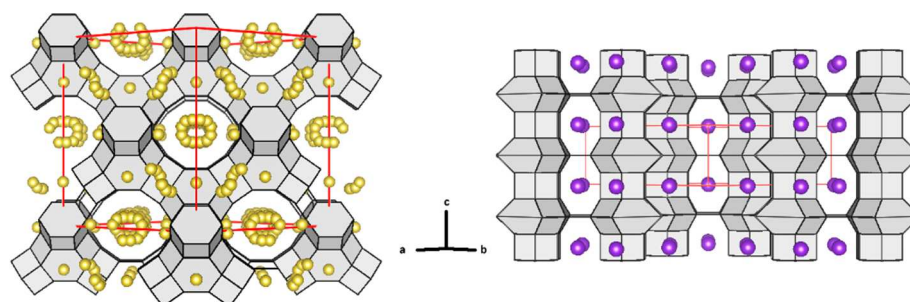


Figure 5-9. Crystal structure of Na faujasite and K L zeolite. The framework is represented by polyhedra with tetrahedral atoms at the corners, while only extraframework cation sites that should be accessible to UVfs are shown (Na in yellow and K in violet).

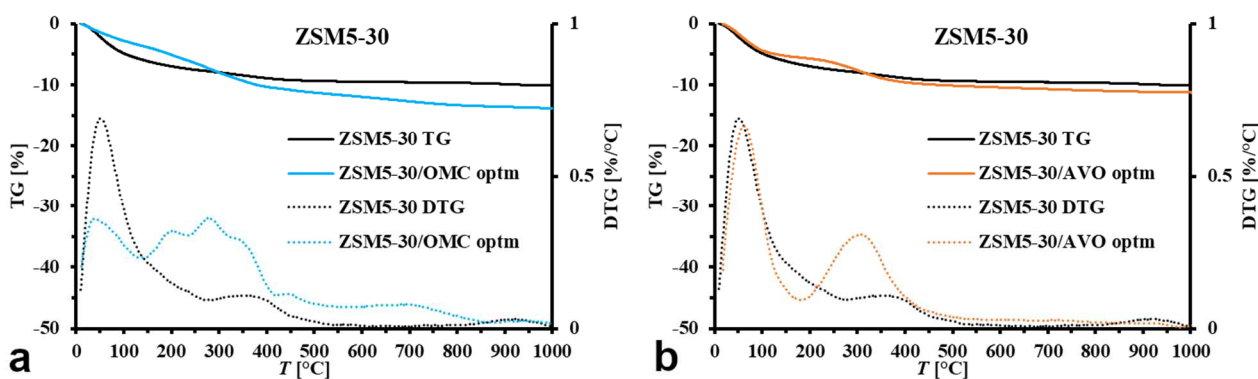


Figure 5-10. TGA of pristine ZSM5-30 and derived ZEOfilters.

ZSM5-30 (**Figure 5-10**), in its protonated form, displays a weight loss of 10.2%, which occurs mostly below 450 °C (9.2%), that was thus used as dehydration temperature during ZEOfilter synthesis. In MFI framework, two straight 10MR channels run along the *b* direction in each unit cell, with a *b* parameter of about 20 Å. Thus the expected maximum loading should be about 2 UVf molecules per unit cell. Slightly higher amounts could also be expected due to the presence of two sinusoidal 10MR channels running in the *a* direction and crossing the other channels. The two channel systems, probably, may not be completely filled simultaneously by UVf but, at the channel intersections, some more room for closer packing may occur. Given these preliminary considerations, the experiments showed that ZSM5-30 traps 7.6% of OMC, and 4.6% of AVO, in good agreement with the values of EA indicating 7.89% and 4.04% for OMC and AVO, respectively. These values correspond to about 2 molecules of OMC (1.8), but just 1 molecule of AVO (**Table 5-2**). The

presence of only H extraframework cations to graft may explain why AVO is less effectively loaded in ZSM5-30, as generally observed in high silica zeolites.

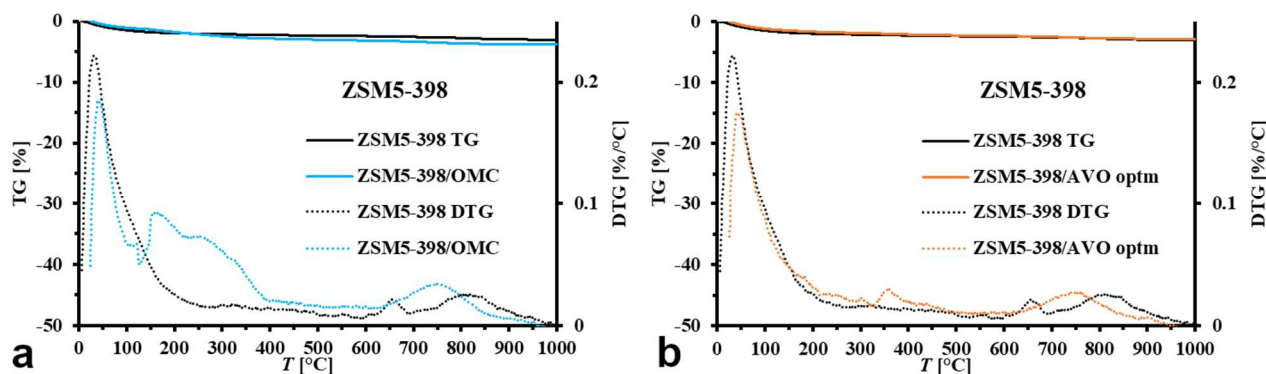


Figure 5-11. TGA of ZSM5-398 and derived ZEOfilters.

The same structural considerations may be done for the high-silica ZSM5-398 (MFI framework). In this case, the pristine ZSM5-398 displays a, very small, total weight loss of 3.0% due to its high hydrophobicity (**Figure 5-11**). Almost all the adsorbed H₂O molecules are released below 200 °C. Also in the case of the two ZEOfilters, the total weight loss is very small, reaching 3.7 and 2.7% for the ZSM5-398/OMC and ZSM5-398/AVO, respectively. With such small losses, the DTG curve is also very noisy, but the signal of UVf release may be located above 120 °C. Above this temperature, the weight loss - and thus the UVf loss - is 2.6 and 1.4% for ZSM5-398/OMC and ZSM5-398/AVO, respectively. These data perfectly match those of EA (2.53 and 1.41%, respectively). The derived loading corresponds to 0.5 and 0.3 molecules of OMC and AVO, respectively, encapsulated in ZSM5-398. The behavior of this sample confirms the same general trend observed for high silica zeolites.

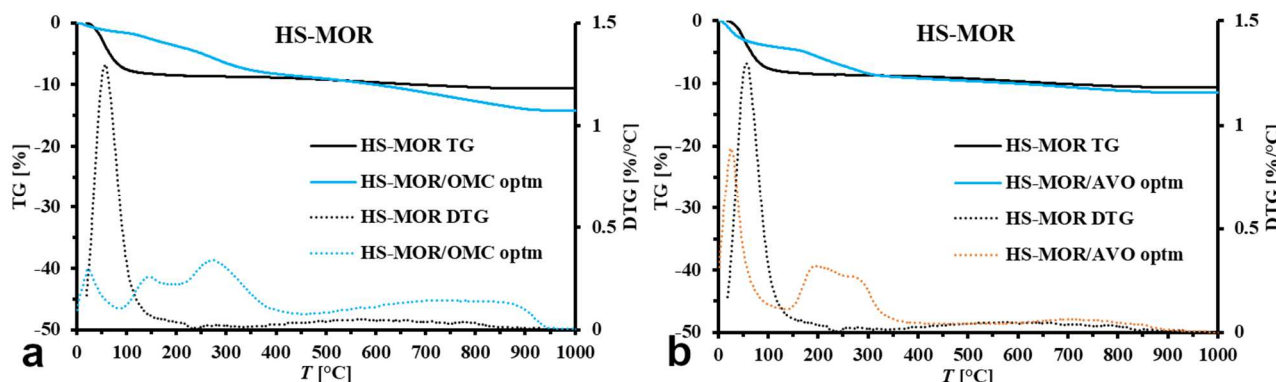


Figure 5-12. TGA of pristine HS-MOR and derived ZEOfilters.

Pristine HS-MOR (**Figure 5-12**) displays a total weight loss of 10.6%, with 8.6% occurring below 250 °C due to adsorbed H₂O, while the remaining part is lost in the 400-900 °C interval, as a consequence of silanols condensation (see **Appendix I**, (189)). Concerning HS-MOR ZEOfilters, UVf losses occur at a slightly lower temperature compared to other systems. OMC is released in a broad interval between 90 and 450 °C accounting for a UVf loss of 7.1%, corresponding to 0.8 molecules p.u.c of OMC. Similarly, AVO is released between 140 and 450 °C with a weight loss of 4.9%, which corresponds to 0.6 AVO molecules p.u.c. Considering that MOR unit cell contains two 12MR channels running along the *c* direction, with *c* being about half of OMC and AVO length, a maximum loading of 1 UVf molecule p.u.c. is expected. Hence, HS-MOR/OMC is almost fully occupied, while HS-MOR/AVO is less occupied. Once again, the trapping of AVO is disfavored in high-silica zeolites compared to OMC. The UVf loss occurring at a lower temperature, compared to other ZEOfilters, can be explained by the presence of mesopores in this HS-MOR sample deriving from its dealumination. The presence of larger mesopores (**Appendix 1**, (189)) can induce an easier release of the molecules at low temperatures.

Based on the EA and TGA results it can be concluded that the encapsulation process is effective for most of the investigated ZEOfilters. Moreover, EA and TGA were confirmed to be reliable and consistent as analytical techniques for ZEOfilter development and characterization.

5.2.2 ZEOfilters' UV filtering properties

Together with the optimization of a synthesis procedure for ZEOfilters, the main aim of this thesis is the evaluation of their UV filtering power, which is most important for their employment. Indeed, ZEOfilters should at least match or, preferably, go beyond the performances of traditional UVfs.

The visible color of UVfs is a further important feature for cosmetic formulations. Indeed, the performance on the skin may determine the success of a sunscreen formulation beyond its protective efficacy. It is thus clear that strongly opaque formulations must be avoided to reduce skin whitening upon topical application and to avoid modification of the rheological properties of cosmetic formulations.

ZEOfilters should desirably fulfill all these requirements, showing a high UV absorption (i.e. low transmittance) in the UV range, but keeping good visible transparency. This shall be conferred by the absence of absorption bands in the visible range and a high UV filtering efficacy, to limit the amount of ZEOfilter – and thus zeolite – in the formulation.

The optical properties of ZEOfilters were measured by UV-Vis spectroscopy on vaseline-ZEOfilter mixtures at different concentrations and were then compared to those of pristine zeolites (25 wt.% in v.o.) and bare UVfs (1 wt.% in v.o., and 8-10 ppm in ethanol, and ethyl acetate) (**Figure 5-13**). The maximum ZEOfilter content that could be added to a given formulation without altering its physical-rheological properties is 20-30%, which corresponds to roughly 1-2% of UVf in the mixture, depending on the ZEOfilter (**Table 5-2**).

As shown in **Figure 5-13a,b**, bare OMC and AVO show minor solvatochromic effects, i.e. little changes in their transmittance spectra in the UV-Vis range (200-800 nm) with changing solvent. The anomalous behavior observed in EtOAc solutions below 250 nm corresponds to the solvent UV cutoff. Bare filters show, and maintain at different concentrations, perfect visible transparency (400–700 nm) and strong absorption in the UVB (OMC) or UVA (AVO) interval, increasing with its concentration, as shown in **Figure 5-13d** for OMC (AVO displays the same features and is thus not reported).

As opposed to UVfs, pristine zeolites in v.o. (**Figure 5-13c**) do not show any absorption band in the visible nor the UV range. Zeolite transmittance continuously decreases with decreasing wavelength, as is typical for particle scattering phenomena. However, different zeolites, at the same weight concentration in v.o., behave differently. Particularly, the high silica zeolites HS-MOR and ZSM5-398 exhibit a very low transmittance in the whole region. By increasing the zeolite concentration in v.o., the transmittance strongly decreases with increasing sample opacity (spectra not shown).

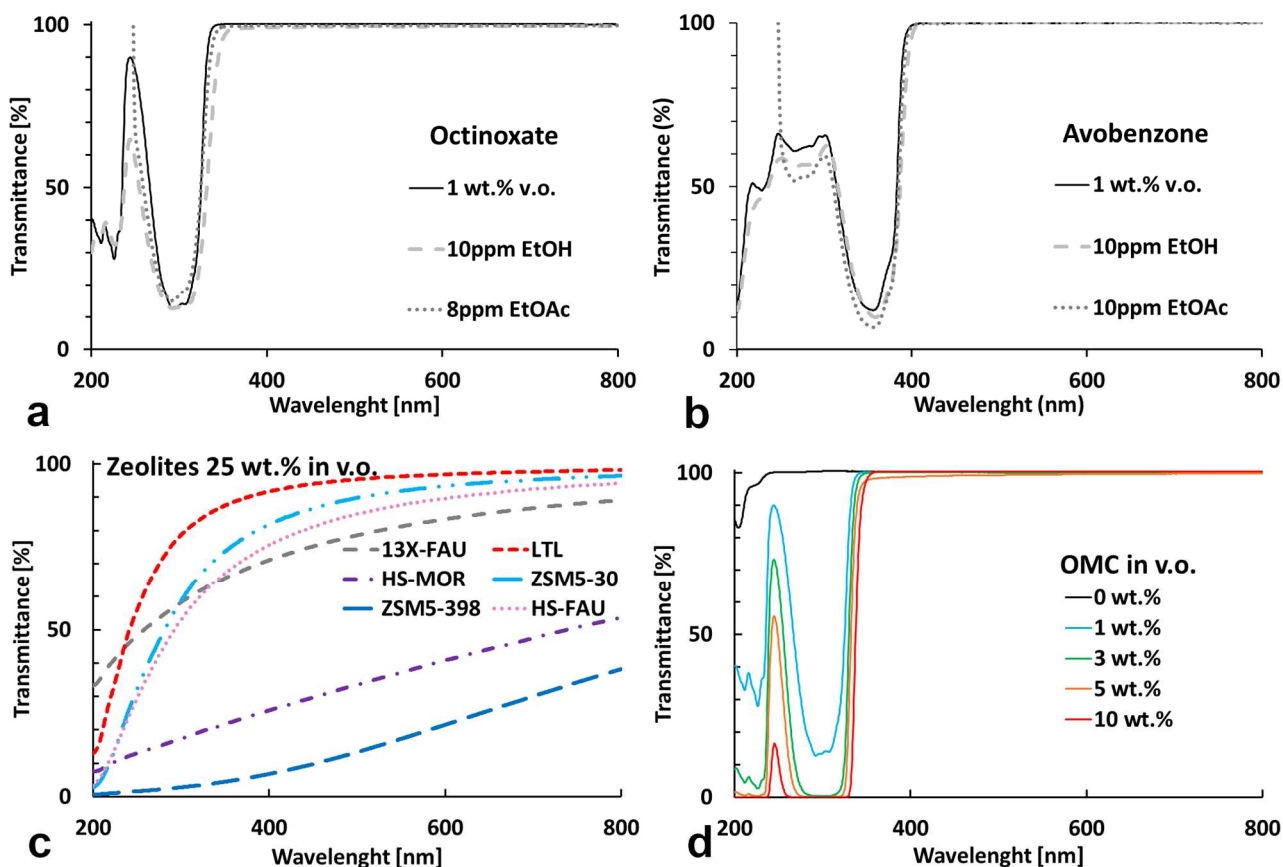


Figure 5-13. UV-Vis spectra of bare OMC (a) and AVO (b) in vaseline oil (v.o.), ethanol (EtOH), and ethyl acetate (EtOAc), of pristine zeolites at 25 wt.% in v.o. (Na-MOR not reported, see **Table 5-2**) (c), and bare OMC at different concentrations in v.o. (d).

Figure 5-14 shows the UV-Vis spectra of ZEOfilters-v.o. mixtures containing OMC (a) or AVO (B) in the concentration of 1 wt.% (i.e. UVf : (ZEOfilter + v.o.) = 1 : 100). This filter concentration was chosen firstly because it allowed the observation of the UV-Vis spectral features (all bands of weak absorptions are evident and few strong bands are out of scale) and secondly in view of further cosmetic applications.

Due to the low UVf loading in ZSM5-398 based ZEOfilters (**Table 5-2**), it was impossible to reach a 1wt. % of UVf in the mixture without inducing strongly modification in the rheological properties of the mixture and on its transparency. Thus, the UV-Vis spectra were collected at 0.5 wt. % of UVf, but still showed a very low transmittance over the whole wavelength range, also indicating a major contribution of zeolite particle scattering to the spectra (Figure 5-14). Conversely, ZSM5-30 ZEOfilters display spectral features similar to other high-silica ZEOfilters, and particularly to HS-MOR, probably because both of them are in protonic form. It is worth noting that the UV absorption band of the ZSM5-30 hybrids, and, to a lesser extent, of the HS-MOR ones, is shifted towards higher wavelengths compared to the other ZEOfilters. This shift towards lower energy can be related to the presence of acid sites in ZSM5-30 and HS-MOR, favoring the keto-

enol form for AVO, and the protonated ester form for OMC (as shown by FT-IR data of HS-MOR, see section 5.6.1).

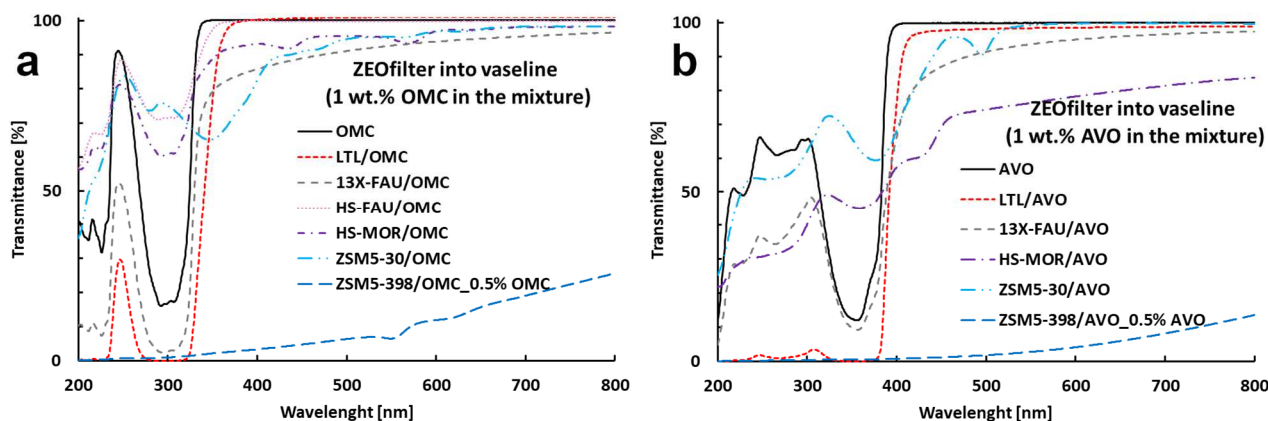


Figure 5-14. UV-Vis spectra of bare UVfs and ZEOfilters in v.o.; HS-FAU/AVO is not reported due to the low UVf loading (**Table 5-2**).

The analyzed ZEOfilters can be split into two groups by comparing their UV transmittance with that of bare UVfs:

- 1) ZEOfilters showing limited UV absorption compared to bare UVfs and possibly some absorptions in the visible region
- 2) ZEOfilters with the same or improved UV absorption compared to UVfs and a good visible transparency

To the first group may be ascribed all ZEOfilters deriving from high-silica zeolites HS-MOR, HS-FAU, and ZSM5-398, and to the low-silica zeolite ZSM5-30. These samples show a too high transmittance in the UV range compared to bare UVfs. Moreover, they also show selective absorptions in the visible light range, leading to the coloration of ZEOfilters powders, which is particularly marked for ZSM5-398, HS-MOR, and ZSM5-30 (**Figure 5-15**). The absorption color of ZEOfilters varies from white to violet or yellow (for OMC and AVO ZEOfilters, respectively) while increasing the zeolite Si/Al ratio, even if for ZSM5-398/AVO, HS-FAU/OMC HS-FAU/AVO colors are very pale.

The explanation for this change in optical properties can be found in the formation of carbocationic species. Indeed, infrared spectroscopy (FT-IR) revealed the protonation of OMC molecules interacting with the HS-MOR acid sites (see section 5.6.1). The protonation of OMC is caused by readily available protons of the zeolite Brønsted acid sites (bridging OH group, Si-OH-Al). The number of available acid sites directly relates to the Al content of the zeolite, while their strength increases with site isolation (222). Due to the high Si/Al ratio, in zeolites such as HS-MOR, ZSM5-398, and HS-FAU all sites are isolated, but the different framework topologies strongly affect their acid catalytic activity. A structure-related reduction of activity per Brønsted acid site was indeed reported passing in the order $ZSM5 \geq MOR > FAU$ (223). Particularly, theoretical modeling and experimental observations revealed an acidity increase with increasing T-O-T angles (up to 180°) (224, 225). This also matches with the reduced activity of faujasite, with T-O-T angles being lower compared to the other two zeolites (FAU $138-147^\circ$, MFI $137-177^\circ$, MOR $143-180^\circ$) (224). Going back to **Figure 5-14**, HS-FAU/OMC is quite peculiar displaying a very low UV filtering power beside a quite high OMC content (**Table 5-2**). Moreover, in this case, the hybrid is almost colorless. Considering that HS-FAU display the highest Si/Al ratio (and thus the lower Al content) tested in this thesis (**Table 4-1**), its lower acid activity can explain the absence of OMC protonation and the consequent very pale tone. However, to deeply understand the associated UV filtering reduction in HS-FAU/OMC deeper investigations are required.

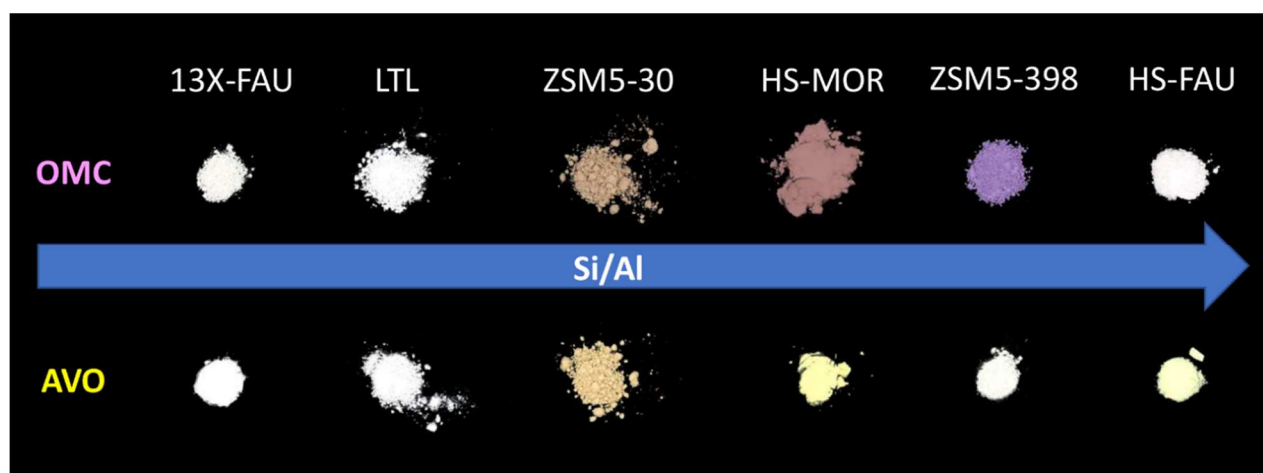


Figure 5-15. Absorption color of ZEOfilters. From left to right Si/Al ratio increases and ZEOfilters show generally darker tones (except for ZSM5-398/AVO and HS-FAU/OMC).

Concerning the second group, it is populated by 13X-FAU and LTL ZEOfilters, which display an equal or enhanced UV filtering power compared to bare UVfs and maintain perfect visible transparency. These optical properties are very promising for their possible future development and exploitation. Indeed, an enhanced UV filtering power can allow reducing the amount of UVfs in cosmetic formulations.

Another important point to pave the way for the use of these ZEOfilters in cosmetic formulations (and in other product categories) is to assess their photostability under protracted UV exposure. Thus, some solar-exposure tests were performed on the most promising ZEOfilters LTL and 13X-FAU, as it is addressed in the next section.

5.2.3 ZEOfilters' stability under UV exposure

Two different tests were performed using a solar simulator lamp on bare UVfs in v.o. and on dry powders of LTL and 13X-FAU based ZEOfilters. In the first test, the samples were exposed for 130 minutes using a lamp irradiance of 500 W/m²; in the second one, they were exposed for 4 hours with an irradiance of 750 W/m² (see section 4.5.2). Thus, in the second test the total radiation on samples was about three times that of the first test. After the irradiation, ZEOfilters were dispersed in v.o. and UV-Vis spectra were acquired and compared to non-irradiated hybrids in v.o. In the first test, about 25 hours occurred between UV exposure and UV-Vis measurements, due to logistical constraints. To observe any time-dependent effect on results, the second test was performed acquiring spectra 2 hours after the solar exposure. **Figure 5-16** shows the irradiated and non-irradiated (blank samples) spectra of the bare UVfs (a OMC, b AVO), and LTL-based (c OMC, d AVO) and 13X-FAU-based (e OMC, f AVO) ZEOfilters. It must be considered an experimental variability of about 10% on transmittance, due to: i) minimal differences in samples thickness, ii) exposed and unexposed ZEOfilters were dispersed in v.o. separately, thus slightly different concentrations are possible. Given this uncertainty, the encapsulated and free filters do not show substantial differences before and after irradiation, regardless the measurements were performed 2 or 25 hours after exposure. Moreover, the spectra acquired on ZEOfilters in the second test almost perfectly overlap the first's, even if (as already mentioned) the radiation dose was three times higher. This confirms the stability of the bare and encapsulated UVfs under irradiation when dispersed separately in v.o.

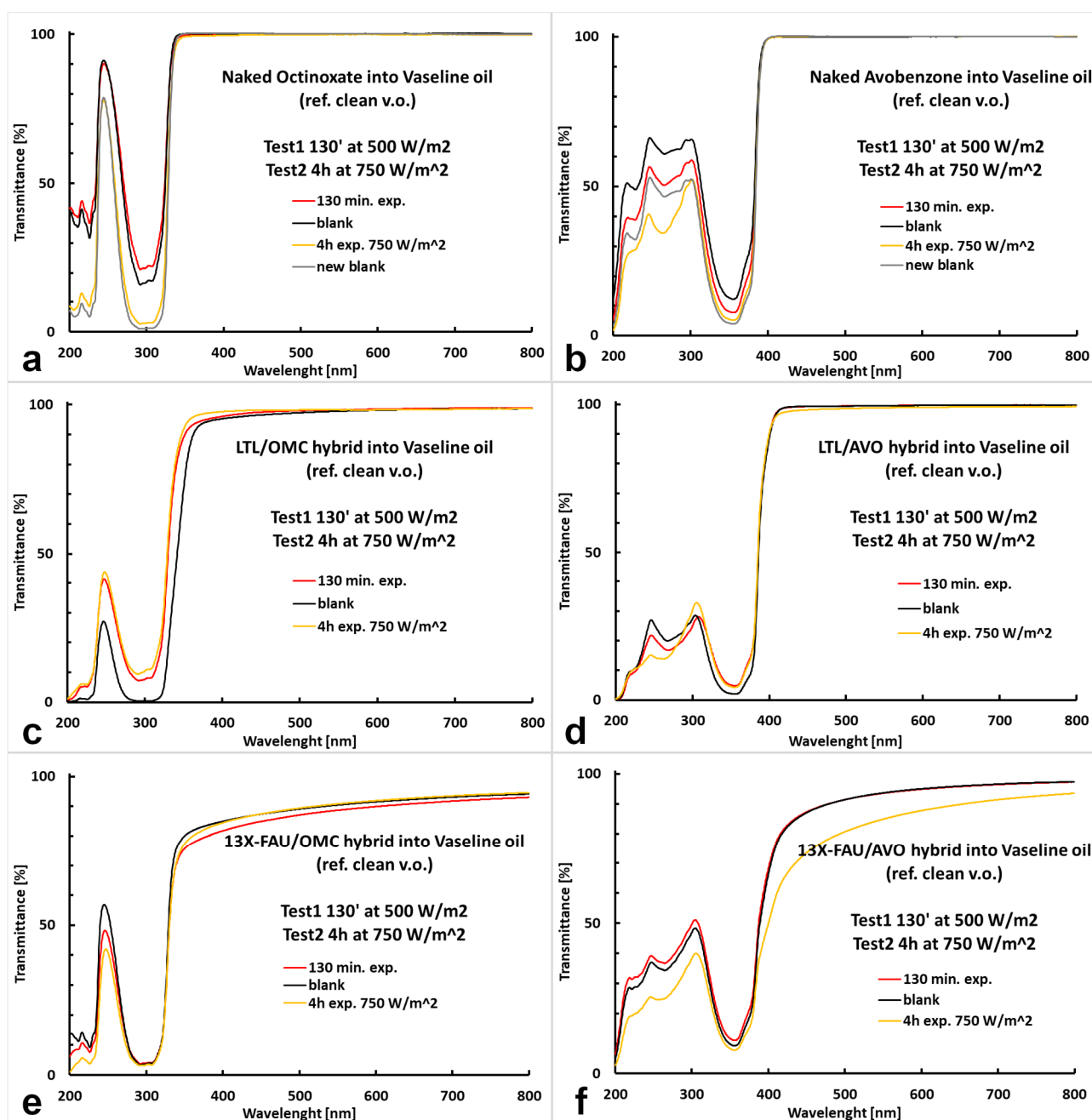


Figure 5-16. UV-Vis spectra of bare UVfs (a,b), and of LTL-based (c,d) and 13X-FAU-based (e,f) ZEOfilters, after exposure to solar simulator lamp (tests 1 and 2). Unexposed samples are also shown for comparison. (blank samples).

In the introduction of this thesis, two main points were highlighted on OMC and AVO stability and efficacy under UV exposure:

- i) under certain conditions, a reversible lowering of AVO absorbance in the UVA region was observed under UV exposure due to the reversible ketonization of the molecule (**Figure 3-11** and section 3.2.2). Similarly, OMC loses, under UV exposure, up to 40% of its absorbance due to the trans-cis photoisomerization (section 3.2.2).
- ii) most degradation phenomena were reported for OMC and AVO mixtures under UV exposure (67, 97), see section 3.3).

UV exposure tests on OMC and AVO ZEOfilters will be repeated in the future to answer these questions, possibly performing *in operando* UV-Vis measurements under UV exposure of OMC and AVO ZEOfilters either separated or mixed. Indeed, the reactions occurring to bare AVO and OMC are mostly reversible, thus 2 hours between UV exposure and spectra acquisition should be too long to observe if ketonization (for AVO) or isomerization (for OMC) occur. Most importantly, the strongest degradation phenomena occur when the two bare filters are associated and mixed in the same formulation. So, the behavior of OMC and AVO ZEOfilters mixtures under irradiation is expected to be significantly higher compared to bare UVfs mixtures, as the filter-filter interaction is inhibited.

5.3 Formulations containing ZEOfilters

5.3.1 Preliminary formulation tests

Optical analysis of formulations was employed to investigate their structure and stability over time. By comparing **Figure 5-17a,b**, it can be noted that, in preliminary formulation tests, the starting O/W emulsion, with only surfactants, displays a quite wide dimensional heterogeneity of droplets (0.05 – 1 mm). The structure is almost retained after 4 days, even if an incipient separation of the two phases is observed, with the disappearance of small-size droplets. The separation is even more marked in the presence of 20% LTL zeolite in the emulsion (**Figure 5-17c**).

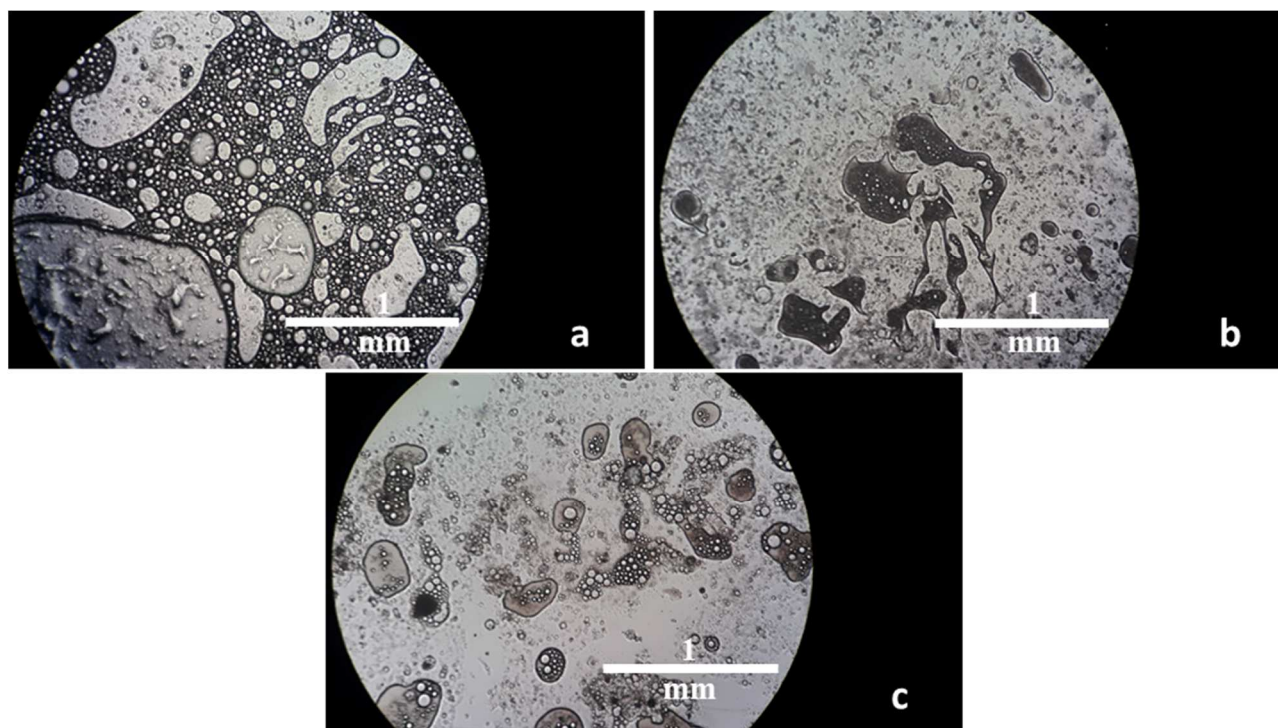


Figure 5-17. Optical microscopy images of O/W emulsion without thickeners. Emulsion immediately (a) and 4 days (b) after preparation; (c) emulsion with 20 % of LTL zeolite.

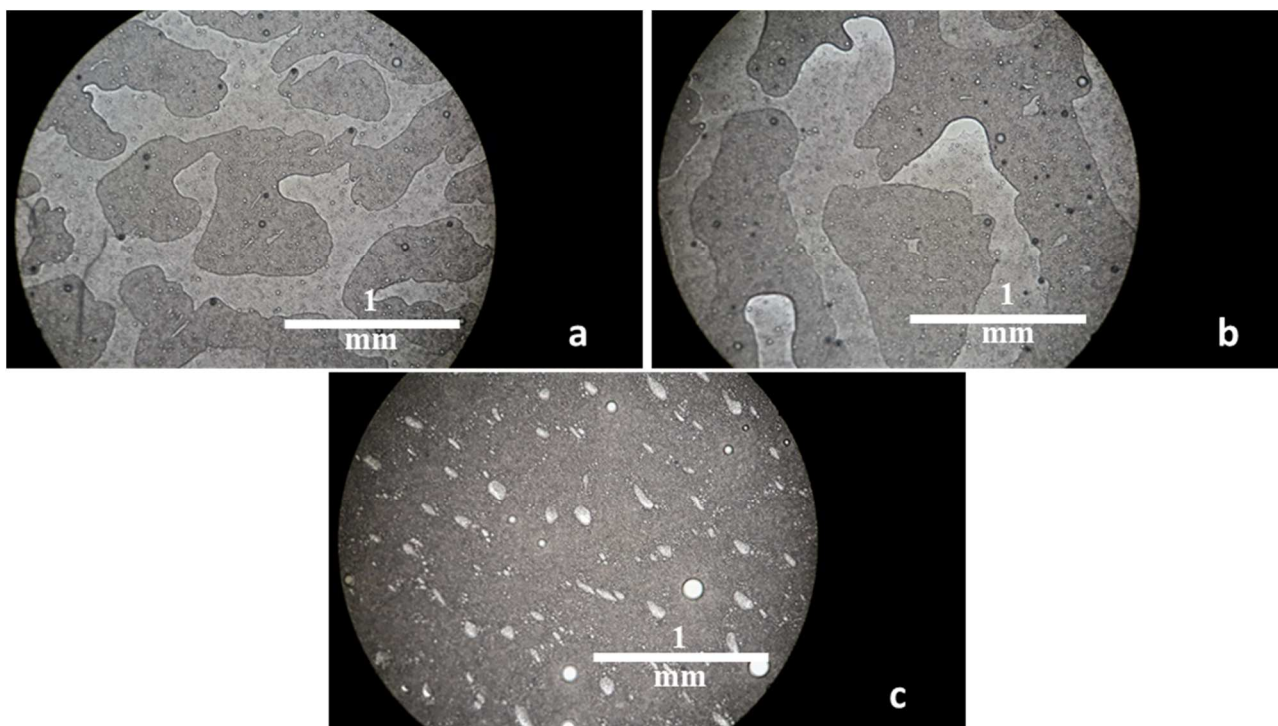


Figure 5-18. Optical microscope images of clean formulations containing thickeners without (a,b) or with (c) bare UVfs. Images were taken immediately (a) and 4 days (b,c) after preparation.

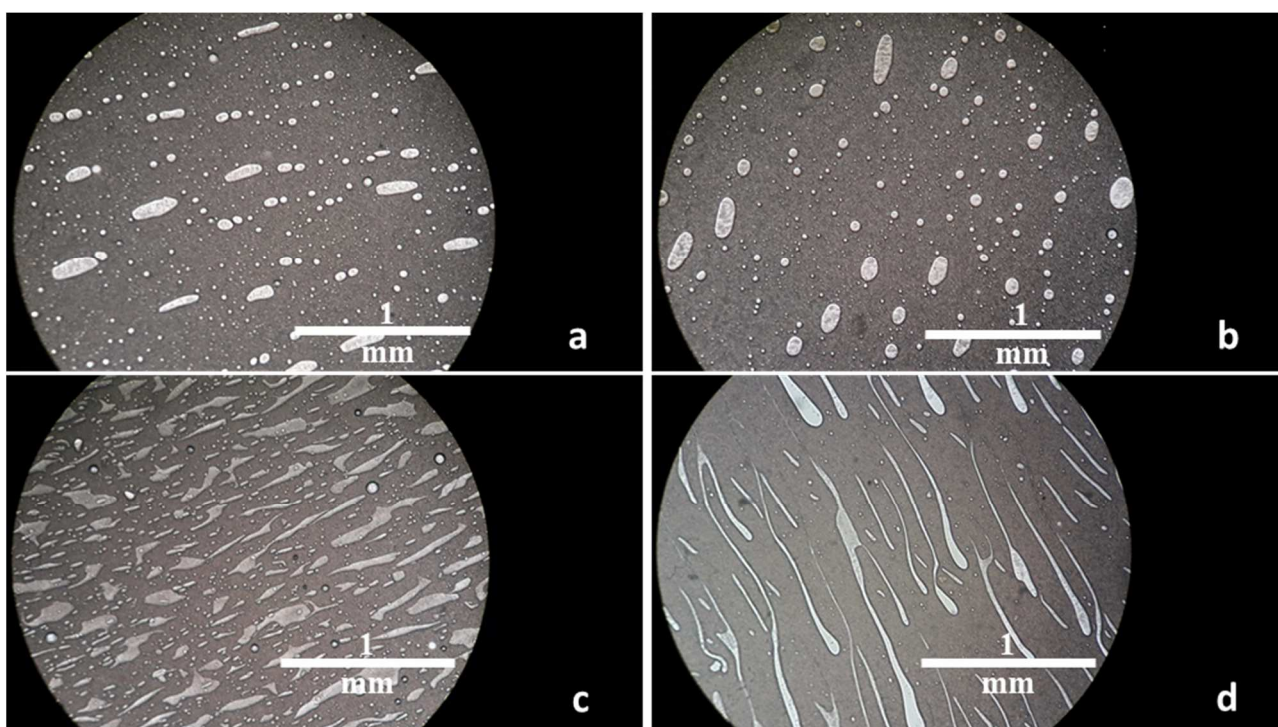


Figure 5-19. Optical microscope images of formulations containing thickeners with 20% 13X-FAU (a,b) or LTL (c,d) zeolites. Images were taken immediately (a,c) and 4 days (b,d) after preparation.

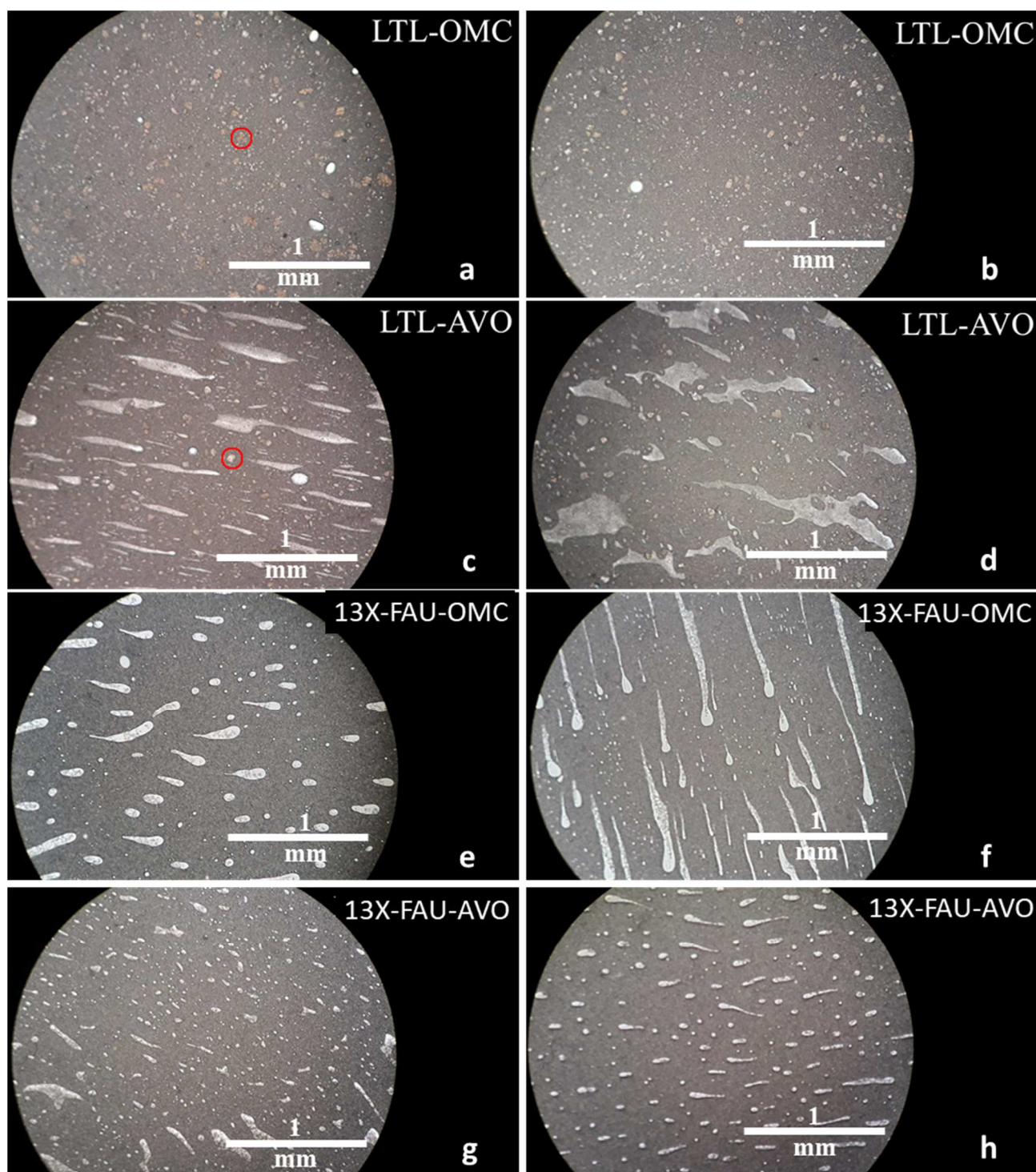


Figure 5-20. Optical microscope images of formulations containing thickeners, with ZEOfilters. (a,b) LTL/OMC; (c,d) LTL/AVO; (e,f) 13X-FAU/OMC; (g,h) 13X-FAU/AVO. For each sample, the image was taken immediately (a, c, e, g) and 4 days (b, d, f, h) after preparation. Red circles in figures (a) and (c) highlight aggregates of LTL ZEOfilters.

After the addition of thickeners, the emulsion appears more homogeneous, and fewer differences are observed after 4 days (**Figure 5-18a,b**). This is true also in the presence of bare UVfs (**Figure 5-18c**). Also, the addition of thickeners to formulations containing zeolites improves their homogeneity making them more similar to the formulation without zeolites (**Figure 5-19**). Moreover, the formulation is stable after 4 days

(**Figure 5-19b,d**). The light and dark structural features observable in most of the images are due to a different abundance of oil and water phases, and their shape, generally elongated, is an artifact of thin-film preparation.

These quick formulation tests were mainly performed to investigate the feasibility and short-term stability of a formulation with 20% of zeolite powder. Indeed, 20% is close to the amount of ZEOfilter (thus roughly of zeolite) required for a complete cutoff of UV radiation in simple vaseline-ZEOfilter mixtures (see section 5.2.2). From an optical analysis of formulations, it is clear that thickeners play a major role in stabilizing zeolite particles inside the formulations. This is probably due to the improved rheology of the formulation.

After the effective integration of bare zeolites inside this simple formulation, LTL-based and 13X-FAU-based ZEOfilters were formulated in the same way, as a proof of concept. **Figure 5-20** displays the obtained formulations, which also appear stable up to at least 4 days. Formulations containing LTL ZEOfilters display small ZEOfilter aggregates up to 0.1 mm (e.g. **Figure 5-20a,c**) which, however, do not affect the product stability.

The prepared formulations were not expected to be stable on a long-term timescale, due to the absence of preservatives. A more refined formulation was subsequently prepared, as it will be shown in the following.

5.3.2 Optimized formulation

The preparation of cosmetic formulations containing ZEOfilters was repeated employing a more complete composition and more refined physical parameters. Particularly, formulations were prepared with LTL/OMC, LTL/AVO, and both ZEOfilters together, prepared after LTL particle size optimization ($D_{90} < 15 \mu\text{m}$). Similarly, formulations were also prepared with bare OMC, AVO, or a mixture of both. All details of the prepared formulations were provided in section 4.5.3.

Figure 5-21 shows that the optimized formulations display a more homogeneous biphasic structure compared to preliminary formulations, with small droplets of oil dispersed in the water phase. As it is possible to observe, the structure of the formulation is highly stable up to at least 3 months after the preparation. Moreover, no precipitation of the zeolites was observed.

Rheological studies (**Figure 5-22**) conducted on the optimized formulation showed that all those present a pseudoplastic behavior without thixotropy (see **Box 5-1**). Pseudoplastic behavior is a desirable characteristic for sunscreen formulation since promotes the formation of a homogeneous film on the skin, ensuring adequate sun protection.

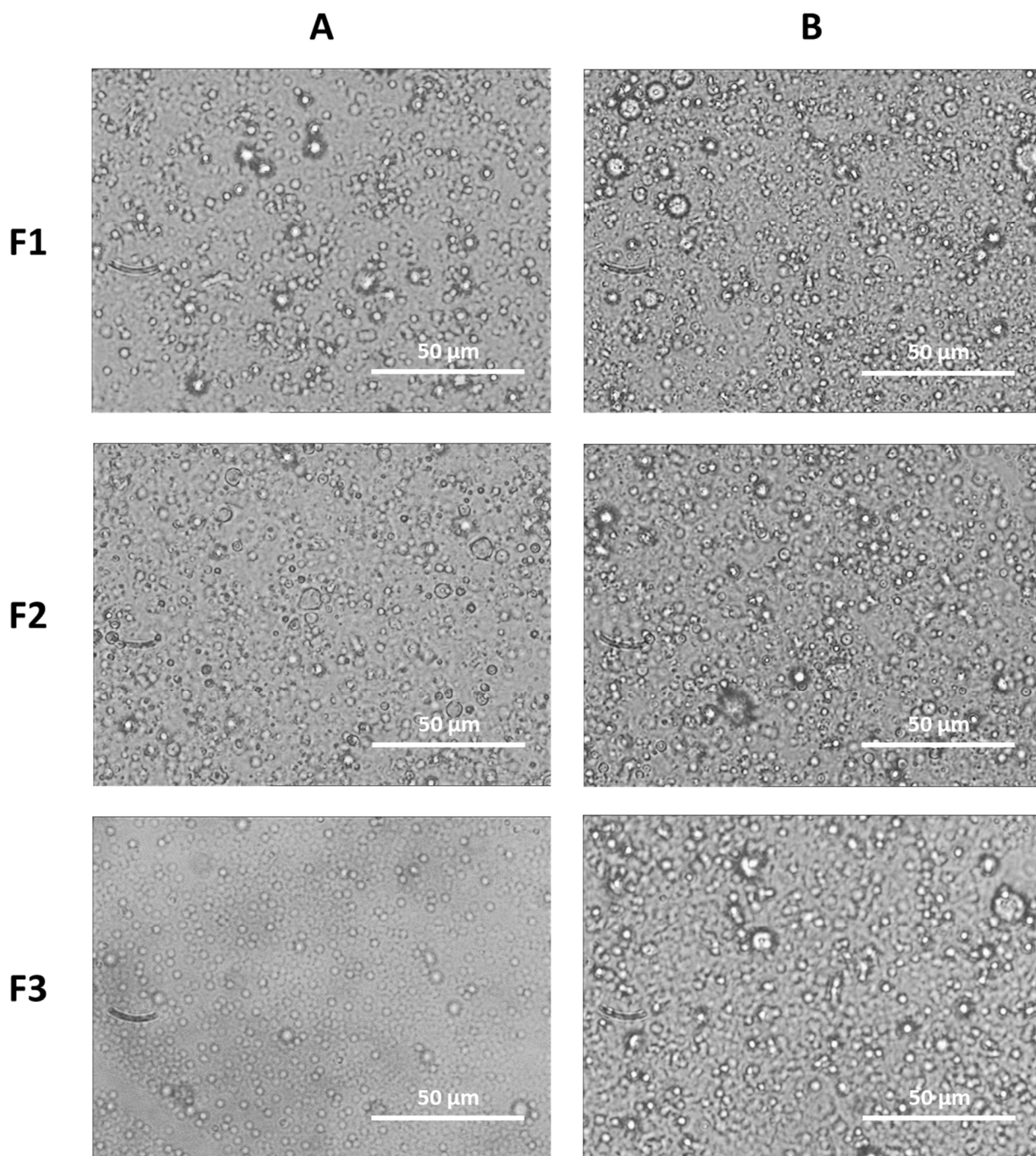


Figure 5-21 Optical microscopy images (magnification 630×) of O/W formulations F1, F2, F3, containing 2% LTL/OMC (F1), 2% LTL/AVO (F2), and 2% of each ZEOfilter, respectively (F3) (see **Table 4-4**). Images were taken immediately (column A) and 3 months (column B) after preparation.

Results and discussion

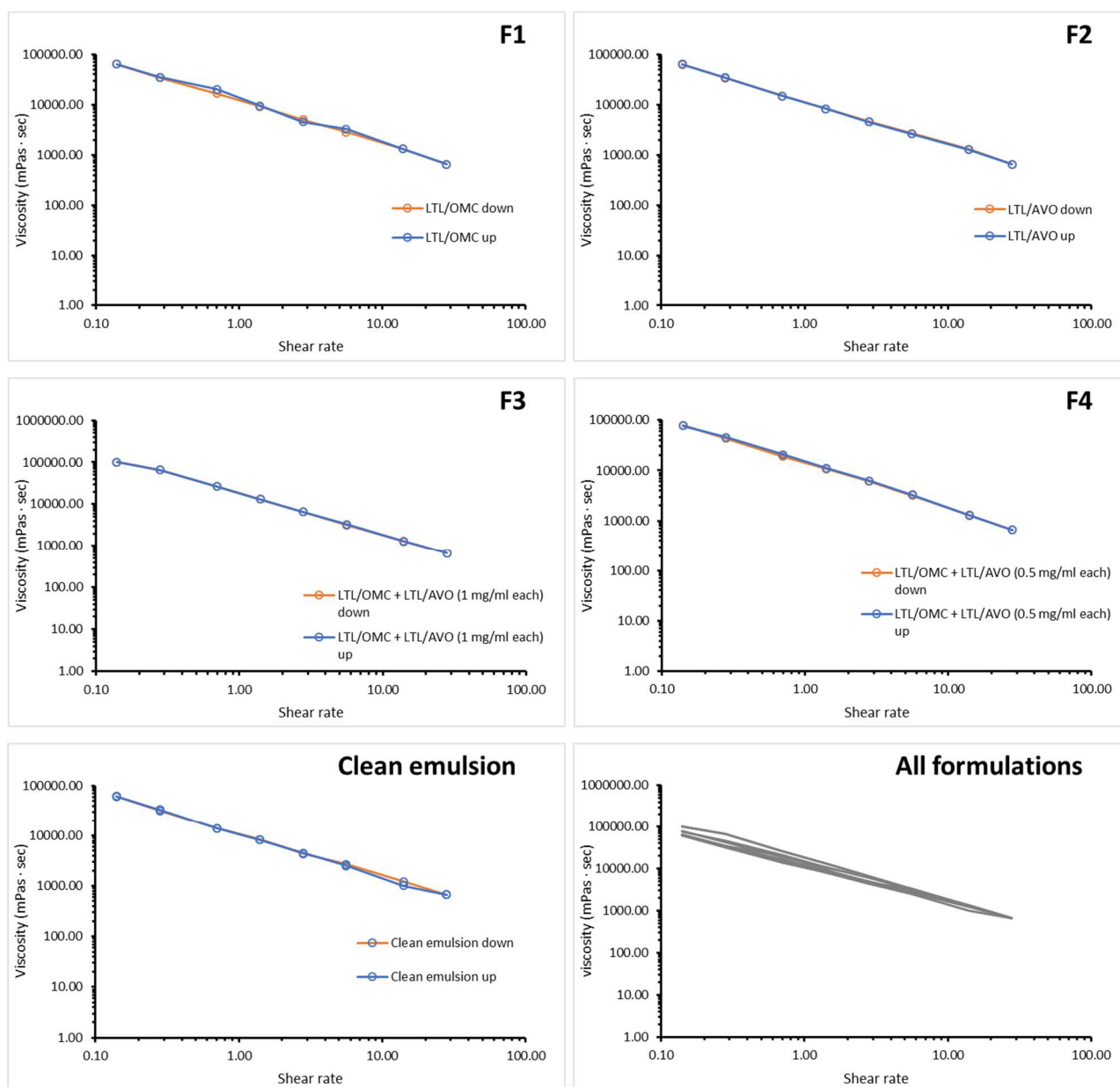


Figure 5-22. Viscosity curves at increasing (up) and decreasing (down) shear rate for ZEOfilter formulations F1, F2, F3, F4 (see **Table 4-4**). Data for the emulsion without ZEOfilters is also shown (Clean emulsion). The bottom-right panel shows all data in the same chart.

As it was stated in the experimental section, the pH of the optimized formulations was measured being an important parameter in determining the skin-sensitizing effects of cosmetic formulations. The observed values are reported in **Table 5-3**.

The observed values, attesting acidic pH for all formulations, are well acceptable values for cosmetic products. Indeed, the skin is acidic, and cosmetics generally display pH values between 4 and 6 to preserve the integrity and activity of the skin (226).

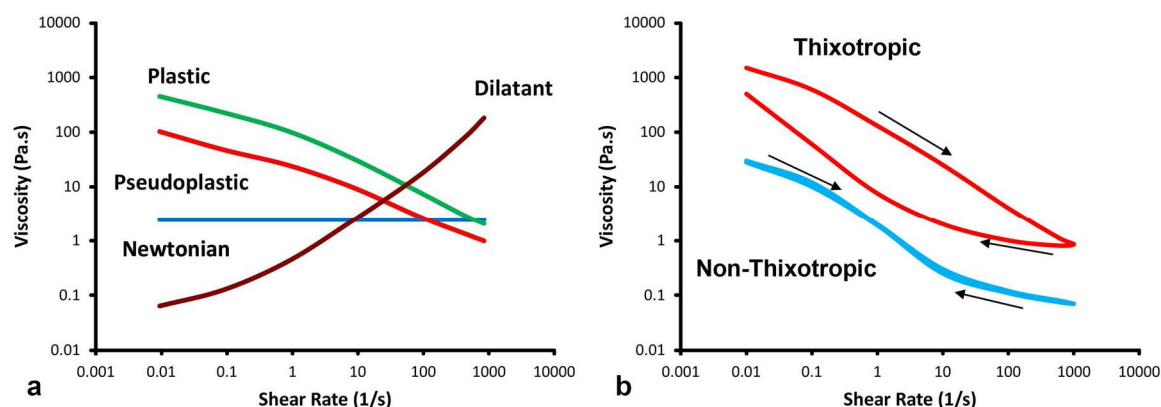
Box 5-1. Rheological behavior of cosmetics.

Figure 5-23. Viscosity trends upon shear rate variations. a) classification of fluids based on viscosity trends. b) Thixotropic and non-thixotropic fluids.

Classification of rheological behavior of fluids, and particularly of cosmetic formulations. **Figure 5-23a:** in Newtonian fluids, viscosity is constant while changing the shear rate. On the contrary, pseudoplastic and dilatant fluids are characterized by shear thinning and thickening with increasing shear rate, respectively. Plastic fluids are similar to pseudoplastic ones, but they behave as solids at rest. **Figure 5-23b:** by considering the behavior of viscosity while increasing and subsequently decreasing shear rate, the fluid is thixotropic if the viscosity displays hysteresis and slowly recovers to the original value, otherwise non-thixotropic if the path up and down overlaps. Modified from (227).

Table 5-3. pH values of the optimized emulsions.

Formulation identifier	sample	pH
F1	LTL/OMC (OMC 1 mg/ml)	5.65 ± 0.02
F2	LTL/AVO (AVO 1 mg/ml)	5.65 ± 0.02
F3	LTL/OMC (OMC 1 mg/ml) LTL/AVO (AVO 1 mg/ml)	5.68 ± 0.02
F4	LTL/OMC (OMC 0.5 mg/ml) LTL/AVO (AVO 0.5 mg/ml)	5.66 ± 0.02
F5	AVO 1 mg/ml	5.60 ± 0.02
F6	OMC 1 mg/ml	5.60 ± 0.02
F7	AVO 1 mg/ml OMC 1 mg/ml	5.62 ± 0.02

5.4 *In vitro* permeation studies

Figure 5-24 shows the amount of OMC (a) and AVO (b) reaching the receiving compartment up to 26 hours of Franz Cell permeation tests. Particularly, Y-axis to the left (solid lines) represents data obtained by using pig skin (PS) in the Franz Cell, while Y-axis to the right (dashed line) indicates data obtained using synthetic membranes (SM). For both OMC and AVO, samples that did not release at all up to 26 hours are not displayed.

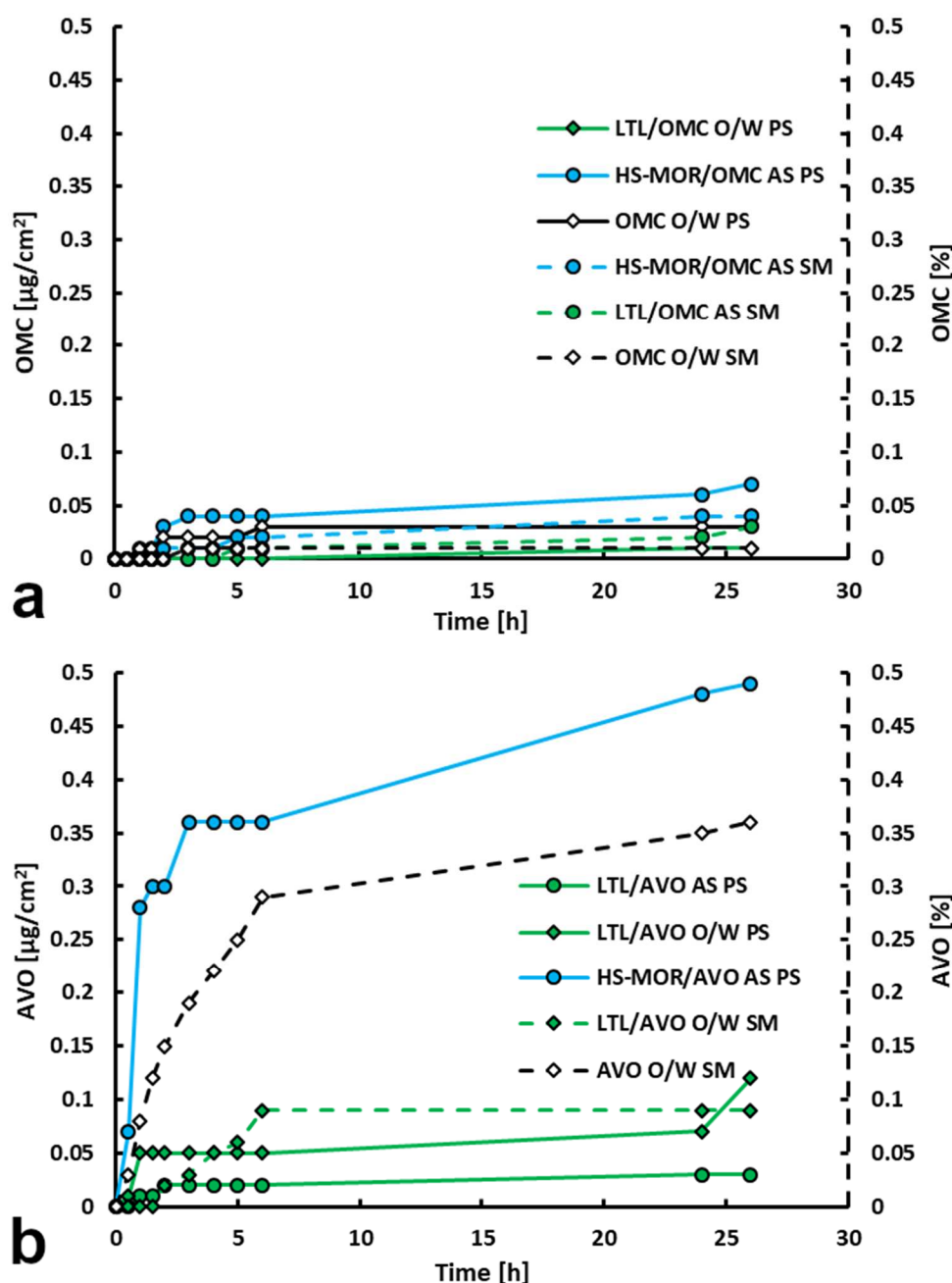


Figure 5-24. Static permeation tests performed with Franz Cell. Curves represent OMC (a) or AVO (b) permeation in the receiving compartment through pig skin (PS) (Y-axis to left, solid lines) or synthetic membranes (SM), (Y-axis to right, dashed lines). Circular markers represent tests performed using aqueous suspensions as donor phases, while diamonds represent O/W emulsions. Black lines are bare OMC and AVO.

The permeation tests performed on ZEOfilters using SM determine the release of the filter molecule from the zeolite. Indeed, zeolite particles (and thus ZEOfilter) can not pass through the SM to the receiving compartment. In the case of zeolites HS-MOR and LTL loaded with AVO, in aqueous suspension (AS), no AVO was detected in the RC up to 26 hours. By repeating the same test on LTL/AVO in an oil-in-water (O/W) emulsion, a negligible release of the filter from the zeolite was observed, reaching after 26 hours 0.09 % of the starting AVO. The same test, performed on an O/W emulsion with bare AVO, showed a still low, but higher, amount of UVf passing to the RC, reaching 0.36 % of the original AVO.

Similar considerations can be done for octinoxate ZEOfilters. The amount of OMC released from HS-MOR and LTL over time in AS is negligible and reaches 0.04 % and 0.03 %, respectively, after 26 h. In the case of LTL/OMC hybrid in O/W emulsion, no OMC passed through the synthetic membrane over time. The unencapsulated OMC, in O/W emulsion, passes through the synthetic membrane barely, reaching 0.01 % after 26 h.

Both results for OMC and AVO indicate that the two molecules are almost not released by zeolites neither in aqueous suspensions nor in O/W emulsion.

Figure 5-24 also displays permeation data obtained using pig skin (PS) membranes. The measurement performed using AS as the donor phase, displayed no AVO in the receiving phase for bare AVO, as well as for 13X-FAU/AVO. On three tests, performed on LTL/AVO ZEOfilters, no penetration of AVO was observed in two of them, and just one test showed a negligible level of $0.03 \mu\text{g}/\text{cm}^2$ after 26 h. In HS-MOR/AVO the penetration through pigskin is higher, and an amount of UVf was detected in the RC reaching $0.49 \mu\text{g}/\text{cm}^2$ after 26 hours. Considering PT performed using O/W emulsion as the donor phase, no AVO penetrated in the RC from an emulsion containing bare AVO, while LTL/AVO led to just $0.12 \mu\text{g}/\text{cm}^2$ after 26 h.

Permeation tests using pig skin membranes were also performed on bare OMC and OMC ZEOfilters. No penetration of the UVf was observed for the bare OMC, HS-FAU/OMC, 13X-FAU/OMC, and LTL/OMC in aqueous suspension. HS-MOR/OMC, in aqueous suspension, led to the permeation of up to $0.07 \mu\text{g}/\text{cm}^2$ after 26 h. Also, bare OMC and LTL/OMC were tested as O/W emulsions. In both cases, a negligible amount of OMC passed in the RC after 26 h, reaching $0.03 \mu\text{g}/\text{cm}^2$ and $0.01 \mu\text{g}/\text{cm}^2$, respectively.

In permeation tests performed using pig skin membranes, the UVf accumulation was also evaluated in each layer of the skin, i.e. stratum corneum (SC), epidermis (E), dermis (D), or epidermis together with dermis (E+D). **Table 5-4** and **Figure 5-25** show the obtained values for each performed test, together with the permeation value obtained with both skin and synthetic membranes. All the observed accumulation values are small. Thanks to the grayscale used in the table, it is easy to note that generally all results are homogeneous and low (total accumulation in the skin about $5 \mu\text{g}/\text{cm}^2$, **Figure 5-25**), with few, slightly higher, exceptions. Moreover, the majority of the filter is retained in the stratum corneum, i.e. the outer layer of the skin, almost all the rest in the epidermis, and almost nothing in the dermis (when E and D separation was performed). In the latter layer, values are so low that can not be represented in **Figure 5-25**.

Concerning OMC, a donor phase constituted by 13X-FAU/OMC dispersed in water displays the highest accumulation of OMC in SC and E+D, accounting for 33.12 ± 0.43 and $20.15 \pm 0.47 \mu\text{g}/\text{cm}^2$, respectively. About one fourth is the accumulation observed for LTL/OMC (7.41 ± 1.04 , 5.02 ± 0.01 , and $0 \mu\text{g}/\text{cm}^2$ for SC, E, and D, respectively), and HS-FAU/OMC (12.61 ± 0.55 , and $2.54 \pm 0.28 \mu\text{g}/\text{cm}^2$ for SC and E+D, respectively), both in AS.

Similarly, AVO highest accumulation was observed for LTL/AVO in AS, while the accumulation is lower for LTL/AVO in O/W emulsion.

By taking into account also the permeation data at 26 h (**Figure 5-25**), it is possible to observe several scenarios:

- i) samples displaying UVf accumulation, even at a high level, in the skin but without UVf permeation in the RC;

- ii) samples with a medium accumulation of UVf in the skin and displaying UVf permeation in the RC only by using PS membranes;
- iii) samples with a medium accumulation of UVf in the skin and displaying UVf permeation in the RC only by using SM;
- iv) samples with a medium accumulation of UVf in the skin and displaying a comparable UVf permeation in the RC by using PS membranes and SM.

The first category includes samples such as the aqueous suspensions of 13X-FAU/OMC, HS-FAU/OMC, LTL/OMC, LTL/AVO, and 13X-FAU/AVO. In all these cases the UVf does not reach the RC and is trapped either as a ZEOfilter particle or as a released molecule in the SC or E. The second category is constituted by samples such as O/W emulsions of LTL/OMC or aqueous suspensions of LTL/AVO and HS-MOR/AVO. These samples indicate that the permeated UVf is probably still encapsulated inside the zeolite, and thus ZEOfilter particles penetrate through the skin without releasing the UVf. Bare AVO O/W emulsions constitute the third group, showing a high affinity for the SC and E of the skin, where it is retained, thus permeating in the RC only by using SM as separation. A similar consideration may be done for sample LTL/OMC in aqueous suspension, even if in this case the permeated UVf is negligible even with SM (0.03%).

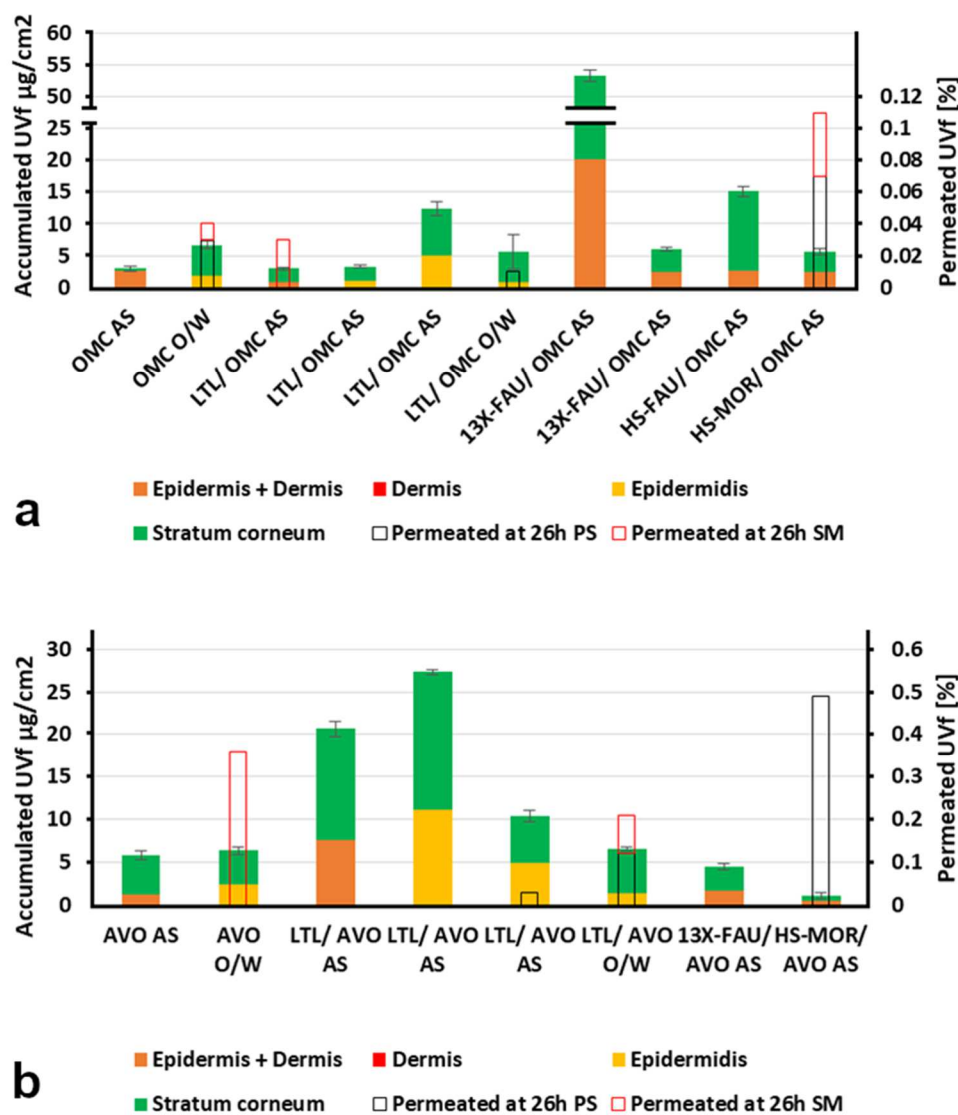


Figure 5-25. Franz Cell permeation tests. Y-axis to left: accumulation data of UVfs in pigskin membranes; values below 0.5 µg/cm² are not appreciable; error bars are the sum of all the errors of single layer measurements. Y-axis to right: the permeation data obtained using pig skin and synthetic membranes.

Moreover, for this latter sample, the small amount of permeated UVf is certainly released by the zeolite, thus behaving as bare UVf. Finally, the fourth category comprises aqueous suspensions of HS-MOR/OMC, and O/W emulsions of bare OMC and LTL/AVO. In the case of bare OMC, the O/W emulsion seems to favor the permeation of the UVf in the receiving phase compared to the AS. Moreover, the value of permeation obtained by PS is slightly higher compared to that from SM, and thus the PS may play an active role in favoring the intake inside the RC. In the case of ZEOfilters HS-MOR/OMC in AS, and LTL/AVO in O/W emulsion, the similar permeation results obtained using PS and SM indicate that the small amount of permeated UVf is probably released by the zeolite either in the DC or in skin layers, but no ZEOfilter particles permeate through the skin.

Permeation and accumulation data obtained by Franz Cell on ZEOfilters are quite similar to those available in literature for bare filters, e.g., (228). However, in the literature, UVfs were detected in many biological fluids of human subjects after topical application of sunscreen formulations containing bare UVfs. Moreover, literature values of UVf skin permeation are generally above 0.5-1% of the applied UVf, with strong differences related to the experimental setup, the donor and receiving medium, and the applied UVf dose (229-231).

Skin permeation results of ZEOfilters may be finally further improved by tuning the particle size of zeolites, which was just marginally investigated during this thesis.

Table 5-4. Accumulation data of UVfs in pigskin membranes. UVf values are associated with a grayscale, darker for higher values. The right column reports permeation data obtained by both pigskin (PS) and synthetic membranes (SM).

→Permeation direction →						
Donor Compartment		Skin			Receiving Compartment	
Sample	Donor phase	Stratum corneum UVf ($\mu\text{g}/\text{cm}^2$)	Epidermis UVf ($\mu\text{g}/\text{cm}^2$)	Dermis UVf ($\mu\text{g}/\text{cm}^2$)	Permeated at 26h PS ($\mu\text{g}/\text{cm}^2$)	Permeated at 26h SM %
OMC	AS	0.30 $\pm$ 0.09	2.62 $\pm$ 0.30		-	-
	O/W	4.81 $\pm$ 0.42	1.86 $\pm$ 0.24	-	0.03	0.01
AVO	AS	4.63 $\pm$ 0.23	1.20 $\pm$ 0.25		-	-
	O/W	3.89 $\pm$ 0.43	2.46 $\pm$ 0.02	-	-	0.36
LTL/ OMC	AS	2.11 $\pm$ 0.15	0.85 $\pm$ 0.06		-	0.03
		2.34 $\pm$ 0.10	0.91 $\pm$ 0.09	0.02 $\pm$ 0.01	-	-
		7.41 $\pm$ 1.04	5.02 $\pm$ 0.01	-	-	-
	O/W	4.80 $\pm$ 2.61	0.85 $\pm$ 0.06	-	0.01	-
LTL/ AVO	AS	13.06 $\pm$ 0.54	7.62 $\pm$ 0.30		-	-
		16.26 $\pm$ 0.10	11.02 $\pm$ 0.19	0.06 $\pm$ 0.01	-	-
		5.44 $\pm$ 0.55	4.98 $\pm$ 0.12	-	0.03	-
	O/W	5.06 $\pm$ 0.16	1.46 $\pm$ 0.07	-	0.12	0.09
13X-FAU/ OMC	AS	33.12 $\pm$ 0.43	20.15 $\pm$ 0.47		-	-
		3.68 $\pm$ 0.21	2.32 $\pm$ 0.16		-	-
13X-FAU/ AVO	AS	2.71 $\pm$ 0.14	1.74 $\pm$ 0.22		-	-
HS-FAU/ OMC	AS	12.61 $\pm$ 0.55	2.54 $\pm$ 0.28		-	-
HS-MOR/ AVO	AS	0.61 $\pm$ 0.21	0.45 $\pm$ 0.14		0.49	-
HS-MOR/ OMC	AS	3.19 $\pm$ 0.32	2.44 $\pm$ 0.22		0.07	0.04

5.5 Leaching tests into seawater

UVfs are an emerging class of contaminants and have been detected in many natural matrices (see section 3.3). One of the objectives of ZEOfilters preparation is to trap permanently UVfs inside zeolites, preventing their release into the environment. Thus, leaching tests into simulated seawater were performed on ZEOfilters, as fully described in section 4.5.5. In a first test, the released UVfs in water were measured by UV-Vis spectroscopy after solvent extraction in ethyl acetate, while in a second test they were quantified by HPLC directly on seawater.

The measurements performed in the first test showed limited release, less than 4 % and 1 % of OMC and AVO originally present in each ZEOfilter (**Table 5-2**), respectively, after about 6 days of testing. The release graphs are shown in **Figure 5-26a** (OMC) and **Figure 5-26b** (AVO). It can be noted that OMC ZEOfilters show a rapid initial release which may be due to the removal of some residual molecules outside the zeolitic grains, while later the release is slower.

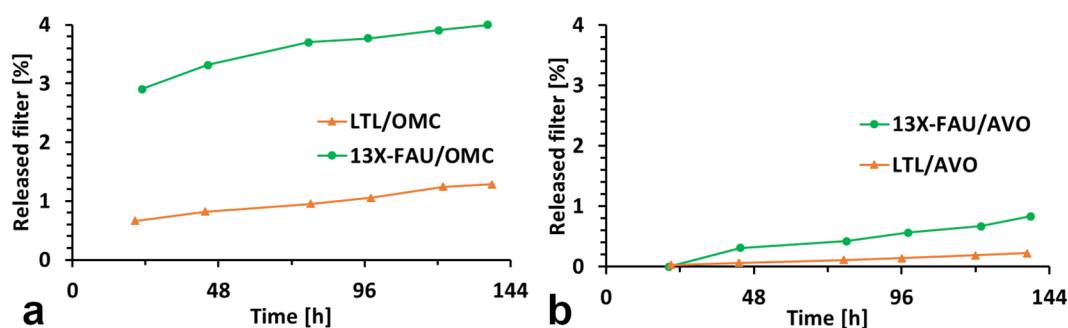


Figure 5-26. Leaching tests of LTL and 13X-FAU ZEOfilters in simulated seawater (first test). Measurements were performed by solvent extraction of water samples in ethyl acetate and UV-Vis spectroscopy.

The second test was performed on the LTL ZEOfilters in two replicates (**Figure 5-27**). In this case, HPLC measurements displayed a lower release percentage for OMC (0.013% at 166 hours vs about 1% in the first test), and a higher 0.42 % for AVO compared to the previous test (about 0.2%).

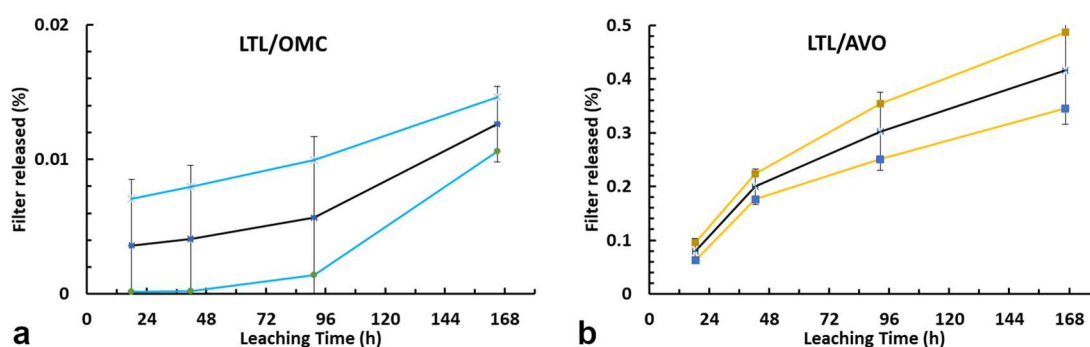


Figure 5-27. Leaching tests of LTL/OMC (a) and LTL/AVO (b) in simulated seawater (second test). Measurements were performed by HPLC directly on water samples. Colored lines are experimental curves while black lines display the average of the two curves with “sample standard deviation” (i.e. standard deviation amplified for too few replicates).

Despite slightly different results shown from the two tests for LTL ZEOfilters, all systems demonstrated very low leaching in salty water. Based on these data it is not possible to hypothesize if this trend would be constant with increasing exposure time or would finally settle on a plateau. Therefore, it is not possible to make a concluding hypothesis regarding the leaching of UVfs from ZEOfilters. Nevertheless, this very low leaching rate, together with the possible reduction of UVf content in sunscreens (see section 5.2.2), possibly make LTL and 13X-FAU ZEOfilters more ecofriendly compared to bare UVfs. Moreover, ZEOfilters may reduce *a priori* the amount of UVfs in the environment by favoring their removal from wastewaters (to capture a micrometric particle is much easier than trapping bare UVfs). In this way, only ZEOfilters entering the water cycle directly from aquatic recreational activities would remain (see section 3.3).

5.6 Structural characterization of ZEOfilters

5.6.1 ZEOfilters FT-IR data

Preliminary FT-IR measurements were performed on bare OMC and HS-MOR/OMC ZEOfilter, mainly to investigate the strong color observed (see section 5.2.2), and to understand the occurrence of molecule photoisomerization under UV exposure. **Figure 5-28** shows the infrared spectra of bare OMC (a) compared to the HS-MOR/OMC ZEOfilter (b). It is noticeable that the interaction with the zeolite causes changes in the structure of the OMC. Indeed, the most characteristic signal responsible for the stretching of the carbonyl group $\nu(\text{C}=\text{O})$ at 1710 cm^{-1} is dampened in the ZEOfilter as well as the signal attributed to the $\nu(\text{C}=\text{C})$ at 1635 cm^{-1} . On the other hand, the signals attributed to the aromatic skeleton at 1604 , 1575 , 1512 , and 1422 cm^{-1} stand out in the ZEOfilter spectrum having a higher relative intensity, compared to the OMC one. A less important modification occurs for the group of signals with a maximum at 1465 cm^{-1} that contain the deformation of CH_2 (δCH_2).

This behavior can be compatible with the protonation of the α,β -unsaturated ester system due to the high amount of acid sites present in the zeolite (**Appendix I**, (189)). This protonation can explain the absorption bands in the visible light range, but a deeper IR investigation of this particular system would be necessary to confirm this hypothesis.

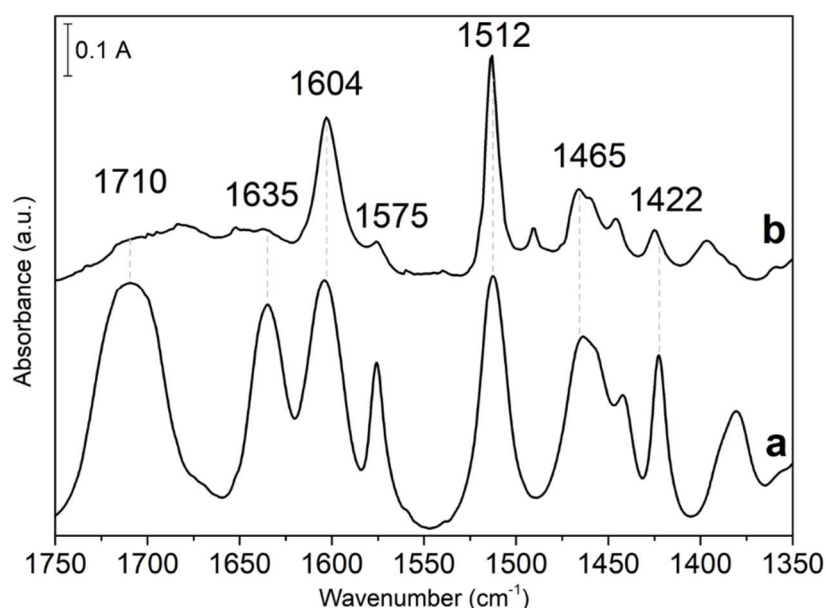


Figure 5-28. FT-IR spectra of OMC (a) and HS-MOR/OMC subtracted for the HS-MOR spectrum (b).

FT-IR results of bare OMC and HS-MOR/OMC before and during UV exposure are shown in **Figure 5-29**. It can be observed that the two spectra of the bare OMC before and during UV exposure (a) are different. The lowering in intensity of signals related to OMC unsaturated carbon skeleton (i.e. double bonds of the aromatic group or conjugated double bond) (black arrows in the figure) indicates the isomerization of OMC during UV exposure. The broadening of the 1710 cm^{-1} signal of OMC is a consequence of O_2 interaction (present in air) during the experiment. The HS-MOR/OMC spectra, subtracted for HS-MOR contribution, show minimal differences in the OMC-related signals before and during UV exposure. The encapsulation of OMC in HS-MOR may thus inhibit the photoisomerization process. This may be explained by the above-mentioned UVf-zeolite interaction and the steric confinement conferred by the zeolite channels, which also make FT-IR spectra of bare OMC and HS-MOR/OMC quite different.

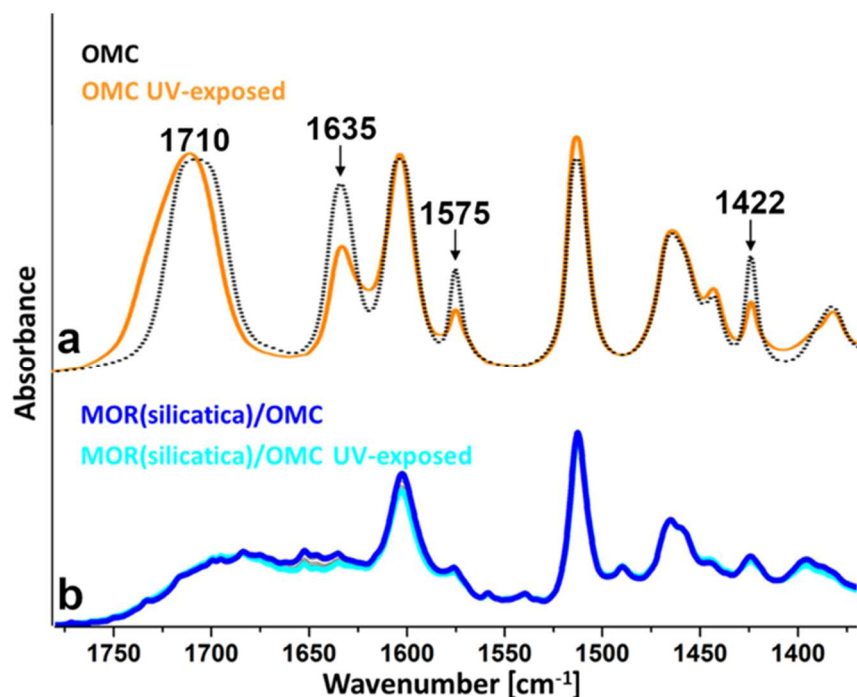


Figure 5-29. Spectra of OMC (a) and HS-MOR/OMC (b) before and after 180 minutes of *in situ* UV exposure of the sample. The exposure was still ongoing during spectra acquisition. Black arrows indicate signals of the unsaturated carbon skeleton of OMC molecule. HS-MOR/OMC spectra are subtracted for zeolite contribution.

However, the spectral features observed in the UV-Vis region for HS-MOR/OMC, and other colored hybrids (see section 5.2.2) make those systems less interesting, in the first instance, for application in sunscreens. Thus, a subsequent FT-IR investigation focused on the more promising LTL/OMC hybrid.

Figure 5-30 shows the FT-IR spectra of pure LTL zeolite (part A) and unoptimized LTL/OMC (i.e. loaded with OMC excess, part B) at increasing outgassing time at room temperature. Concerning pristine LTL, most of the signals are related to H_2O molecules and their interactions. Prolonged outgassing in these conditions leads to the almost complete disappearance of the main spectroscopic features. In particular, a marked decrease is observed of the H_2O bending mode at 1635 cm^{-1} and, in parallel, of the broad adsorption in the $3700\text{--}3000\text{ cm}^{-1}$ range, assigned to the $\nu(\text{O-H})$ mode of hydrogen-bonded H_2O molecules. Conversely, in the unoptimized LTL/OMC sample (**Figure 5-30B**), most of the signals are related to OMC molecules. The outgassing for 60 minutes at room temperature removes only a fraction of the OMC molecules, as testified by the intense signals still present in the $1700\text{--}1250$ and $3000\text{--}2800\text{ cm}^{-1}$ spectral regions, the latter due to $\nu(\text{C-H})$ vibrations.

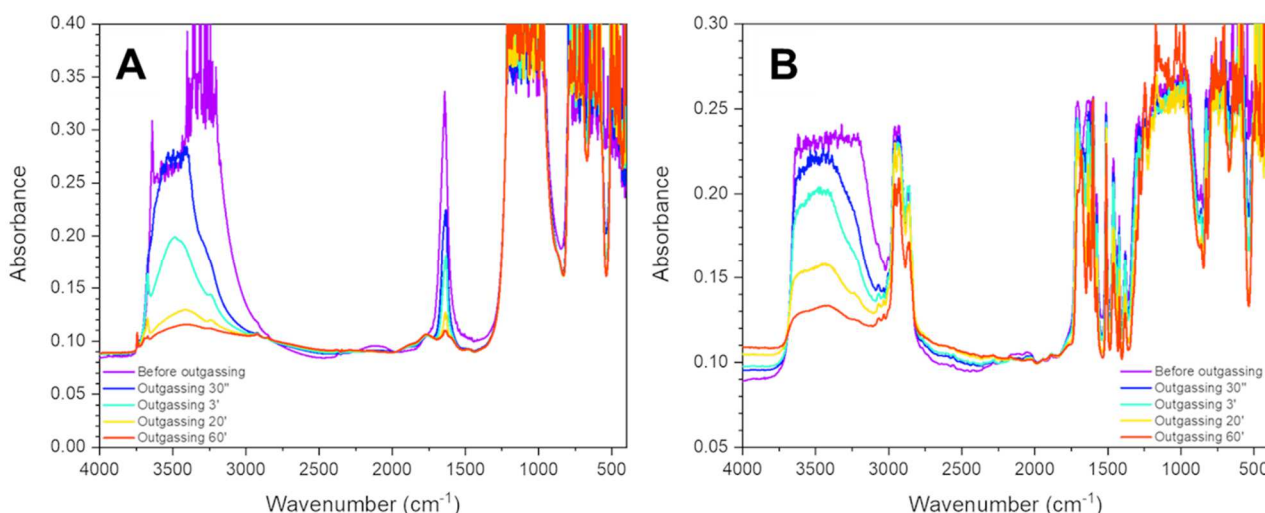


Figure 5-30. FT-IR spectra of pure LTL zeolite (A) and unoptimized LTL/OMC (B) at increasing outgassing time, at room temperature.

Closer inspection of the IR fingerprint region (**Figure 5-31** and **Figure 5-32B**) of unoptimized LTL/OMC, shows a decrease of all bands, except for a specific (OMC-related) component at 1680 cm^{-1} . This signal is initially superimposed with the main absorption at 1708 cm^{-1} (another OMC-related signal) and progressively emerges during the outgassing. Heating at increasing temperatures (**Figure 5-31**), after 60 minutes of outgassing, leads to the complete disappearance of the band at 1708 cm^{-1} and, then, to the almost total disappearance of OMC-related signal at $400\text{ }^{\circ}\text{C}$, indicating the desorption of OMC in agreement with the thermogravimetric results.

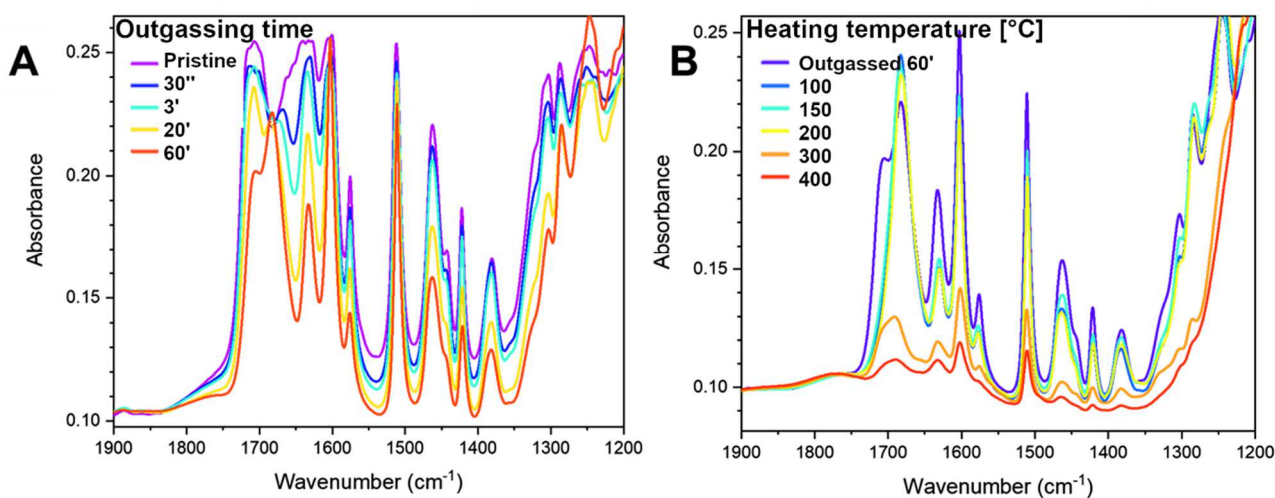


Figure 5-31. FT-IR spectra of unoptimized LTL/OMC: (A) increasing outgassing time at room temperature up to 60 minutes and (B) after 60 minutes outgassing, increasing temperature up to $400\text{ }^{\circ}\text{C}$. Each temperature was kept for 30 minutes.

To achieve deeper insights into the origin of the two IR signals at 1708 and 1680 cm^{-1} , we acquired the spectra of the bare OMC diluted in CCl_4 – an almost IR transparent solvent – at increasing concentrations. As visible in **Figure 5-32A**, the $\nu(\text{C}=\text{O})$ mode of the isolated molecule appears at 1710 cm^{-1} . Therefore, we can conclude that the band observed at 1708 cm^{-1} , in LTL/OMC, is due to free carbonyl groups, while the peak at 1680 cm^{-1} is associated with perturbed carbonyls, likely interacting with the K^+ cations present in the zeolite channels. The behavior is different compared to OMC in HS-MOR, where protonation of the α,β -unsaturated

ester occurs inducing the disappearance of the $\nu(\text{C}=\text{C})$ signal, present at 1635 cm^{-1} in the isolated molecule (compare **Figure 5-28** and **Figure 5-32A**). In LTL/OMC, the UVf structure seems to be perturbed, as suggested by the shift of the $\nu(\text{C}=\text{O})$ to 1680 cm^{-1} , but preserved since the $\nu(\text{C}=\text{C})$ at 1635 cm^{-1} mode is still clearly visible.

Finally, **Figure 5-32B** shows a comparison of the three differently loaded LTL/OMC ZEOfilters, after prolonged outgassing at room temperature. As expected, the most intense spectrum is recorded for the unoptimized LTL/OMC (dark blue curve), followed by the sample loaded with an *ad hoc* filter amount (violet curve) and, finally, by optimized LTL/OMC washed (light blue curve). Moreover, the unoptimized LTL/OMC is the only sample still showing the $\nu(\text{C}=\text{O})$ band at 1708 cm^{-1} , suggesting that, even after 60 minutes of outgassing at room temperature, some OMC molecules remain with free carbonyls, not interacting inside the zeolite channels.

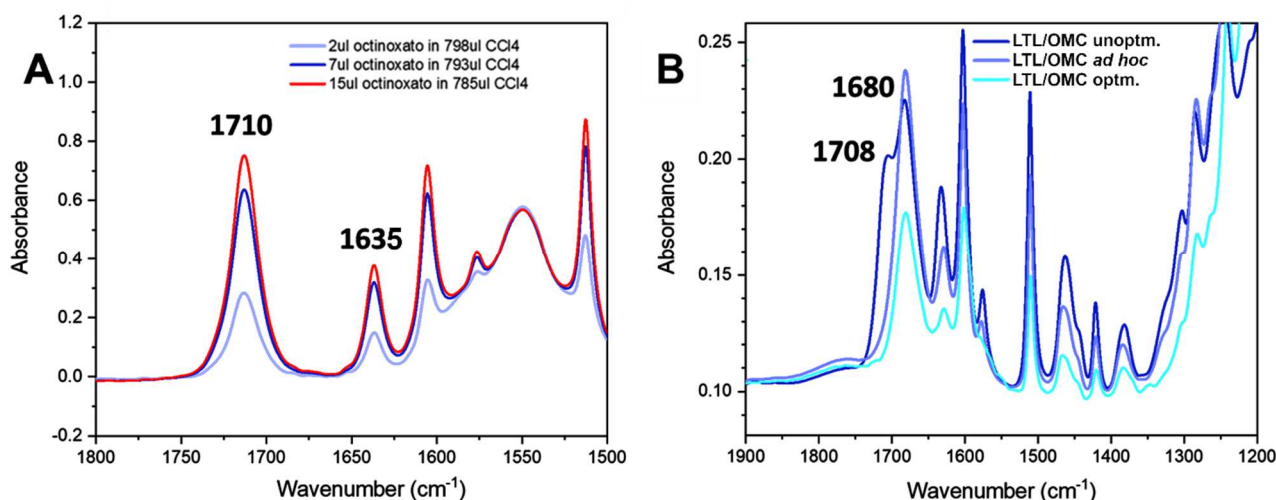


Figure 5-32. (A) FT-IR spectra of pure OMC in CCl₄ at increasing concentrations. (B) Comparison of the FT-IR spectra, acquired after 60 minutes under outgassing at room temperature, of unoptimized LTL/OMC (dark blue curve), optimized LTL/OMC (light blue), and LTL/OMC loaded with an *ad hoc* filter amount (violet curve).

The stronger signals of OMC in the *ad hoc* loaded LTL/OMC, compared to the optimized one, may indicate that a good encapsulation may be obtained without starting the ZEOfilter synthesis with UVf excess. Probably, the presence of a great excess of UVf, during loading, can hinder the diffusivity of the molecules in the channels due to the presence of a large number of molecules accumulated between zeolite grains, thus preventing the entry of molecules into the pores. Accordingly, in the future, the washing step of the preparation process may be reduced, but maintained to prevent the retention of unencapsulated UVfs.

5.6.2 Structural refinement of LTL/OMC ZEOfilter

Two different XRPD experiments were performed on ZEOfilters at ELETTRA (Trieste, Italy) and ESRF (Grenoble, France) synchrotrons. The adopted experimental conditions are reported in section 4.4.2.

The main scope of the first experiment was to confirm the eventual encapsulation of UVfs inside the zeolite frameworks. Different batches of LTL/OMC ZEOfilter, with variable, and generally high, C% from elemental analysis (EA), were collected to observe: i) possible variations of unit cell parameters; ii) possible differences in extraframework content (i.e. intensity of the low angle peaks). Neither appreciable variation of unit cell parameters was observed with changing C%, nor even any superstructure peak. Similarly, no evident intensity differences were detected among different batches of LTL/OMC. Conversely, a marked difference in

the intensity was observed after *in situ* dehydration at 120 °C of pristine LTL and LTL/OMC ZEOfilter. Particularly, the first reflection (2.5° 2θ with a wavelength of $0.70000 \text{ \AA}$) of the dehydrated LTL/OMC is intense about half that of dehydrated LTL (**Figure 5-33**), indicating a higher extraframework content in the ZEOfilter.

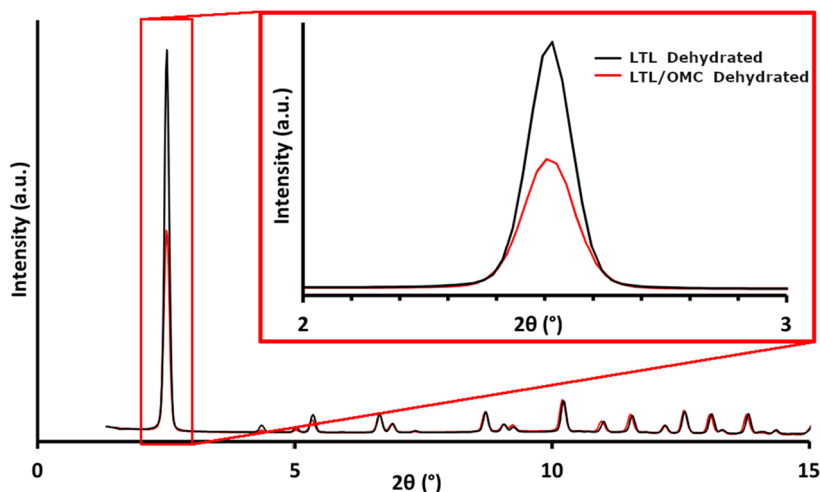


Figure 5-33. XRPD patterns of the dehydrated LTL zeolite and dehydrated LTL/OMC ZEOfilter.

The absence of differences between diffracted intensities of ZEOfilters with different C% indicates that the higher C% (and thus UVf) does not affect the diffraction phenomena, thus the exceeding UVf is outside the zeolite. On the other hand, the lower intensity of the first peak in the dehydrated LTL/OMC, compared to the dehydrated LTL, indicates that some extraframework species i.e. OMC are present in the ZEOfilter. Thus the effectiveness of UVf encapsulation was confirmed.

In the following, the results of the LTL/OMC structural refinement – of XRPD data collected during the second experiment – are reported. The main aim was to find the position assumed by OMC molecules in zeolite channels and the host-guest interactions possibly explaining the observed stable encapsulation of the UVf. Details of the structural refinement were provided in section 4.4.2. The starting model of LTL was taken from (208) excluding H_2O molecules. The original space group (s.g.) is $P6/mmm$. The diffraction data (**Figure 5-34**) used in the refinement were collected at -193°C and did not reveal superstructure reflections as could have been expected because of the relation between the periodicity of the zeolite (c unit cell parameter $7.52 \text{ \AA}$, direction of the main 10MR channel) and the length of the OMC molecule (up to about $18.5 \text{ \AA}$).

The comparison between the observed and calculated intensities showed a poor fit (**Figure 5-34**) resulting in a high R_w of 22.25 %. This misfit is generally related to a lack of electron density in the model or changes in the sample symmetry.

Leaving aside symmetry changes for a while, the misfit indicates a lack of electron density in the zeolite channels of the model. In fact, in the LTL/OMC ZEOfilter, no H_2O molecules are expected (the sample was dehydrated *in situ* before data collection), and channels are occupied, besides K ions, by OMC molecules with higher electron density compared to H_2O . Further analyses were hence performed to determine the organic location and its interactions with the zeolite.

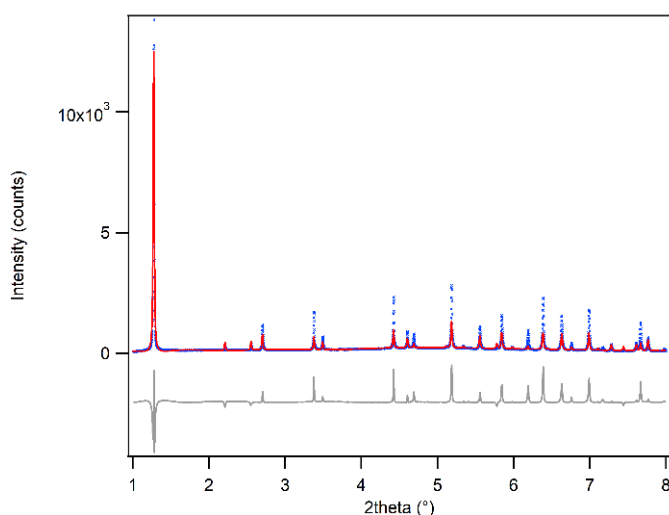


Figure 5-34. Observed XRPD pattern of LTL/OMC (blue markers) and calculated pattern (red line) of LTL model (excluding H₂O molecules), in the *P6/mmm* space group. The observed-calculated difference curve is in grey.

The structural refinement was firstly performed in the original space group of LTL, *P6/mmm*, inserting the OMC as a rigid body. **Table 5-5** reports and compares the unit cell parameters of the ZEOfilter and that of the pristine LTL. Both *a* and *c* parameters show a slight contraction, this can be due to the presence of the molecule and its interaction with the framework (the same effect was already observed for small molecules (232, 233)).

OMC is located in the 12MR channel running along *c*, occupying two unit cells in this direction. The refined occupancy factors and site symmetry lead to 0.7 OMC molecules p.u.c. occupying statistically (due to hexagonal symmetry) the whole available space in the channel (**Figure 5-35a**).

Table 5-5. Unit cell parameters of pristine LTL, and LTL/OMC ZEOfilter modeled with different space groups.

	L zeolite <i>P6/mmm</i>	LTL/OMC ZEOfilter		
		<i>P6/mmm</i>	<i>Cmmm</i>	<i>C2/m</i>
<i>a</i> (Å)	18.37294(5)	18.3673(1)	31.8104(8)	31.8123(7)
<i>b</i> (Å)			18.3690(4)	18.3677(4)
<i>c</i> (Å)	7.52458(3)	7.5126(6)	7.5127(5)	7.51287(6)
β (°)				90.057(2)
γ (°)	120	120		

The refined position of OMC indicates a non-bonding distance between framework oxygen atoms and UVf carbon atoms (~2.8 Å). A possible interaction distance is observed between the extraframework K cation and the oxygen of OMC carbonyl group (~2.84 Å). Despite the quite good R_{wp} value (9.04 %), some misfits remained between observed and calculated intensities. Particularly, the (200) reflection displayed a null intensity in the calculated pattern (**Figure 5-36a**), suggesting a symmetry lowering.

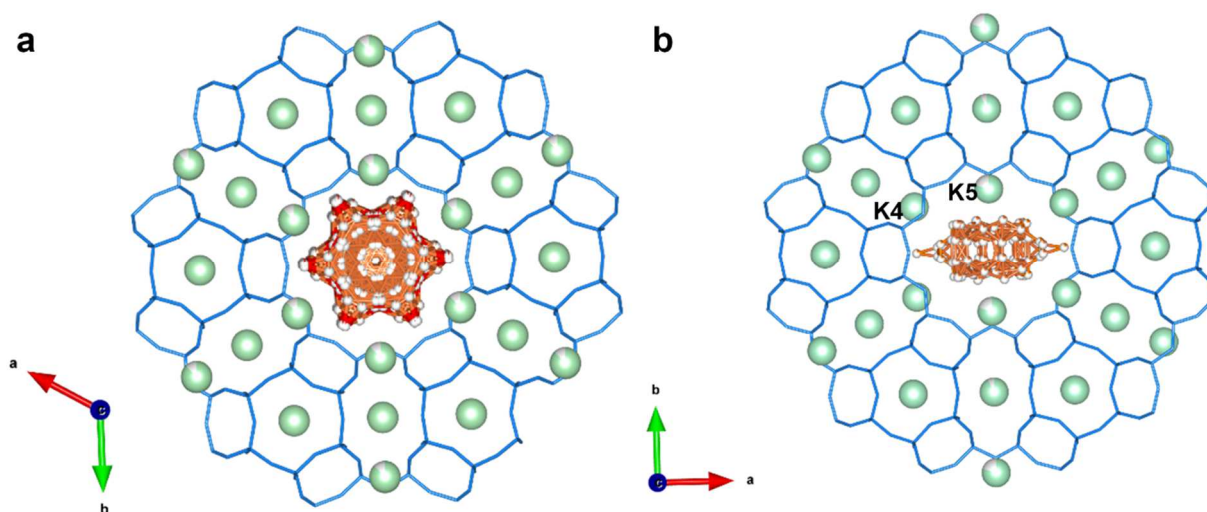


Figure 5-35. Structure of LTL/OMC in the $P6/mmm$ (a) and $C2/m$ space groups (b), respectively. Potassium (green), carbon (orange), and oxygen atoms of OMC (red).

An attempt with $P6$ space group did not improve the calculated intensity on the (200) reflection. Thus, the 6 fold axis was removed passing to the orthorhombic subgroup with highest symmetry, $Cmmm$. Refinement performed in $Cmmm$ ($a=31.8104(8)$, $b=18.3690(4)$, $c=7.5127(5)$) leads a R_{wp} of $\sim 7\%$ and better fit of the peak (400) (*i.e.* the (200) reflection in the $P6/mmm$) (**Figure 5-36b**). It has to be noted that the new unit cell in $Cmmm$ has a volume double that in $P6/mmm$. By lowering symmetry, the number of refined variables (N_{var}) increases, but tests performed on the pristine LTL indicated no significant effects on the improvement of the R_{wp} value compared to $P6/mmm$. However, the number of OMC molecules found p.u.c. is 1.6, *i.e.* higher than the one obtained by the thermogravimetric analysis (*i.e.* 1 p.u.c. considering the doubling of the unit cell, see section 5.2.1). The high occupancy factors and large isotropic thermal parameter of OMC atoms (about $9 \text{ \AA}^2$) indicate a certain disorder degree – both static and dynamic – of OMC in the 12MR channel.

To better fit the peak intensity of the (400) reflection, the symmetry was further reduced to the monoclinic $C2/m$ space group. The obtained refinement R_{wp} is even $\sim 7\%$ (**Table 5-6**), however, the refined model displays a better fitting of (400) reflection (**Figure 5-36c,d**), a lower content of OMC (1.4 molecules p.u.c.), and lower isotropic thermal parameters ($1.8 \text{ \AA}^2$). Moreover, the multiplicity of OMC atom sites decreases from 24 to 16 and 8 passing from the $P6/mmm$, $Cmmm$, and $C2/m$ space group, respectively, and in the $C2/m$ model the molecule is no more distributed in the whole main channel (**Figure 5-35b**).

Table 5-6. Refinement details for LTL/OMC at -193°C modeled in $C2/m$.

T (K)	100
Space Group	$C2/m$
a (Å)	31.8123(7)
b (Å)	18.3677(4)
c (Å)	7.51287(6)
β (°)	90.057(2)
Rp (%)	5.31
R _{wp} (%)	7.74
R _{exp} (%)	2.97
No. of variables	163
No. of hkl	7726

It must be stressed that it is very challenging to find the correct symmetry in a so complex system. However, thanks to the above-made considerations, the $C2/m$ model was selected as the best description of the LTL/OMC ZEOfilter, especially thanks to the higher reliability, and physical and chemical significance of the results.

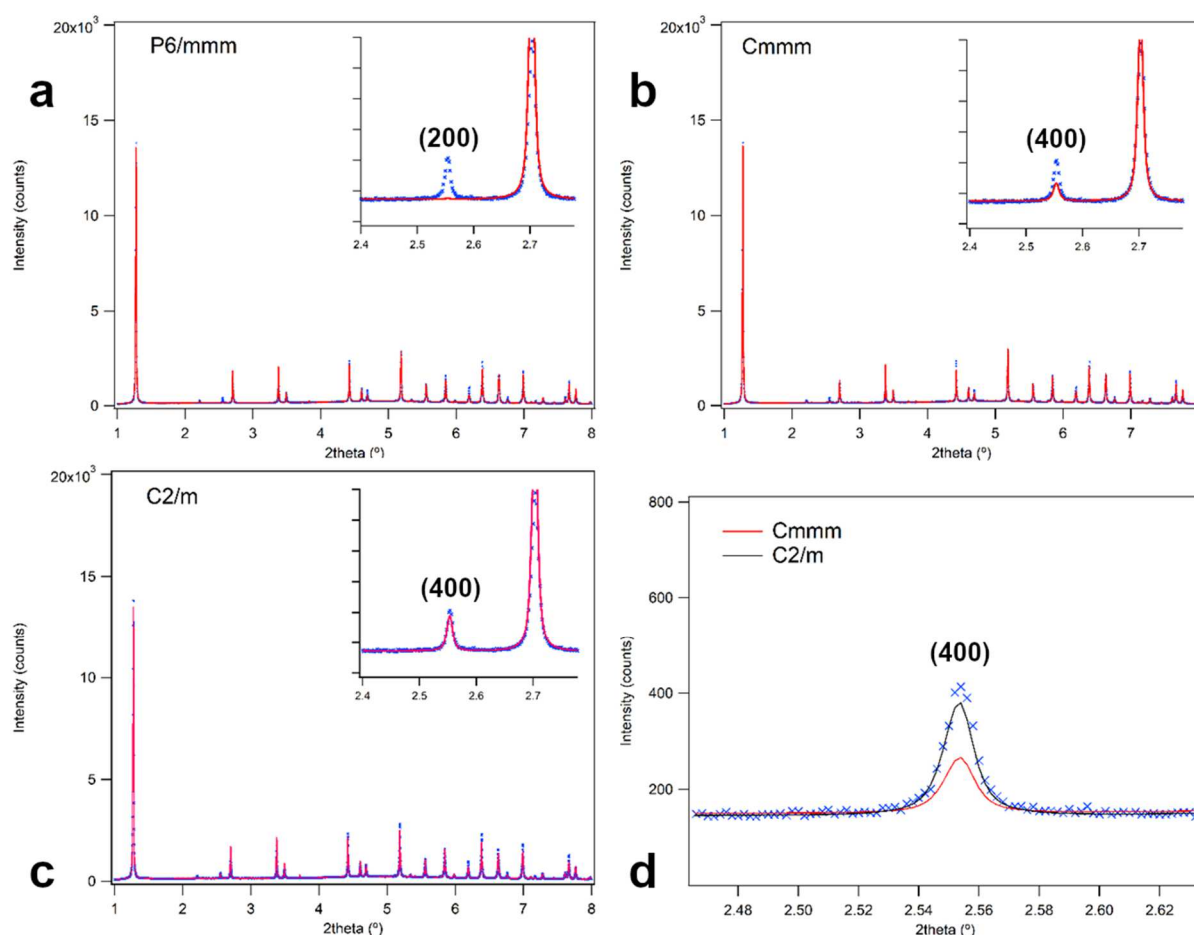


Figure 5-36. Observed (blue markers) and calculated (red line) diffraction patterns from Rietveld refinement of LTL/OMC in the $P6/mmm$ (a), $Cmmm$ (b), and $C2/m$ space groups. d) Zoom on the (400) reflection (observed: blue markers; calculated ($Cmmm$): red line; calculated ($C2/m$): black line).

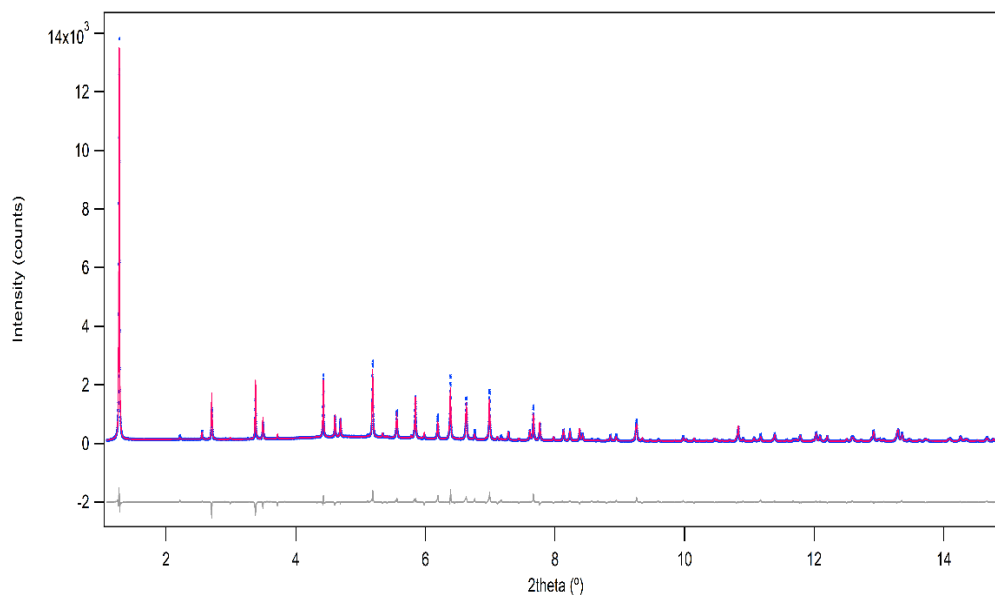


Figure 5-37. LTL/OMC diffraction patterns of the final Rietveld refinement in $C2/m$ space group (observed: blue markers; calculated: red line; difference curve: grey line).

The final data fitting in the $C2/m$ s.g. is shown in **Figure 5-36c** and **Figure 5-37**. The refinement details (fractional coordinates, occupancy factors, thermal parameters, and atomic distances) are reported in **Table 5-5**, **-7**, and **-8**, respectively, with **Figure 5-38** showing the OMC atoms labeling. Cell parameters are $a=31.8123(7)$ Å, $b=18.3677(4)$ Å, $c=7.51287(6)$ Å, $\beta = 90.057(2)^\circ$, with only slight monoclinic distortion.

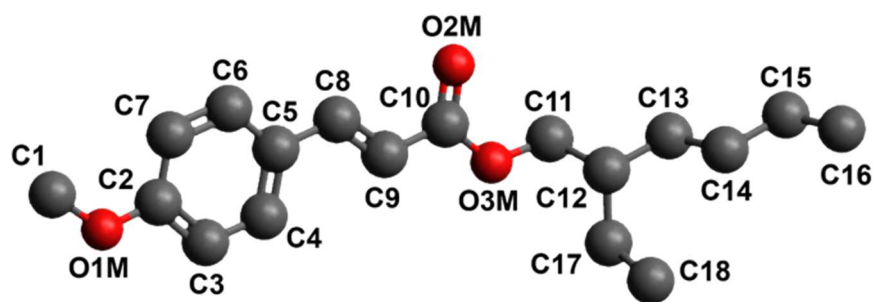


Figure 5-38. Octinoxate molecule and labels used in the following tables. Hydrogens are omitted.

Results and discussion

Table 5-7. Fractional coordinates, occupancy factors, and isotropic thermal parameters for LTL/OMC refined in *C2/m* s.g.

	x	y	z	occ.	B (Å ²)		x	y	z	occ.	B (Å ²)
Si1	0.1318(5)	0.7764(9)	0.500(6)	1	0.67(2)	C1	-0.0585(16)	-0.092(3)	-0.040(2)	0.1801(7)	1.8(7)
Si2	0.5456(5)	0.8091(9)	0.500(6)	1	0.67(2)	O1M	-0.0729(16)	-0.090(3)	-0.232(2)	0.1801(7)	1.8(7)
Si3	0.3220(5)	0.4135(7)	0.500(6)	1	0.67(2)	C2	-0.0345(17)	-0.083(3)	-0.348(2)	0.1801(7)	1.8(7)
Si4	0.1659(12)	0.670(3)	0.214(5)	1	0.67(2)	C7	0.0096(16)	-0.079(3)	-0.264(3)	0.1801(7)	1.8(7)
Si5	0.8341(12)	0.330(3)	0.214(5)	1	0.67(2)	C6	0.0483(17)	-0.065(4)	-0.382(4)	0.1801(7)	1.8(7)
Si6	0.5818(11)	0.916(3)	0.217(5)	1	0.67(2)	C5	0.0430(18)	-0.056(4)	-0.585(4)	0.1801(7)	1.8(7)
Si7	0.4182(11)	0.084(3)	0.217(5)	1	0.67(2)	C4	-0.0011(18)	-0.060(4)	-0.669(3)	0.1801(7)	1.8(7)
Si8	0.2506(12)	0.416(3)	0.216(5)	1	0.67(2)	C3	-0.0399(18)	-0.074(3)	-0.551(2)	0.1801(7)	1.8(7)
Si9	0.7495(12)	0.584(3)	0.216(5)	1	0.67(2)	C8	0.0809(19)	-0.038(5)	-0.704(4)	0.1801(7)	1.8(7)
O1	0.1347(7)	0.8640(18)	0.500(7)	1	0.76(5)	C9	0.075(2)	-0.035(5)	-0.894(4)	0.1801(7)	1.8(7)
O2	0.5	0.7681(14)	0.5	1	0.76(5)	C10	0.111(2)	-0.012(6)	-1.018(5)	0.1801(7)	1.8(7)
O3	0.0833(11)	0.7522(14)	0.500(10)	1	0.76(5)	O3M	0.107(2)	-0.027(6)	-1.215(5)	0.1801(7)	1.8(7)
O4	0.3345(12)	0.5	0.5	1	0.76(5)	C11	0.072(2)	-0.079(6)	-1.258(4)	0.1801(7)	1.8(7)
O5	0.1305(17)	0.607(4)	0.261(12)	1	0.76(5)	C12	0.031(2)	-0.040(6)	-1.205(3)	0.1801(7)	1.8(7)
O6	0.8695(18)	0.393(4)	0.261(12)	1	0.76(5)	C17	0.037(3)	0.042(6)	-1.221(5)	0.1801(7)	1.8(7)
O7	0.237(3)	0.5	0.269(13)	1	0.76(5)	C18	-0.005(1)	0.081(6)	-1.18(2)	0.1801(7)	1.8(7)
O8	0.764(3)	0.5	0.269(13)	1	0.76(5)	C13	-0.005(2)	-0.064(6)	-1.326(3)	0.1801(7)	1.8(7)
O9	0.155(2)	0.744(6)	0.323(9)	1	0.76(5)	C14	-0.044(2)	-0.080(6)	-1.21(1)	0.1801(7)	1.8(7)
O10	0.845(2)	0.255(5)	0.323(9)	1	0.76(5)	C15	-0.073(2)	-0.013(6)	-1.20(2)	0.1801(7)	1.8(7)
O11	0.550(2)	0.860(5)	0.321(9)	1	0.76(5)	O2M	0.154(2)	0.008(6)	-0.942(6)	0.1801(7)	1.8(7)
O12	0.450(2)	0.139(5)	0.321(9)	1	0.76(5)	C16	-0.106(2)	-0.023(7)	-1.06(2)	0.1801(7)	1.8(7)
O13	0.294(2)	0.395(6)	0.322(9)	1	0.76(5)						
O14	0.706(2)	0.605(6)	0.321(9)	1	0.76(5)						
O15	0.2128(19)	0.359(5)	0.273(7)	1	0.76(5)						
O16	0.787(2)	0.641(5)	0.272(7)	1	0.76(5)						
O17	0.073(3)	0.5	0.28526	1	0.76(5)						
O18	0.927(3)	0.5	0.28576	1	0.76(5)						
O19	0.1653(9)	0.6866(14)	-0.000(12)	1	0.76(5)						
O20	0.5735(9)	0.9109(13)	-0.000(11)	1	0.76(5)						
O21	0.2586(9)	0.4116(14)	-0.000(12)	1	0.76(5)						
K1	0.1639(5)	0.5	0.499(8)	0.932(5)	0.43(5)						
K2	0.25	0.75	0.5	0.883(9)	0.43(5)						
K3	0.5	0	0.5	0.74(2)	0.43(5)						
K4	0.1534(2)	0.8418(5)	0.001(3)	0.874(5)	0.43(5)						
K5	0.5	0.7218(7)	0	0.568(7)	0.43(5)						

Table 5-8. Bond distances < 3.2 Å for LTL/OMC in *C2/m* s.g.

Framework-Framework											
Si1-	O1	1.61(4)	Si2-	O3	1.64(4)	Si3-	O4	1.64(2)	Si4-	O15	1.65(8)
	O3	1.61(3)		O2	1.64(2)		O1	1.65(3)		O19	1.64(9)
	O9	1.63(8)		O11	1.65(9)		O14	1.65(8)		O9	1.63(9)
	O10	1.63(8)		O12	1.65(8)		O13	1.64(8)		O5	1.65(8)
Si5-	O16	1.65(8)	Si6-	O5	1.64(7)	Si7-	O6	1.64(7)	Si8-	O7	1.65(6)
	O19	1.64(9)		O17	1.65(5)		O18	1.65(5)		O21	1.64(9)
	O10	1.64(9)		O20	1.65(9)		O20	1.67(9)		O13	1.65(8)
	O6	1.65(8)		O11	1.64(9)		O12	1.64(9)		O15	1.65(9)
Si9-	O8	1.65(6)									
	O21	1.64(9)									
	O14	1.65(8)									
	O16	1.64(9)									
Framework-Extraframework											
O1-	O1M	2.94(4)	O1-	C6	3.17(6)	O6-	K1	2.86(3)	O10-	K4	3.02(4)
	C8	2.92(7)	O4-	O3M x2	2.88(4)	O7-	K1	2.86(2)	O13-	K4	3.10(5)
	O3M	3.05(9)		C14 x2	3.17(6)	O8-	K1	2.89(8)	O14-	K4	3.08(8)
	C11	2.90(6)	O5-	K1	2.86(6)	O9-	K4	3.00(2)	O15-	K2	2.89(6)
O16-	K2	2.89(8)	O21-	K4	3.08(7)						
O17-	K3	2.84(8)									
O18-	K3	2.3(8)									
O19-	K4	2.88(9)									
Extraframework-Extraframework											
K4-	O2M	2.8(1)									
	C16	2.96(9)									
	C10	3.00(9)									
	O2M	3.09(1)									
	O10x	3.11(9)									
K5-	C1 x2	3.04(5)									

OMC molecules are sited along the main channel, occupying two adjacent unit cells in this direction. From the occupancy factor 1.4 molecules p.u.c. are calculated (half in each of the two channels of the C centered cell). As already mentioned (**Figure 5-35**), in the *P6/mmm* model OMC is statistically spread over the whole channel, while in *C2/m* the molecule position appears distributed preferably along the *a* direction.

In the hexagonal space group, the two diameters of the main channel are 10.69 Å and 9.83 Å (perpendicular to and along the *b* axis, respectively), while in the monoclinic model those are 10.54 Å and 9.86 Å along *a* and *b* axis, respectively. The shortening of the main diameter of the channel along the *a* axis could be caused by the molecule position, which may act by contracting the distance with the framework, even if no direct bonding with the framework was found. Along the *a* direction, the molecule establishes a bond with the potassium K4 (**Figure 5-35b**) through the oxygen O2M (**Figure 5-38**) belonging to the carbonyl group (length equal 2.9(2) Å).

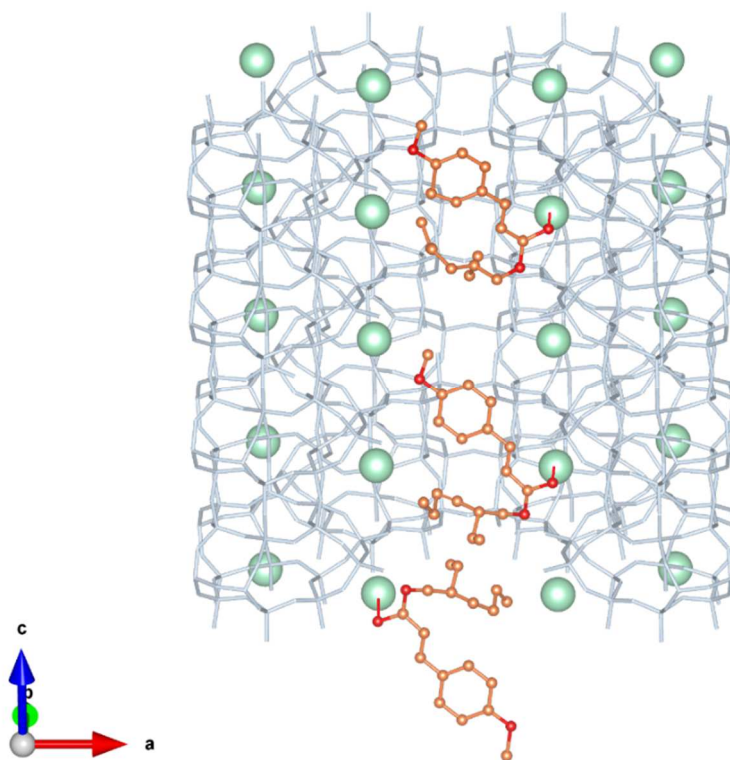


Figure 5-39. Structure of LTL/OMC refined in $C2/m$ s.g., showing 4 cells along the c axis. Only potassium atoms interacting with the filter molecules are drawn in green, while OMC Oxygen and C atoms are shown in red and orange, respectively. The figure shows only one of the symmetrically equivalent positions of OMC molecule in each unit cell.

It is interesting to notice that the presence of the OMC molecule influences also the position of the potassium atoms (K5, **Figure 5-35**) along the shorter diameter (b axis in figure 4) of the main channel. These cations are shifted towards the inner part of the channel, where more space remains available compared to that of the hexagonal model. Apart from the bond previously mentioned, the OMC molecule shows just slight interactions with the framework and potassium atoms keeping distances of at least 2.8 Å (**Table 5-8**).

In **Figure 5-39** the structure of LTL/OMC is shown. In all the models tested, the part of the molecule comprising the benzene ring up to the carbonyl group is almost in the same position. This part is quite rigid compared to the rest of the molecule and is bonded with K4 through O2M which is placed in a site very close to the mirror plane. Thus, we can affirm that this part of the molecule is practically ordered, while the more flexible tail assumes slightly different configurations in the different models.

Interestingly, for all of them, we observe a kind of bending of the tail that shorts the molecule length to about 10 Å (**Figure 5-39**). This can be due to the reciprocal interactions between molecules, indeed, the bending of the tail allows to maintain a distance of ~ 2.6 Å (carbon-carbon) between two molecules in the case of tail-against-tail position (**Figure 5-39**). Despite this can be one of the explanations, we have to keep in mind that the sites belonging to the tail are very close to the ones of the more rigid part. Thus, the refined tail position can be affected by an artifact due to the residual electron density always present around the benzene rings.

Beyond the uncertainties on the tail positioning and disorder, the refinement points out a bonding of the carbonyl oxygen with the LTL potassium atoms, and a certain ordering of the rigid part of the molecule.

6 Conclusions

The encapsulation of UV filters (UVfs) octinoxate (OMC) and avobenzone (AVO) into zeolites with MOR, FAU, MFI, and LTL topologies and different Si/Al ratio (low-silica: Na-MOR, LTL, ZSM5-30, 13X-FAU; high-silica: HS-MOR, ZSM5-398, HS-FAU) was tested and discussed. The obtained hybrid materials are referred to as ZEOfilters, and the project addressed: i) the optimization of their synthesis procedure; ii) the evaluation of their UV filtering performances; iii) the assessment of efficacy and safety of ZEOfilters in simulated field conditions; iv) the investigation of host-guest and guest-guest interactions.

Different tests were performed by varying the synthesis parameters (temperature, UVf/zeolite ratio, solvent). Finally, a four-step loading procedure was optimized: 1) zeolite dehydration to remove H₂O molecules from channels; 2) UVf loading into the zeolite at 100 °C to promote molecule diffusivity; 3) ZEOfilter washing with acetone to remove unencapsulated UVf molecules; 4) ZEOfilter drying at 60 °C for solvent removal. The final UVf content differs varying zeolite topology, Si/Al ratio, and/or UVf. The optimized ZEOfilters, (i.e. without UVf molecule on the external surface of zeolite particles) display a UVf content variable from 13.2 (HS-FAU/OMC) to 1.4% (ZSM5-398/AVO). Particularly, OMC was found to be loaded more evenly in both high- and low-silica zeolites compared to AVO, which is conversely more efficiently trapped in low-silica zeolites compared to their high-silica counterparts (**Table 5-2**).

High silica ZEOfilters generally display a low UV filtering power and are colored possibly due to UVf protonation (see sections 5.2.2 and 5.6.1). Concerning low-silica zeolites, Na-MOR is the sole displaying no UVf loading with both OMC and AVO, while others hold both molecules. ZEOfilters of ZSM5-30 present strong absorption colors like high-silica zeolites, possibly due to the strong acidity of this zeolite. LTL and 13X-FAU are the two more promising zeolites for ZEOfilters production, with LTL slightly overcoming 13X-FAU. Indeed, they both display a high UVf content, an enhanced UV filtering power compared to bare UVfs, and almost complete transparency in the visible range. Thus, most of the tests performed in this thesis focused on these two systems, and especially on LTL.

To investigate the interaction between UVfs and the zeolite scaffold, FT-IR experiments and structural refinements were performed on selected samples. Firstly, the HS-MOR/OMC ZEOfilter was studied by FT-IR to investigate the phenomenon inducing sample coloring. It was found that the molecule, indeed, undergoes protonation, probably by interacting with the zeolite acid sites. Moreover, experiments performed with *in situ* UV exposure highlighted in HS-MOR an inhibition of the trans-cis photoisomerization of OMC. As for host-guest interaction, FT-IR highlighted a perturbation (from 1708 to 1680 cm⁻¹) of the $\nu(\text{C=O})$ mode of the OMC carbonyl group when it is encapsulated into LTL, while no protonation of the molecule was observed. The structural refinement of LTL/OMC XRPD data, found a possible bonding interaction of OMC carbonyl oxygen with an extraframework potassium site, possibly explaining the observed perturbation in FT-IR data. The major role of carbonyl groups in the organic-zeolite interaction has been reported in the literature. Fois et al. (2010) found the same carbonyl-K interaction of the fluorenone dye molecule in the L zeolite, also indicating how this interaction is responsible for the fluorenone resistance against H₂O substitution (153).

The stability of UVfs under solar UV exposure is crucial for the safety and efficacy of sunscreen products. UV exposure tests performed on bare UVfs, and LTL and 13X-FAU ZEOfilters demonstrated high stability of all samples when the compounds were tested independently (Section 5.2.3). In the literature, OMC and AVO are known to degrade under UV exposure in formulations containing both filters, with potentially harmful effects. Unfortunately, exposure tests on mixed ZEOfilters could not be performed during this thesis. It is expected that formulations containing OMC ZEOfilters and AVO ZEOfilters (simultaneously) should display a high UVf stability since OMC-AVO interactions are inhibited by the zeolite scaffolds. OMC was also found to degrade easily if aggregated in thin films (68, 70); also in this case the encapsulation of OMC into the zeolite structure should prevent this kind of interaction, thus enhancing OMC stability.

The assessment of UVfs skin permeation is also important for sunscreen safety. In this thesis, skin permeation tests were performed on bare UVfs, and HS-FAU, HS-MOR, LTL, and 13X-FAU ZEOfilters in aqueous suspensions. All systems displayed a very low permeation through the employed pigskin membrane, with the highest record of 0.49 $\mu\text{g}/\text{cm}^2$ (about 0.2% of the starting amount) for HS-MOR/AVO after 26 hours

Conclusions

of test. LTL ZEOfilters and bare UVfs were more deeply investigated, and tests were performed also dispersing those in oil-in-water (O/W) emulsions. In these conditions, the highest permeation was observed for LTL/AVO, but with a very low value of $0.12 \mu\text{g}/\text{cm}^2$. Accumulation data of UVfs in the different skin layers demonstrated that most of the UVfs accumulate in the stratum corneum, the outermost skin layer, while a generally very low quantity is detected in epidermis. The UVf accumulated in the dermis was found to be almost negligible (up to $0.06 \mu\text{g}/\text{cm}^2$). The amount of UVf accumulating in the deep strata of the skin is of particular concern due to potential adverse effects. Overall, skin permeation tests showed similar results for bare UVfs and ZEOfilters. Since bare OMC and AVO are currently used in cosmetics and are thus compliant with legislation, ZEOfilters should have a good chance of being compliant with safety regulations too, even if further *in vitro* and *in vivo* tests would be required.

In view of future employment, in this thesis, some O/W formulations were prepared with different ZEOfilter content (2 or 20 wt.%). The good rheological properties observed demonstrated the feasibility of their inclusion in cosmetic products (see section 5.3). The use of ZEOfilters in cosmetics should provide several advantages. The encapsulated UVfs should not interact with the skin, and their amount in formulations may be reduced (thanks to the enhanced filtering power) together with that of other compounds, such as stabilizers.

As was mentioned in the introduction, UVfs are emerging as a new class of pollutants, especially in the aquatic environment. In leaching tests here reported, LTL and 13X-FAU ZEOfilters showed very slow but continuous leaching of UVfs, leading, in the worst-case scenario, to a release of 4% OMC from 13X-FAU after 6 days of testing (see section 5.5). In the case of LTL/OMC, the low leaching rate can be attributed to OMC-K interaction, as already mentioned here above for the fluorenone dye (153). The observed leaching trends do not display an evident flattening up to 160 hours, thus in the future new and more protracted leaching tests should be made. Indeed, stable trapping of the UVf inside the zeolite could prevent or at least reduce the adverse effects those have on living organisms. ZEOfilters, by the way, would reduce the amount of UVfs entering the water cycle by reducing their amount escaping from wastewater treatment plants. Indeed, ZEOfilters particles will be more easily trapped compared to the bare UVfs, reducing the burden on the ecosystem.

This thesis is by no means exhaustive of the project, and the development and understanding of these zeolite-based UV filters are still ongoing.

Concerning the ZEOfilter optimization, the zeolite particle size will be optimized to improve its stabilization into formulations and consequently the final filtering efficacy. Moreover, the particle size can be optimized for the exploitation of ZEOfilters in products different from cosmetics, eg. plastics and dyes. UVfs are indeed employed also in packaging, where ZEOfilters should also contribute to the product rheology and performance. Also, the synthesis process will be possibly further optimized in view of a possible future scale-up. The UVf amount will be reduced to a minimum so to reduce the employment of organic solvents. The recovery of UVf from the washing process is also possible, so to reduce waste. Moreover, all the working temperatures (e.g. zeolite dehydration, filter loading, and final drying) will be lowered as much as possible.

Concerning the exploitability of ZEOfilters, many tests deserve to be performed before their use in cosmetics is launched. Particularly, deeper dermatological and toxicological studies must be performed. The stability of ZEOfilters under UV exposure would also be evaluated with *in operando* UV-Vis and FT-IR measurements, possibly verifying the production of reactive oxygen species and other undesired decay products.

Certainly, the development of such a broad project will require the engagement of industrial partners, bringing expertise and sharing ideas, and thus a patent application has already been filed.

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8 Acknowledgment

A research project is not only a matter of science but also, and maybe most, of team-working, ideas- and knowledge-sharing. Thus I want to thank many people that have made their experience, advice, and support available to me.

First of all, I am deeply grateful to my supervisors Prof. Giovana Vezzalini and Prof. Rossella Arletti for leading me patiently and outstandingly through the whole project, especially during thesis writing.

Then, I would like to express my sincere gratitude to Prof. Simona Quartieri and others that helped me and contributed to the project in various ways; in Modena: Dr. Cecilia Baraldi, Dr. Monica Caselli, Prof. Erika Ferrari, and Prof. Alfonso Zambon; in Turin: Dr. Monica Argenziano, Prof. Roberta Cavalli, Prof. Gianmario Martra, and Dr. Lorenzo Mino; in Montpellier: Dr. Sylvie Bégu, Dr. Francesco Di Renzo, and Dr. Julien Haines; finally Prof. Giuseppe Cruciani and Prof. Annalisa Martucci from Ferrara, Dr. Andy Fitch from Grenoble, and Dr. Michael Fischer from Bremen.

I would like to offer my sincere gratitude to Prof. Barbara Onida and Prof. Svetlana Mintova for the careful proofreading of my thesis.

My special thanks to my “zeolite-team” colleagues Dr. Giorgia Confalonieri (especially acknowledged for XRPD data collection and analysis at ID22, ESRF), Dr. Michelangelo Polisi, Dr. Marco Fabbiani, and Francesco Colombo, who shared with me labs, office, and many coffees.

It was fundamental for the good outcome of the project also the work of Monica Malavasi and Daniele Bernardeschi for elemental analyses, Dr. Simona Bigi and Dr. Simona Marchetti Dori for TGA, and laser diffraction particle size analysis. Many thanks also to grad students Flavia, Benedetta, and Giulia for their support in sample preparation, and Chiara, Laura, and Nicolò for IR measurements. ID22 (ESRF) and XRD1 (ELETTRA) beamline staff are acknowledged for the granted beamtime and support.

This work would never be possible without the support of many friends that made unforgettable these (historically) enlivened years. My first thanks to my Ph.D. mates, soon Dr.s Fabrizio Poletti, Laura Maletti, Laura Tomassetti, Léna Verhoest, Eleonora Clò, and to our dear Fabio. Not to forget anyone I won't list names, but I warmly thank each and every one of the other Ph.D. students and post-doc who brightened up every working day. Then my thanks to all other friends outside university, and especially Alle and Chia, Ali and Andre, Guido, Anna, Elos, Fre, and Vane, that are almost part of my family.

Of course, in the end, but above all others, endless gratitude to my family, my parents Denise and Dino, my sister Janette and my dear Giuseppe, that patiently grew me up and to whom I owe what I am. Finally, my all to my darling Giorgia, who since long walks beside me sharing dreams, and soon sharing home.

9 Appendixes

- I) Thermal Behavior of High Silica Mordenite
- II) Boosting Sunscreen Stability: New Hybrid Materials from UV Filters Encapsulation

Appendix I



Thermal behavior of high silica mordenite

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ARTICLE INFO

Keywords:

Mordenite

High temperature

XRPD

Infrared spectroscopy

ABSTRACT

This work studies the thermal stability, heat-induced structural deformations, and dehydration/rehydration dynamics of a synthetic high silica mordenite. It is of special interest because this particular phase has proven to be an ideal host for the encapsulation of several kinds of organic molecules making it a promising scaffold for drug delivery. The dehydration process was followed by thermal analysis, infrared spectroscopy in controlled atmosphere, in situ synchrotron XRPD, and structural refinement. Overall, all the results indicate weak interactions of H₂O molecules with the silicatic mordenite framework and evidence the presence of hydroxyl groups with different condensation responses at high temperature. Infrared characterization highlighted how the desorption of adsorbed H₂O molecules under degassing is already complete at rT. The unit cell parameters exhibit very slow and almost isotropic changes upon heating. Above 550 °C an increase in slope is observed for all parameters. This corresponds to the marked silanol condensation and consequent framework reassessment observed at this temperature by infrared characterization. Overall cell contractions are 0.67%, 1.18%, and 0.81% for a, b, c, respectively and 2.64% for cell volume. HS-MOR undergoes very moderate *T* induced deformations, indicating a very rigid and stable framework.

1. Introduction

Establishing the thermal stability of a zeolite is of particular importance since its properties can change in the dehydrated/calcined state and under operating conditions. Understanding the mechanisms governing heat-induced structural deformations is crucial for many technological applications, e.g. Ref. [1]. Zeolites are exploited in diverse complex applications, ranging from catalysis to drug delivery. Due to their physicochemical stability, uniform porosity, large surface area, and biocompatibility, zeolites are widely employed as drug delivery carriers since they have proven to be ideal hosts for organic molecule encapsulation, including photoactive species [2–5]. The first step in the preparation of zeolite/organic molecule hybrid materials is the dehydration of the zeolite to facilitate the penetration of the desired molecules. Consequently, it is essential to thoroughly investigate how H₂O is released, at what temperature, and how this affects the zeolite framework.

Many studies and reviews report the thermally induced dehydration

and consequent structural deformations of alumino-silicate hydrated phases, see e.g. Refs. [6,7]. In general, it is widely accepted that: a) thermal stability increases with Si/Al ratio as a consequence of the higher energy required to break the Si–O bond compared to the Al–O bond; b) lower dehydration temperatures are observed in zeolites with higher Si/Al ratios since their surfaces become more hydrophobic. On the basis of the collapse temperature obtained by X-ray structural investigations, Cruciani [6] introduced the so-called “stability index” (SI) and demonstrated a clear correlation between SI and the Si/(Si + Al) ratio.

Several data sets are also available on the thermal behavior of pure and high silica phases [8–14]. Since most high silica zeolites are obtained by dealumination, their properties are affected by the presence of connection defects and their investigation assumes particular importance, especially if the SiOH connectivity can be defined. For most of these materials, the silicatic framework undergoes negative thermal expansion (NTE) of variable entity.

This work aims to define thermal stability, heat-induced structural

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<https://doi.org/10.1016/j.micromeso.2019.109882>

Received 7 August 2019; Received in revised form 11 October 2019; Accepted 7 November 2019

Available online 9 November 2019

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deformations, and reversibility of these processes in a high silica mordenite. This phase has proven to be an ideal host for the encapsulation of several kinds of organic molecules (hydrocarbons, ethylene glycol, etc.), e.g. Refs. [15–17], and is a promising scaffold for several other applications in the drug delivery field. For the reasons set out above, understanding framework modifications of high silica mordenite under preloading treatment (i.e. high temperature) is of great importance.

2. Experimental methods

2.1. Material

High silica mordenite (HS-MOR) with an $\text{SiO}_2/\text{Al}_2\text{O}_3$ molar ratio of 220, was purchased (code HSZ-690HOA) in its protonated form from Tosoh Corporation (Japan). This material was previously characterized by our group by different techniques (SEM, surface area, porosimetric analysis, thermogravimetric analysis, and FTIR spectroscopy) [17] and was used in previous work on the adsorption of pollutants from waste water [15,16,18–21]. FTIR spectroscopy revealed the presence of a large quantity of silanol defects produced by the dealumination process. The nominal particle size is 10 μm .

Mordenite (framework type MOR [22]) crystal structure exhibits a 1D channel system characterized by two parallel channels running along the *c* axis, comprising a large 12 MR channel and a strongly elliptical 8 MR channel. These channels are interconnected along the [010] direction through side pockets delimited by double 8 MRs that, in turn, form a sinusoidal channel running parallel to the *b* axis [23].

2.2. Infrared spectroscopy in controlled atmosphere

The infrared measurements were carried out on a PerkinElmer 2000 spectrophotometer equipped with Globar source and MCT detector, operating at a resolution of 2 cm^{-1} and averaging 64 scans for each spectrum collected. The zeolite powder was compressed into a self-supporting pellet and enclosed in a gold-frame, then inserted into a traditional quartz-glass infrared cell where both the thermal treatment and infrared analysis were conducted. The cell was closed and connected to a vacuum line (residual pressure 5.0×10^{-4} mbar). The thermal treatment consisted of heating the material in dynamic vacuum from rT to 800 °C for 30 min. Isotopic exchange was achieved by exposing the outgassed material to D_2O vapor pressure for 5 cycles of 5 min.

The Fit Curve routine of Bruker's OPUS 5.0 software was used to fit the νOH experimental profile.

2.3. Thermogravimetric (TG) analysis

TG analysis of HS-MOR was made using a Seiko SSC/5200 thermal analyzer. About 10 mg of the sample was loaded into a Pt crucible and heated in air from room temperature to 1050 °C, at a heating rate of 10 °C/min, the same heating rate used for in-situ XRPD collections.

2.4. Synchrotron X-ray powder diffraction (XRPD) experiments

The temperature-resolved synchrotron XRPD patterns were collected at ID22 beamline at ESRF (Grenoble) at a fixed wavelength of 0.3544 Å. The wavelength was calibrated with Si NIST standard reference material. The powder sample was loaded and packed into a 0.5 μm quartz capillary. The capillary was mounted on a standard goniometric head and kept spinning during pattern collection. The sample was heated in situ using a hot-air blower from rT to 800 °C at a heating rate of 10 °C/min.

Temperature was calibrated against the thermal expansion of a standard Pt reference material. Diffraction patterns were recorded with a high-resolution multi-analyzer stage composed of nine analyzer crystals in the 2θ range 0–25°. Between 50 and 600 °C the patterns were collected every 50 °C, while above 600 °C every 100 °C. During

temperature decrease, two data collections were performed at 150 °C and room temperature (labeled 150 °C_{rev} and rT_{rev} , respectively).

2.5. Structure refinements

The GSAS package [24] with the EXPGUI interface [25] was used for Rietveld structure refinements. The starting coordinates adopted and site labels are from Ref. [17]. The refinements were tested in both *Cmc* and *Cmc*₂₁ s.g. The *Cmc*₂₁ s.g. refinements were found to be more satisfactory and hence this space group was adopted for all the investigated temperatures (only *Cmc*₂₁ data are here reported).

The Bragg-peak profiles were modeled by a pseudo-Voigt function [26] with a peak intensity cut-off set to 0.001 of the peak maximum. A 24-term Chebyshev polynomial was used to fit the background curve. The overall scale factor, the 2θ -zero shift, and the unit-cell parameters were refined for each histogram over the entire temperature range. Si^{4+} and O^{2-} scattering curves were used for the framework species, and the O^{2-} used again for H_2O molecules. Soft constraints were imposed on the tetrahedral bond lengths T-O (1.63 Å), with a tolerance value of 0.03 Å. Isotropic thermal displacement parameters were constrained to the same value for the same atomic species.

The refinement details at selected temperatures (rT , 300, 800 °C, and rT_{rev}) are summarized in Table 1. The final observed and calculated patterns for the selected refinements are shown in Fig. 2S a,b,c,d of the Supplementary Materials. Tables 1S and 2S respectively report the atomic coordinates and bond distances. Table 2 reports the unit-cell parameters refined for all the investigated temperatures.

3. Results and discussion

3.1. Infrared spectroscopy in controlled atmosphere

Fig. 1 shows the IR spectra of HS-MOR at increasing dehydration/dehydroxylation steps for the ranges in which signals were observed deriving from OH stretching (νOH) of silanols and H_2O molecules (section A), and overtone/combination bands of lattice modes and H_2O ($\delta\text{H}_2\text{O}$) molecule deformation band (section B).

For the material in air (curve a), most of the νOH signal is out of scale (section A), because of the large number of H_2O molecules present in the system. The only observable features are at 3662 cm^{-1} , caused by the stretching of OH moieties without interaction with other H_2O molecules [27], along with a weak component at 3747 cm^{-1} , due to highly hydrophobic isolated silanols unable to adsorb H_2O molecules at the relative humidity of the ambient conditions during the measurement.

At lower frequency (section B), the spectrum of the material in air is dominated by a peak at 1630 cm^{-1} due to the $\delta\text{H}_2\text{O}$ of adsorbed molecules, accompanied by signals at 2000 and 1880 cm^{-1} , resulting from lattice mode combinations, while a partner signal resulting from an overtone of lattice modes expected at ca. 1650 cm^{-1} is obscured by the $\delta\text{H}_2\text{O}$ mode [28]. The disappearance of the $\delta\text{H}_2\text{O}$ band at 1630 cm^{-1}

Table 1
Unit-cell parameters and details of structural refinements at selected temperatures.

T (°C)	rT	300	800	rT_{rev}
Space group	<i>Cmc</i> ₂₁	<i>Cmc</i> ₂₁	<i>Cmc</i> ₂₁	<i>Cmc</i> ₂₁
<i>a</i> (Å)	18.0609(2)	18.0440(2)	17.9394(4)	17.9881(5)
<i>b</i> (Å)	20.2095(2)	20.1824(2)	19.9711(4)	20.0432(5)
<i>c</i> (Å)	7.4546(1)	7.4470(1)	7.3943(2)	7.4111(2)
<i>V</i> (Å ³)	2720.9(1)	2712.0(1)	2649.2(1)	2672.0(2)
<i>R</i> _p (%)	5.70	6.05	5.11	5.07
<i>R</i> _{wp} (%)	7.26	7.69	6.65	6.65
<i>R</i> F ² 2 (%)	7.59	7.21	8.01	6.62
No. of variables	114	91	91	91
No. of observations	11601	10933	7946	7946
No. of reflections	1411	1202	539	559

Table 2

Cell parameters of HS-MOR at all the investigated temperatures.

T (°C)	Space group	a (Å)	b (Å)	c (Å)	V (Å ³)
RT	Cmc2 ₁	18.0609(2)	20.2095(2)	7.4546(1)	2720.9(1)
50	Cmc2 ₁	18.0598(2)	20.2058(2)	7.4542(1)	2720.1(1)
100	Cmc2 ₁	18.0658(2)	20.2115(2)	7.4539(1)	2721.7(1)
150	Cmc2 ₁	18.0609(2)	20.2095(2)	7.4532(1)	2720.4(1)
200	Cmc2 ₁	18.0553(2)	20.2015(2)	7.4518(1)	2718.0(1)
250	Cmc2 ₁	18.0500(2)	20.1919(2)	7.4499(1)	2715.2(1)
300	Cmc2 ₁	18.0440(2)	20.1824(2)	7.4470(1)	2712.0(1)
350	Cmc2 ₁	18.0379(3)	20.1728(2)	7.4438(1)	2708.6(1)
400	Cmc2 ₁	18.0309(2)	20.1612(2)	7.4403(1)	2704.7(1)
450	Cmc2 ₁	18.0227(2)	20.1474(2)	7.4361(1)	2700.1(1)
500	Cmc2 ₁	18.0142(2)	20.1330(2)	7.4319(1)	2695.4(1)
550	Cmc2 ₁	18.0040(3)	20.1138(2)	7.4269(1)	2689.5(1)
600	Cmc2 ₁	17.9924(3)	20.0899(3)	7.4212(1)	2682.5(1)
700	Cmc2 ₁	17.9631(3)	20.0280(3)	7.4071(1)	2664.8(1)
800	Cmc2 ₁	17.9394(4)	19.9711(4)	7.3943(2)	2649.2(1)
150 rev.	Cmc2 ₁	17.9814(5)	20.0333(5)	7.4095(2)	2669.1(2)
RT rev.	Cmc2 ₁	17.9881(5)	20.0432(5)	7.4111(2)	2672.0(2)

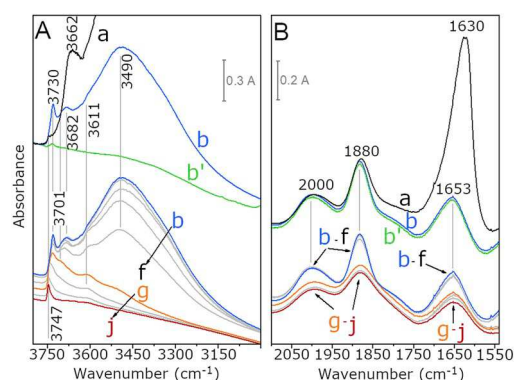


Fig. 1. Infrared spectra in the νOH (A) and overtone/combination lattice modes and $\delta\text{H}_2\text{O}$ (B) regions of: HS-MOR in air (a) and outgassed from rT (b) up to 800 °C (j) in steps of 100 °C. Curve b': HS-MOR after H/D isotopic exchange by contact with D_2O at vapor pressure at rT and subsequent outgassing. The signal of the sample in air (a) is out of scale because of the large amount of H_2O molecules present in the system.

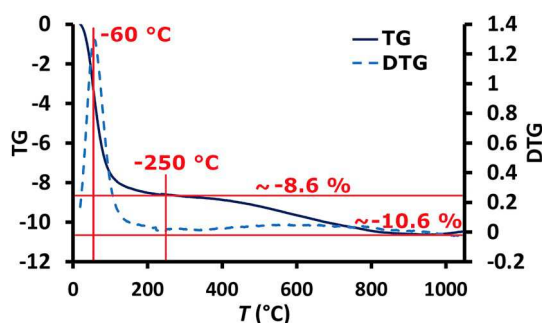


Fig. 2. TG and DTG curves of HS-MOR.

after outgassing under high vacuum at rT for 30 min (curve b), now revealing an overtone at 1653 cm^{-1} , testifies the removal of adsorbed H_2O molecules. The completeness of desorption is proven by the invariance of the spectral profile in the $1700\text{--}1600\text{ cm}^{-1}$ range of the sample after H/D isotopic exchange (curve b') by contact with D_2O at vapor pressure at rT, which should have depleted any $\delta\text{H}_2\text{O}$ component (converted to a lower frequency $\delta\text{D}_2\text{O}$ signal), if still present after outgassing.

Regarding the νOH region (section A), the spectral profile remaining after water desorption (curve b) is due only to hydroxy groups,

overwhelmingly silanols, $\equiv\text{SiOH}$, because of the very high Si/Al ratio. Only traces of hydroxy group patterns are still present in the spectrum of the H/D exchanged sample (curve b') indicating that almost all of them are accessible to H_2O molecules (when dosed at water vapor pressure at rT). For the sample in air, all signals due to hydroxy groups were displaced towards lower frequencies by the interaction with H_2O (except for a small fraction due to highly hydrophobic isolated silanols), and then hidden by the νOH band of H_2O molecules.

In more detail, the outgassed sample pattern is dominated by a broad band with maximum at 3490 cm^{-1} , typical of H-bonded silanols like those in so-called “silanol nests” and expected in highly dealuminated zeolites [29]. An ill-resolved shoulder at 3611 cm^{-1} can be attributed to Brønsted acid $\equiv\text{Si}(\text{OH})\text{--Al}\equiv$ sites [30], while components at 3682, 3701, and 3730 cm^{-1} are due to silanols involved in interactions becoming weaker as the νOH frequency rises [28]. Finally, the presence of isolated silanols, evidenced by the component at 3747 cm^{-1} in curve a, should contribute to the high frequency side of the 3730 cm^{-1} band.

The intensity of the overall νOH pattern decreases as the outgassing temperature is increased up to 800 °C (curve j), leaving a more intense component at 3747 cm^{-1} , indicating some increase in the quantity of isolated silanols (curves b–j). As a whole, this evolution indicates a progressive condensation of hydroxyl groups forming Si–O–Si linkages in the case of silanols.

It is noteworthy that two different regimes can be observed as a function of temperature. The components at 3490 cm^{-1} and 3682 cm^{-1} exhibit the largest decrease in intensity when the outgassing temperature is increased from 400 to 500 °C (curves f, g), while most of the decline in other components occurs at higher temperatures (curves g–j). This behavior is consistent with the strength of the inter-silanol interactions, directly proportional to their distance. Indeed, the shorter the distance (i.e. silanols with νOH 3490 and 3682 cm^{-1}), the easier the condensation between silanols, which therefore occur at lower temperatures.

The thermogravimetric data presented below indicate that the hydroxyl groups might be ca. 6 p.u.c. in the pristine HS-MOR. To establish a relative quantification of the various types of hydroxy groups contributing to the νOH pattern, the experimental profile in the $3800\text{--}3000\text{ cm}^{-1}$ range was fitted. The integrated intensity of the resulting components were recalculated on the basis of the relationship between OH stretching frequency and the relative decadic absorption coefficient proposed by Carteret [31], making it possible to take into account the increase in this coefficient as the strength of the inter-silanol interaction increases [31]. The data analysis results are reported in Fig. 1S, indicating that the silanols responsible for the components at 3490 and 3682 cm^{-1} account for ca. 90% of hydroxy groups. Clearly, condensation of this number of silanols has an impact on the zeolite lattice, as evidenced by the changes in the combination and overtone modes responsible for the bands at 2000, 1880, and 1653 cm^{-1} when the outgassing temperature was increased from 400 to 500 °C (curves f, g in section B of Fig. 1).

3.2. Thermogravimetric analysis

Fig. 2 shows the thermogravimetric analysis results. As highlighted by the DTG curve, weight-loss starts at very low temperatures, with the main weight-loss at about 60 °C. At 250 °C the TG curve indicates a weight-loss of 8.6%. Above this temperature, a continuous slow weight loss leads to a total loss of 10.6%.

The initial weight loss, between rT and 250 °C, can be ascribed to the release of H_2O molecules from the zeolite porosity/surface, and corresponds to $15.1\text{H}_2\text{O}$ p.u.c. The main weight loss in this range is at low temperature and is due to weakly bonded H_2O present in the channels and/or on the zeolite surface, as evidenced by the infrared spectra of the outgassing process at rT. The remaining 1.72%, lost at higher temperatures (400–900 °C), is consistent with IR results and corresponds to the H_2O release resulting from silanol condensation.

3.3. Structure refinements

3.3.1. Structure of HS-MOR at room conditions

The structure refinement of HS-MOR at room conditions indicates the presence of seven partially occupied H₂O sites, corresponding to 10.34H₂O molecules p.u.c. The difference between this value and that resulting from the TG analysis (15.1 molecules) can be ascribed to the presence of disordered and lowly occupied sites not identifiable in the refinement, and/or to the contribution of H₂O molecules physisorbed on the surface. The structure derived from the refinement at rT is reported in Fig. 3 a, b, and in Tables 1S and 2S.

The W2, W3, W5, W6, and W7 sites are mainly 12 MR channels parallel to [001], while W1 and W4 are in the side pocket. All H₂O molecules, with the exception of those in W2, are sited on the mirror

plane perpendicular to the *a* axis (Table 1S and Fig. 3). W1 is near to site D' found in natural mordenite from Pashan ((Na_{3.51}K_{0.14}Ca_{1.89}Mg_{0.09}Sr_{0.01}) [Fe³⁺_{0.03}Al_{7.40}Si_{40.53}O₉₆] · 27.26H₂O) [32], W2 is near to site E, W3 to D, W4 to B, and W6 to site F. Site G in the Pashan sample is close to the W5 and W7 sites of HS-MOR, which are almost equivalent in *Cmcm* s.g.

In general, the structure refinement at rT shows that H₂O molecules are weakly or not bonded to the framework oxygen atoms (distance ~3.25 Å), with the exception of W7, which is strongly bonded (2.61(8) Å) to O10 (Table 2S). This H₂O molecule's distribution is consistent with the TG analysis, justifying the large weight loss observed at low temperature, and with IR data under degassing.

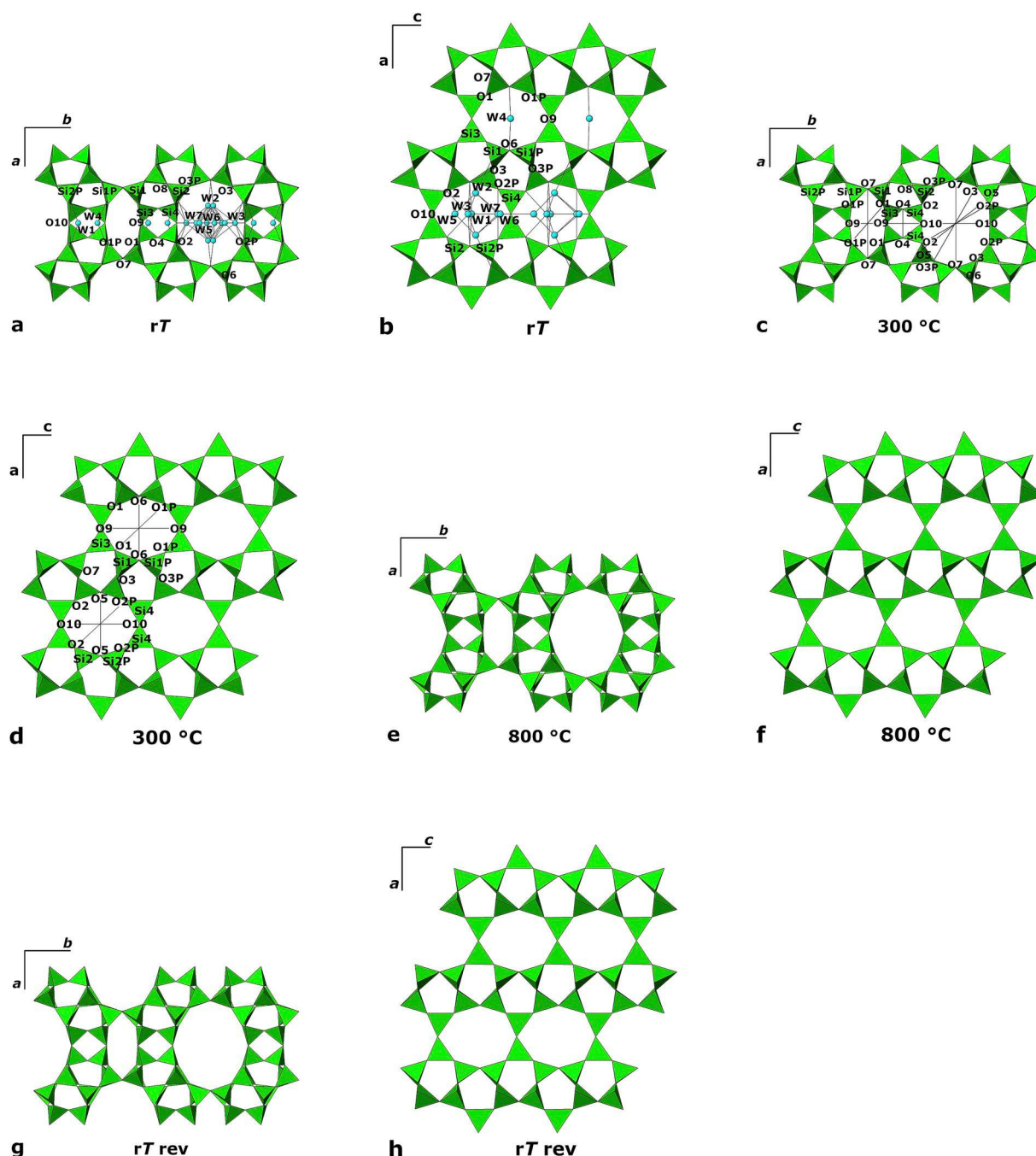


Fig. 3. Projection along [001] and [010] of HS-MOR structure at rT (a,b), 300 (c,d) 800 °C (e,f), and rT_{rev} (g,h).

3.3.2. Cell parameter behavior

The structural refinements of HS-MOR in the $Cmc2_1$ s.g. were successful at all the investigated temperatures. Details of the Rietveld refinement parameters at rT , 300, 800 °C, and rT_{rev} are reported in Table 1. No phase transitions or symmetry changes were observed with increasing temperature and the zeolite was stable up to 800 °C. Some diffraction peaks were broadened at the tails, and this led to a misfit in intensities between observed and calculated patterns after Rietveld refinement. This effect was particularly marked for peak (111), which could be due to framework defectiveness, probably induced by the dealumination procedure. Similarly, Simonic and Armbruster [33] reported the presence of diffuse scattering in both natural and synthetic mordenite due to disorder in the MOR framework.

Fig. 4 reports the evolution of the HS-MOR lattice parameters with T . The unit cell parameters show very slow and almost isotropic changes upon heating. The c parameter decreases right across the studied T range, while a and b undergo a very small decrease below 50 °C, followed by an increase to values slightly higher than those observed at rT . Above 100 °C, and up to 800 °C, all parameters shrink. Above 550 °C an increase in slope is observed for all parameters. This corresponds to marked silanol condensation and resulting framework modification, also highlighted by changes in the combination and overtone modes of the infrared bands. The overall lattice contractions are 0.67%, 1.18%, and 0.81% for a , b , c , respectively, and 2.64% for cell volume.

The odd trend in HS-MOR parameters between rT and 100 °C corresponds to the main dehydration step observed in the TG curve (Fig. 2). The expansion of a and b between 50 and 100 °C can thus be explained as a response of the framework to the H_2O flow through the 12 MR and 8 MR channels. A comparable “breathing” effect was found in analcime [34], where the six-member ring apertures of the channels parallel to (111) are opened as widely as possible during dehydration. During HS-MOR cooling, the unit cell does not recover its original dimensions, but maintains - at both 150 °C_{rev} and rT_{rev} - values close to those found at 700 °C.

Comparing the variation of the unit cell parameters of HS-MOR with those of Pashan mordenite [32], it is possible to identify some differences in thermal behavior. The cell volume contraction of the natural sample (~1.9% mainly due to b parameter decrease) is lower than that observed for HS-MOR. This is clearly due to the presence of extra-framework cations, which sustain the framework during dehydration.

In general, the high stability and low deformability of the MOR structure under heating is confirmed even in the high-silica sample.

3.3.3. H_2O release induced by heating

Fig. 5 reports the variation in the number of H_2O molecules at the

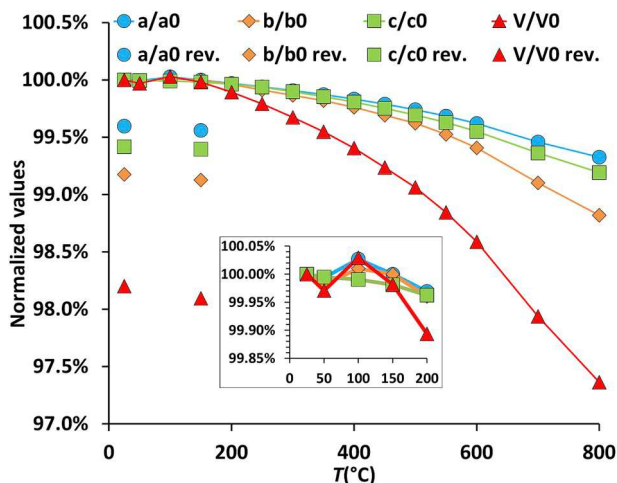


Fig. 4. Normalized unit-cell parameters of HS-MOR vs. temperature.

different W sites. The sample weight loss in the range rT -300 °C is also shown for comparison. A decrease in occupancy factors for almost all the H_2O sites is observed during the initial heating stage, thus confirming the TG data that indicate dehydration already starts between rT and 50 °C. Only the W3 and W7 sites show a slightly higher occupancy at 50 °C with respect to rT , favored by the better coordination of these sites with the framework oxygens. At 100 °C the H_2O molecules at W2, W5, and W7 hosted in the 12 MR channel are completely lost. Subsequently, in the range 100–150 °C, the molecules at W1 and W6, respectively located near the middle of the side pocket and of the 12 MR channel, are removed, while the W3 and W4 molecules remain in the center of the 8 MR windows of the side pocket, coordinated to framework oxygen atoms. At 200 °C even W4 is completely lost and only 0.6 H_2O molecules persist at the W3 site. Dehydration is complete at 300 °C.

Infrared characterization revealed that the desorption of adsorbed H_2O molecules by degassing is already complete at rT . It is worth noting that the evolution of the H_2O and hydroxy group content revealed with infrared spectra was obtained by outgassing HS-MOR at various temperatures in a dynamic vacuum regime, while the XRPD experiments were carried out under static pressure conditions that discourage H_2O diffusion.

3.3.4. Framework structural distortions induced by heating

Fig. 3 shows the refined structure of HS-MOR at rT , 300 °C, 800 °C, and rT_{rev} , viewed along [001] (a, c, e, g) and [010] (b, d, f, h).

The small unit cell volume contraction observed in the investigated T range is mainly due to a decrease in the b parameter, which starts above 150 °C (Fig. 4) and is enhanced at about 550 °C. The shrinking of b is related to the deformation of the 8 MR channel aperture. Fig. 3 c and e show the decrease in the O9–O1–O7 angle, which induces a strong deformation of the 8 MR. Summarizing, HS-MOR undergoes very moderate T induced deformations, which indicates a very rigid and stable framework.

3.3.5. Thermal expansion

The thermal behavior of HS-MOR can be described using thermal expansion coefficients:

- Between rT and 300 °C (temperature at which all the H_2O molecules are released), the values are $-2.19 \times 10^{-6} K^{-1}$, $-3.17 \times 10^{-6} K^{-1}$, $-2.29 \times 10^{-6} K^{-1}$, $-7.62 \times 10^{-6} K^{-1}$, for a , b , c , and V , respectively;
- Between 300 and 800 °C the values are $-11.59 \times 10^{-6} K^{-1}$, $-20.94 \times 10^{-6} K^{-1}$, $-14.15 \times 10^{-6} K^{-1}$, $-46.31 \times 10^{-6} K^{-1}$ for a , b , c , V , respectively.

These results appear to indicate that HS-MOR undergoes a negative

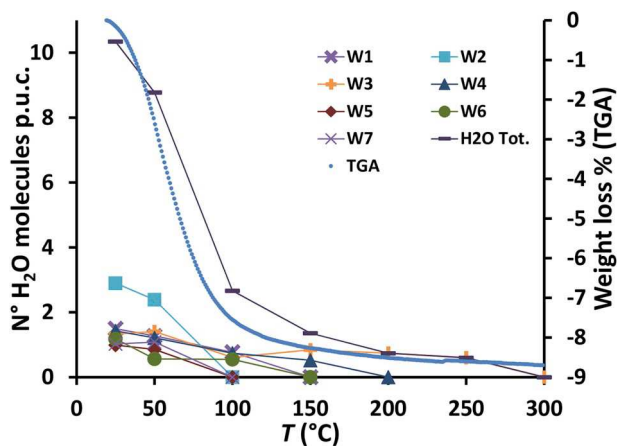


Fig. 5. Total H_2O content per unit cell and for each extraframework site vs. temperature compared with the TG curve.

thermal expansion (NTE) above 300 °C. However, this interpretation is not strictly rigorous, since the sample's weight loss, associated to the release of hydroxyls, continues up to the highest investigated temperature (Fig. 2). It is likely that the condensation of silanols, with the formation of siloxane bridges between silica tetrahedra, contributes to the shrinkage of cell parameters.

Negative thermal expansion (NTE) is defined as a reversible contraction of the material unit cell upon heating, and it was originally determined in structures with M-O-M linkages like metal oxides [35–37]. Recently, NTE was observed in the dehydrated forms of many microporous materials with Si–O–Si linkages [6,11,38]. Most of the high silica synthetic zeolites, with 2D or 3D channel system, exhibit this thermal behavior. In open frameworks like zeolites, the main mechanism was explained by Sleight [35] as the presence of transverse thermal vibrations of the oxygen atoms in Si–O–Si linkages. These motions may occur cooperatively and large void volumes are required to accommodate the cooperative rotations of tetrahedra. Since the thermal expansion of the tetrahedra is negligible, they are free to rotate as rigid units with little or no internal distortions. This mechanism has been justified on the basis of the so-called rigid unit mode (RUM) model [39]. The increase in vibrational amplitude of RUMs as a function of temperature is thus the underlying mechanism of NTE in framework structures ([40] and references therein). Based on lattice dynamics calculations for 18 siliceous and non-siliceous zeolites, Tschaufeser and Parker [41] suggested that NTE is more the norm rather than the exception for these materials.

It is clear that the condensation of silanols induces the rotation of the corresponding tetrahedra to establish new Si–O–Si bonds. This phenomenon explains both the shrinkage of the cell lattice (the “apparent” NTE), and the failed recovery of original cell values by HS-MOR during cooling (150 °C_{rev} and rT_{rev}). The HT induced condensation of silanols does not allow their complete rehydration, thus hindering complete recovery of the initial cell volume.

4. Concluding remarks

Strictly following Baur's classification [42], HS-MOR can be defined as flexible and collapsible, similarly to natural mordenite.

This phase is a very thermally stable zeolite, since up to at least 800 °C it does not undergo phase transition or amorphization, and overall unit cell contraction is less than 3%. The Stability Index (SI) - as defined by Cruciani [6] is 5, corresponding to the temperature of structural breakdown > 800 °C. This result was reasonably predictable, due to: i) the high Si/Al ratio (~110); ii) the high energy required to break the Si–O bond; iii) the presence of columns of five and four-membered rings that stiffen the framework [43,44].

The thermal expansion coefficients seem to indicate that HS-MOR undergoes a negative thermal expansion (NTE) above 300 °C. However, this interpretation is not strictly rigorous, since the sample's weight loss, associated with the release of H₂O molecules due to the condensation of silanols (widely present in this dealuminated sample) continues up to the highest investigated temperature.

Overall, all the data indicated a weak interaction of the H₂O molecules with the high silica mordenite framework, and provided evidence for the presence of different types of hydroxy groups with their different responses to thermal condensation. Infrared characterization showed that the desorption of adsorbed H₂O molecules by degassing is already complete at rT .

This interpretation of all the observed data might provide some insight into the thermal behaviour of other dealuminated zeolitic materials.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

the work reported in this paper.

Acknowledgements

The authors thank the staff of the ID22 beamline of ESRF (Grenoble, France) and Dr. Simona Bigi for the TG analysis. This work was supported by the Italian MIUR (PRIN2015 Prot. 2015HK93L7).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.micromeso.2019.109882>.

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Appendix II



Boosting sunscreen stability: New hybrid materials from UV filters encapsulation

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ARTICLE INFO

Keywords:

Encapsulated UV Filter
Eco-friendly sunscreen
Zeolite
Absorption
Hybrid material
Host-guest interaction

ABSTRACT

Unprotected exposure to solar UV is the main recognized cause of the spreading of skin cancer that has occurred in the last decades. Organic and inorganic UV filters are the main defense against UV exposure and have become ubiquitous in personal-care products, packaging, plastics, dyes, and many other sectors. UV filters still have some stability and efficacy issues making it important to find stable and broad-spectrum UV absorbers, safer for human health and the environment.

In this work UV filters octinoxate and avobenzone were encapsulated into zeolites with different chemistry and topology leading to the production of hybrid zeolites/organic filter sunscreens. The obtained materials were deeply characterized and their filtering capacity evaluated.

The encapsulation of UV filters in cationic zeolites resulted in an enhanced UV filtering capacity, whereas that in acid zeolites seem less effective in absorbing UV radiation, with emerging visible coloring.

The enhancement of UV filtering power is of paramount importance for the future development and exploitation of ZEOfilters, possibly being the key to reduce the quantity of actives, stabilizers, and co-formulants employed, with benefits for humankind and the environment.

1. Introduction

The solar UV radiation reaching the Earth's surface is increasing since the 1970s at middle-high latitude, even if, after the Montreal Protocol (1989), the trend significantly slowed down due to the recovery of the ozone layer [1]. While the UV irradiance is also affected by local factors [2], its rise leads to an increased UV exposure for human beings, and specifically for open-air workers, with growing health concerns, particularly, UV exposure is considered the main cause of skin carcinogenesis [3,4].

The number of annually diagnosed skin cancers, including both malignant melanoma (MM) and non-melanoma skin cancer (NMSC), is growing year after year. The American Cancer Society estimates 106,110 new diagnosed melanomas in the United States for 2021, with over 7000 deaths [5]. European countries have also shown an overall increase in melanoma incidence rate in the last decades [6].

These alarming numbers explain why sunscreen products are becoming of utmost importance in recent times. Organic and inorganic

UV filters (hereafter UVfs) are the main means of UV protection and are components of many personal-care products. Moreover, due to the detrimental effect of UV radiation on many goods, UVfs have also become ubiquitous in packaging, plastics, dyes, and many other sectors where UV radiation can promote product degradation (e.g. Refs. [7–10]).

Despite the massive use of organic UVfs, some issues linked to their stability and efficacy are still unresolved. It is well known that organic UVfs undergo photodegradation under UV exposure, losing protection efficacy and decaying in by-products of unknown toxicity [11]. The combination of different UVfs, to reach a broad-spectrum UV protection, may foster the photodegradation process. As an example, a sunscreen lotion thin film containing both octinoxate and avobenzone (two of the most used organic UVfs) loses completely its UV blocking property under 4 h of light exposure [12].

Various strategies were explored to stabilize UVfs and obtain more efficient and safer sunscreens. Among them, co-formulants are often added as stabilizers (e.g. Refs. [13,14]), although they may increase the

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<https://doi.org/10.1016/j.micromeso.2021.111478>

Received 22 July 2021; Received in revised form 24 September 2021; Accepted 29 September 2021

Available online 2 October 2021

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system complexity fostering allergic reactions [15,16], and photochemically incompatible ingredients must be avoided.

Recently, encapsulation has also been investigated as an alternative approach to the stabilization of organic and inorganic UVfs. Inorganic UVfs (e.g. TiO_2 and ZnO) are commonly encapsulated to reduce their photocatalytic activity [13]. Indeed, uncovered oxide particles cause the formation of reactive oxygen species (ROS) and enhance the photo-degradation of organic UVfs [17]. As for organic UVfs, different studies explored the stabilizing effect of their encapsulation into organic and inorganic materials (for a review see Ref. [18]). The use of inorganic matrices - such as hydrotalcites [19], amorphous silica [20–22], and MOF [23] - has been proposed to increase sunscreen stability and to prevent their absorption across the skin. In most cases, the encapsulation systems demonstrated to be effective under the usage timescale (few hours) but showed generally high filter leaching on longer timescales, such as those of storing and end-of-life disposal.

Zeolites have been only marginally investigated [24–26] as a scaffold for the encapsulation of UVfs: among them, only zeolite Y was studied as a host for Oxybenzone (OXY) and Para-Aminobenzoic Acid (PABA), the latter being no longer added to cosmetic sunscreens due to health issues (U.S. Food and Drug Administration, FDA, Federal Register 84FR6204, 2019–03019).

Reducing UVfs interaction with the skin and their transdermal permeation was the focus of most of the studies on encapsulated UVfs (e.g. Ref. [27]), but a deeper investigation of encapsulation properties and filter stability is needed before these materials could be employed in commercial formulations.

In this study, we report the synthesis and characterization of hybrid materials (hereafter ZEOfilters) obtained by the encapsulation of UVfs into zeolites. Among all, two of the most commonly employed organic UVfs were selected: the UV-A filter avobenzone (AVO) and the UV-B filter octinoxate (OMC) (Fig. 1). As for the zeolites, we chose framework types suitable for hosting small molecules, particularly MOR, LTL, FAU, and MFI as reported in Fig. 2 [28].

This research is part of a broader project aimed at the manufacture of stable UV filters effective in blocking radiation damage, but also safe for human health as well as for the environment. The ZEOfilters are expected to overcome the issues linked to both the use of the bare UVfs and the matrices other than zeolites. Eventually, this investigation proves the efficacy of zeolites in encapsulating UVfs and the capacity of the hybrid materials to absorb UV radiation, with interesting perspectives for new-generation sunscreens.

2. Experimental section

2.1. Materials

2.1.1. UV filters

Octinoxate ($\text{C}_{18}\text{H}_{26}\text{O}_3$, liquid, molar weight (MW) 290.40 g/mol,

specific gravity (SG) 1.01 g/ml, purity >96,0%) and avobenzone ($\text{C}_{20}\text{H}_{22}\text{O}_3$, powder, MW 310.39 g/mol, SG 1.08 g/ml, purity >98,0%) were purchased from TCI (Tokyo Chemical Industry Co., Ltd.).

2.1.2. Zeolites

All the synthetic zeolites used in this work (High Silica Mordenite (hereafter HS-MOR), Zeolite L (hereafter LTL), High Silica Faujasite (hereafter HS-FAU), Sodium Faujasite (hereafter 13X-FAU), High Silica ZSM-5 (hereafter ZSM5-398), low silica ZSM-5 (hereafter ZSM5-30)) were purchased from commercial suppliers as detailed below. Table 1S summarizes the main characteristics of the employed zeolites. All zeolites appear as white powders in their pristine form.

Mordenite (framework type MOR [28], Fig. 2a) was purchased from Tosoh Corporation (Japan, code HSZ-690HOA) in its protonated high-silica (dealuminated) form (HS-MOR; $\text{Si}/\text{Al} = 110$). The mordenite framework presents a 1D channel system with two parallel channels running along the *c* axis: a large 12-membered-ring channel (12 MR, maximum diameter of a sphere that can diffuse along it: 6.45 Å), and a strongly elliptical 8 MR channel. HS-MOR was thoroughly investigated by our group and was demonstrated to be a suitable host for organic molecules under different conditions [30–33]. We have previously shown that the HS-MOR sample is strongly defective as a consequence of the dealumination process and shows some degree of acidity [33].

Zeolite L (framework type LTL [28], Fig. 2b) was purchased from Tosoh (code HSZ-500KOA, $\text{Si}/\text{Al} = 2.9$) and used by our group in other studies (e.g. Refs. [34–37]). The LTL framework has a 1D channel system constituted by a circular 12 MR channel (maximum diameter of a sphere that can diffuse along it: 7.5 Å) and a smaller elliptical 8 MR one, both running along the *c* axis. The extra-framework K cations are sited into three distinct crystallographic sites as fully described by Ref. [35].

Faujasite zeolite (framework type FAU [28], Fig. 2c) was used in both high- and low-silica forms [38,39]. High silica faujasite (HS-FAU, $\text{Si}/\text{Al} = 280$) was purchased from Tosoh Corporation (Japan, code HSZ-390HUA), while low-silica faujasite (13X-FAU, $\text{Si}/\text{Al} = 1.2$) from BDH Chemicals, (Product 54017, out of stock). The FAU structure is characterized by a tridimensional 12 MR channel system (maximum diameter of a sphere that can diffuse along them: 7.35 Å). While HS-FAU has almost no extraframework cations, 13X-FAU has Na cations spread over different crystallographic sites, accounting for about 100 Na per unit cell (p.u.c.).

ZSM5 zeolites (framework type MFI [28], Fig. 2d) were purchased from China Catalyst (China) in both high- and low-silica protonated forms (ZSM5-398, code CCG05Z4001, $\text{Si}/\text{Al} = 237$ [40], and ZSM5-30, code CCG05Z301, $\text{Si}/\text{Al} = 14$ respectively). The MFI topology consists of straight 10 MR channels running along *b* direction intersecting a sinusoidal 10 MR channel running along *a* axis (maximum diameter of a sphere that can diffuse along them: 4.46 Å and 4.7 Å respectively).

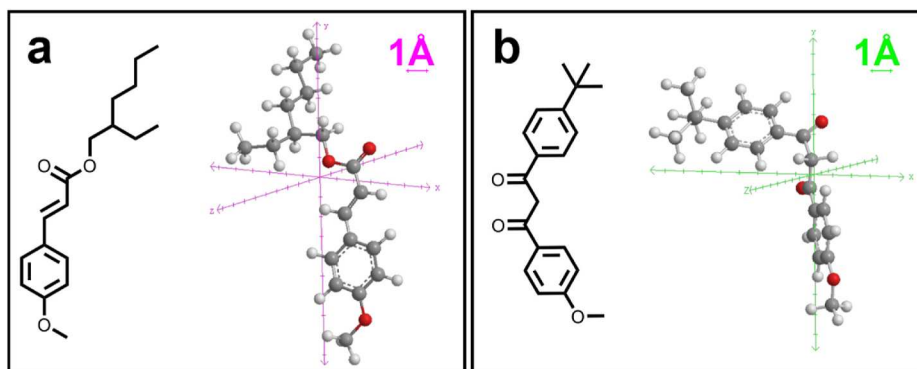


Fig. 1. Structures and molecular models of a) octinoxate (OMC) and b) avobenzone (AVO); ticks on the molecular axis are in Å, 1 tick = 1 Å.

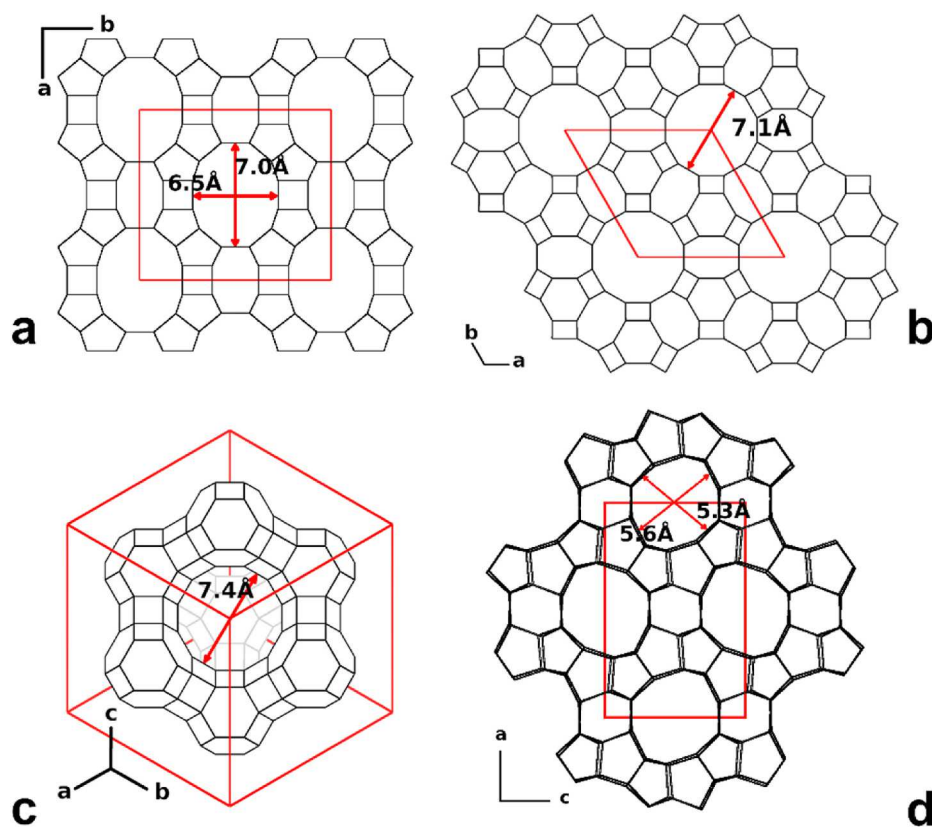


Fig. 2. The framework of a) MOR, b) LTL, c) FAU, d) MFI zeolites [29].

Table 1

Summary table of the selected hybrid samples reporting synthesis conditions and results from elemental (EA) and TG analyses (* = optimized washing, i.e. Total UVf wt.% = encapsulated UVf wt.%). TGA was not performed on the HS-FAU/AVO system due to the low UV-filter content. All samples were loaded at 100 °C for 48 h.

Label	Synthesis conditions		EA		TG		
	UVf/Zeolite [mol/mol]	l/s [ml/mg]	C [wt.%]	UVf [wt.%]	Total UVf [wt.%]	Encapsulated UVf [wt.%]	UVf molecules p.u.c.
13X-FAU/OMC	55.91	0.10	13.53	18.19	16.0	9.9	6.9
		0.16*	4.91	6.60	6.6	6.6	4.3
13X-FAU/AVO	13.20	0.00	17.29	22.34	20.7	16.1	11.2
		0.06*	7.61	9.83	10.6	10.6	6.6
HS-FAU/OMC	87.46	0.60*	10.29	13.83	13.2	13.2	6.1
HS-FAU/AVO	14.88	0.20*	0.46	0.59	–	–	–
HS-MOR/OMC	19.96	0.15	8.21	11.03	8.5	8.5	0.9
HS-MOR/AVO	1.30	0.19*	4.60	5.94	5.6	5.6	0.6
LTL/OMC	17.31	0.84	4.17	5.60	5.88	5.3	0.5
LTL/AVO	0.57	0.22*	4.42	5.71	5.3	5.3	0.5
ZSM5-30/OMC	40.31	1.71*	5.87	7.89	7.6	7.6	1.8
ZSM5-30/AVO	5.44	1.55*	3.15	4.07	4.6	4.6	1.0
ZSM5-398/OMC	40.50	1.71*	1.88	2.53	2.6	2.6	0.5
ZSM5-398/AVO	5.83	0.81*	1.09	1.41	1.4	1.4	0.3

2.1.3. ZEOfilters synthesis

The zeolite loading procedure, aimed at the preparation of hybrid ZEOfilters, can be summarized in 4 phases: 1) Zeolite activation; 2) UVf loading; 3) ZEOfilter washing; 4) ZEOfilter drying, according to the following procedure.

All zeolites were dehydrated at 450 °C for 3 h before UVFs loading to remove all the H₂O molecules.

Dehydrated zeolites were then mixed, at room temperature, with the organic UV filter (AVO or OMC, separately) into glass tubes. The mixtures were stirred and homogenized for a few minutes and then sealed with Teflon stoppers. All tubes, covered with aluminum foil to prevent light exposure, were heated at 100 °C for 48 h. The samples were frequently checked and homogenized. Since at 100 °C both OMC and AVO are liquid, the loading is actually performed by soaking the zeolites

with the neat UV filters.

The samples were then washed to remove the unloaded UV filter present on the external surface of the zeolite grains. Two different washing techniques were tested and compared in terms of efficacy and efficiency: Soxhlet extraction (SE) and ultrasound-assisted extraction (UAE). The Soxhlet extraction was carried out using a 70 ml Soxhlet extractor with acetone as solvent. Ethanol was tested too, but it was discharged since less effective (see results). A small amount of hybrid was sampled at regular intervals during the washing procedure and analyzed by elemental analysis (EA) to follow the evolution of the system over washing. An overall liquid-over-solid ratio (l/s) parameter was used to evaluate the washing degree from the chemical data since the amount of hybrid powder prepared and then washed varied. The l/s parameter is defined by the following equation:

$l/s = (\text{number of washing cycles}) \times (\text{solvent volume}) / (\text{hybrid sample mass}) = [\text{ml/mg}]$

The samples washed with UAE were split into various portions and washed with acetone using a constant solid/liquid ratio of 0.03 ml/mg. The aliquots underwent a different number of cycles of 20 min ultrasonic bath followed by centrifugation (the solvent was refreshed at each cycle). Samples of the hybrids at different degrees of washing were analyzed by EA to monitor the washing process as done for the Soxhlet method. The same l/s parameter was employed for both SE and UAE. Before analysis, all samples were dried for 48 h at 60 °C for solvent removal after the washing process. The obtained dried material is referred to as ZEOfilter.

The loading/washing protocol was optimized to yield ZEOfilters with the maximum possible filter loading and without molecules on the zeolite grains surface, as detailed in the Result section. Then, hybrids were produced on a multi-gram scale to allow their complete physico-chemical characterization.

As mentioned, the maximum possible UV filter loading was not known in advance for the investigated zeolites. Thus, the first exploratory, loading were made with large UV filter excess. Further syntheses of ZEOfilters were performed by significantly reducing the initial excess of UV filter.

2.2. Elemental analysis (EA)

Elemental analyses were performed using a Thermo-Fisher CHNS FLASH 2000 analyzer. The samples were brought at 1800 °C with a “FLASH” dynamic combustion. After the reduction, the elementary gases released by the decomposition were analyzed in a GC (gas-chromatograph) comprising a chromatographic column and a sensitive TCD detector. The amount of sample used for the analyses ranges from 0.7 mg to a few mg. The analyzed elements are C and H.

2.3. Thermogravimetric analysis (TGA)

TG analyses were carried out using a Seiko SSC/5200 thermal analyzer. TGA were performed on about 20 mg of ZEOfilters loaded into an open Pt crucible and heated under helium stream from room temperature to 1050 °C, at a heating rate of 10 °C/min.

Samples at different washing stages were analyzed by TG to determine their filter content and to determine weight losses due to filter molecules in the zeolite cavities and on the surface of the grains. TGA were also performed on pure octinoxate and avobenzone in the same conditions used for the hybrids, and on pristine zeolites in an air stream.

2.4. UV-Vis spectroscopy

UV-Vis measurements were performed with a UV-Vis V-570 Jasco spectrophotometer in transmission mode. UV-Vis spectra were collected in the 200–800 nm interval with 1 nm resolution, at 25 °C.

Solution spectra of octinoxate and avobenzone in ethanol and ethyl-acetate were collected employing a 1 cm quartz cell at different concentrations ($1 \text{ ppm} < c < 200 \text{ ppm}$).

UV-Vis spectra of pure filters in vaseline oil (v.o.), zeolites in v.o., and of hybrids in v.o. were collected using a quartz slide sandwich [41].

2.5. Infrared spectroscopy

FTIR spectra were collected on a Bruker IFS66 spectrophotometer equipped with a La-DTGS detector and a KBr beamsplitter. Each spectrum is the average between 128 scans in the 4000–400 cm^{-1} range with a resolution of 4 cm^{-1} . The spectra of OMC were collected by the thin film method by putting a drop of liquid between two KBr windows, while the ZEOfilter spectra were obtained by making a self-supporting pellet of powder with an optical thickness of about 10 mg/cm^2 and by

evacuating it (residual pressure 10^{-4} mbar) into a traditional infrared cell equipped with KBr windows.

3. Results and discussion

3.1. ZEOfilter loading

Zeolite loading represented a challenging aspect in the preparation of the hybrid ZEOfilters, particularly because the UVfs maximum loading was unknown and the washing procedure had to be effective in removing the surface excess of the UVfs without affecting the encapsulated molecules. These two achievements are crucial for the realization of safe and effective sunscreen hybrid materials. The selected samples of ZEOfilters are summarized in Table 1 along with their loading conditions and chemical data.

As already mentioned, all ZEOfilters were initially prepared by using a high UV filter excess. Once the maximum loading of each system was experimentally determined, subsequent samples were obtained with a smaller UV filter excess (+1–2 wt%). Whatever the reagent excess, all samples of the same zeolite/UV filter system displayed the same final composition and features. In Table 1 are reported samples with very variable initial UV filter/zeolite ratio (i.e. from a more than ten-fold excess in the case of 13X-FAU/OMC and HS-FAU/OMC, to an almost ad-hoc loading of LTL/AVO).

The carbon content (C%) variation of the different hybrid materials was followed upon washing by EA. The different washing effect of ethanol and acetone on the LTL/OMC system is shown in Fig. 3a that exhibits the decrease of C wt.% under the effect of SE. Both solvents induce a significant decrease in UVf content in the first cycles, followed by a smoothing of the curve upon successive washing cycles, leading to a compositional final plateau. Conversely, the residual C% is different for the two solvents attaining the final value of about 4% and 1% for acetone and ethanol respectively. Taking into account the molecular weight of OMC, the plateau of the acetone-washed curve corresponds to about 0.5 OMC molecule p.u.c. of LTL (Table 1), which given the size of the molecule and of the LTL channel could account for the maximum OMC loading. We can thus assume that at the plateau the unadsorbed UVf molecules on the surface are removed, leaving only the more strongly trapped ones in the cavities. The washing profiles indicate that ethanol is not suitable for this purpose, as it tends to remove the OMC molecules even from the zeolite channels. Instead, acetone is able to remove the physisorbed molecules on the surface of the grains without affecting those hosted in the cavities. Nevertheless, we have noticed that upon prolonged washing even with acetone the C% decreases constantly albeit slowly (data not shown); it is thus essential to stop the washing procedure once the plateau is reached. Based on these results, acetone was used as the solvent for all the other samples.

Soxhlet extraction (SE) and ultrasound-assisted extraction (UAE) were both evaluated as washing methods, and the results for LTL/OMC system are shown in Fig. 3b. Both SE and UAE led to similar final UVf concentrations in the hybrid material, even if at different l/s values. We deem the UAE more suitable for large-scale preparation since no heating source is required, a larger volume can be obtained faster and the procedure is more easily tunable, even if it is more labor-intensive. On the contrary, the SE fits better for small-scale operations. We then decided to choose the appropriate washing technique on a case-by-case basis, and hereafter no specification of the employed method will be given for each sample.

The optimum loading for each sample was estimated as the plateau of the washing curve, corresponding to the maximum encapsulated filter content (wt.%). These data are those reported in Table 1 together with the TG results (see below for discussion), showing the number of UVf molecules actually encapsulated p.u.c.

As different framework types have different pores volume, it is to be expected that FAU can host more molecules compared to the other investigated zeolites. Indeed, FAU accessible volume corresponds to

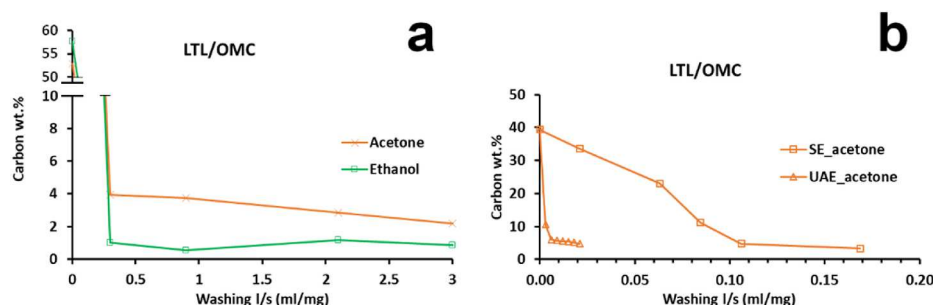


Fig. 3. Example of washing curves of ZEOfilters. a) Soxhlet extraction (SE) of hybrid LTL/OMC with ethanol (green curve) and acetone (orange curve); b) comparison of ultrasound-assisted extraction (UAE) and SE washing methods for LTL/OMC sample. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

27.42% of the total cell volume (more than $14000 \text{ \AA}^3$), compared to 12.27 and 15.37% for MOR and LTL framework, respectively (cell volumes about $3000 \text{ \AA}^3$ and $2000 \text{ \AA}^3$, respectively). The two UVfs behave differently when encapsulated in different matrices: AVO seems to be more suitable to be hosted in cationic zeolites - particularly, 13X-FAU shows the highest loading - while in high silica zeolites it seems to be not loadable at all, probably for the absence of cationic sites to graft. Conversely, OMC can be loaded in all the investigated zeolite types, both cationic and high silica. Interestingly, zeolites LTL and 13X-FAU can host almost the same amounts of both filters. Both the UVfs have hydrophobic character, although AVO behaves as a weak acid due to the β -diketo group. The keto-enol tautomerism is hampered in the solid-state within the zeolite channels, but the proximity to zeolite acid sites may catalyze the interconversion of the keto-enolic form into the diketo one. On the other hand, the presence of metal ions in the zeolite cavities could account for a shifting of the tautomeric equilibrium toward the keto-enol due to its enhanced metal-binding ability [42–44]. The slight differences in loading between AVO and OMC can be attributed to their steric hindrance. OMC is bulkier and characterized by a hydrophobic and mobile aliphatic side chain, while AVO, particularly in the keto-enol form is an almost linear rigid structure, probably able to better fit into zeolite channels.

3.2. ZEOfilter characterization

Elemental analysis performed during and after washing allowed a first, quick, estimation of UV filter content in each ZEOfilter. However, EA does not provide any information about the effectiveness of encapsulation. Thus, thermogravimetric analyses were performed under inert atmosphere (He) on the selected hybrid samples before and after the washing process to investigate the differences in the desorption temperatures of physisorbed molecules on the grain surface and within the zeolite pores (Table 1). The pristine zeolites and pure UVfs OMC and AVO were used as reference systems. The results are reported in Table 1. The differences among the values obtained by EA and TGA may arise from various factors. First of all, even if samples were homogenized before analysis, some inhomogeneities can be present at the scale of

sampling (1 mg for EA and 20 mg for TGA). Then, low-C measuring by EA is challenging in silicate matrixes. Finally, the possible water content variability in zeolites can induce weight variation of the samples. Thus TGA was preferably used for the final UVf p.u.c determination.

The pure UVfs (Fig. 4) decompose over a 100-degrees range below $\sim 300^\circ\text{C}$ (OMC) and $\sim 350^\circ\text{C}$ (AVO). These temperature ranges are lower than those reported in the literature for their boiling temperature (i.e. 382°C and 400°C at 1 atm for OMC and AVO, respectively [45], as expected for a TGA in the open crucible setup [46].

The thermal profiles for the systems with the highest loading, i.e. FAU13X and LTL hybrids, are reported in Fig. 5 and Fig. 6, respectively, while the weight losses of the whole sample set are reported in Table 1.

The pristine 13X-FAU (Fig. 5a and b, black line plot) displays a single broad weight loss below 400°C , accounting for 23% weight loss, that can be correlated to the removal of H_2O molecules in the solvation sphere of cations in different sites, consistently with what reported in the literature [47]. The two 13X-FAU hybrids reported in Fig. 5a and b (13X-FAU/OMC, 13X-FAU/AVO) show a DTG peak at about 100°C that can be attributed to H_2O molecules readsorbed during the preparation and/or storing of the ZEOfilters. The lower temperature at which these losses occur suggests that H_2O molecules are more loosely bonded in ZEOfilters than in the pristine zeolites. This hypothesis is supported by the insertion of mostly hydrophobic UVfs into the zeolite channels that prevent the access to H_2O molecules. The DTG curves of the optimized samples (l/s 0.16 and 0.06 for OMC and AVO hybrids, respectively) show a shoulder at slightly higher temperature (about 150°C), which is not visible in the unoptimized ones in which an excess of UVfs is on the surface of zeolite particles (l/s 0.10 and 0 for OMC and AVO, respectively) as shown in Fig. 5. A possible explanation is that the physisorbed UVfs on the surface hamper the access of the H_2O molecules to the zeolite pores; upon washing the removal of UVfs excess from the grain makes the channels more accessible to water once again and allows the formation of some more stable H_2O -zeolite bonds, similarly to what observed in the pristine sample.

At higher temperatures, the DTG curves of 13X-FAU ZEOfilters show two peaks of different breadth. Unoptimized 13X-FAU/AVO DTG (l/s = 0) displays a noticeable peak at 250°C (Fig. 5b) that completely

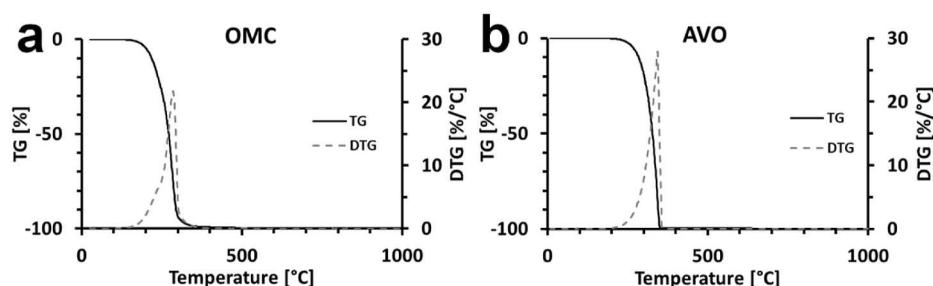


Fig. 4. TGA of OMC (a) and AVO (b) in a helium atmosphere.

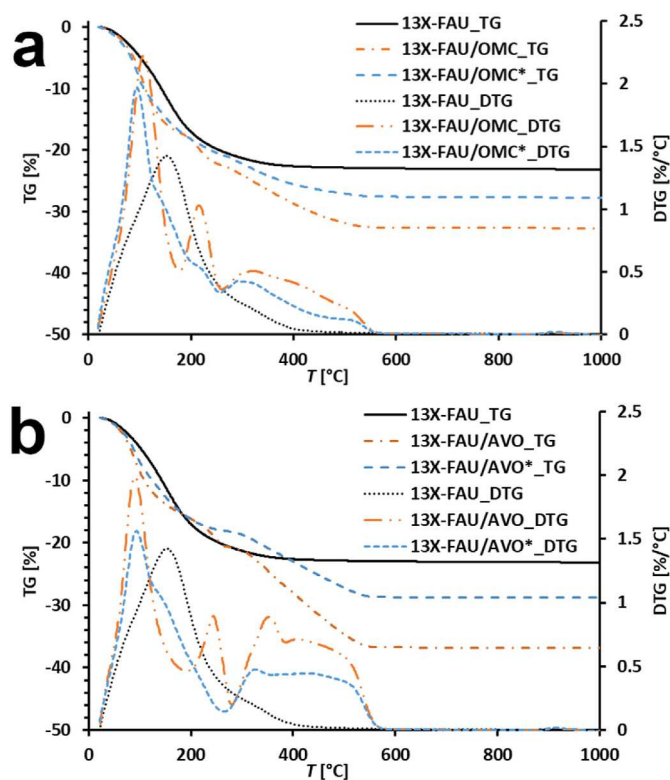


Fig. 5. TGA of FAU-13 hybrids with OMC (a) and AVO (b). *optimized samples.

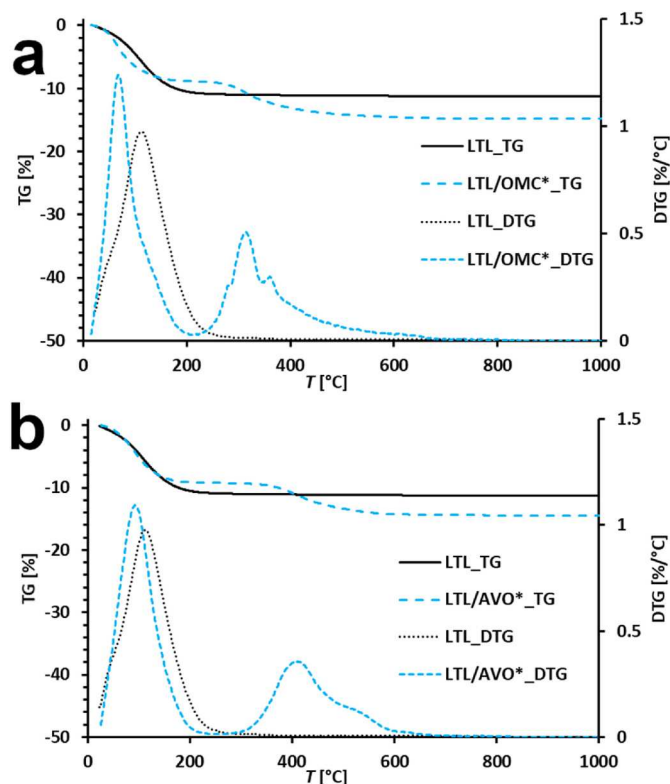


Fig. 6. TGA of pristine LTL zeolite and optimized LTL hybrids with OMC (a) and AVO (b).

disappears in the optimized sample and can be attributed to UVfs loosely bound to the surface. Similarly, unoptimized 13X-FAU/OMC shows a DTG peak at 220 $^{\circ}\text{C}$ but, in this case, a small signal remains in the optimized sample ($l/s = 0.16$, Fig. 5a), indicating incomplete removal of the UVf molecules from the zeolite grains surface. The DTG broad bands registered in the range 270–550 $^{\circ}\text{C}$ can be attributed to the decomposition of the UVfs encapsulated into the zeolite porosities, which are calculated as 6.6% and 10.6% wt. for the 13X-FAU/OMC and the 13X-FAU/AVO systems, respectively. Since the TG losses corresponding to these peaks are higher for the unoptimized samples, we cannot exclude a contribution of molecules more strongly bonded on the zeolite grains surface. It is worth noting that the decomposition temperatures observed for the UVf molecules encapsulated into the zeolites are higher than those observed for the pure filters, as a clear consequence of the UVf-zeolite interactions. By comparing the total UVf loss with the weight of the anhydrous zeolite it can be calculated that 13X-FAU/OMC samples host 4.3 molecules of OMC per unit cell while the 13X-FAU/AVO hosts 6.6 molecules of AVO p.u.c. These data are in good agreement with those obtained from elemental analyses (Table 1).

All DTG signals -relative to the organic decomposition-of 13X-FAU/AVO are shifted toward higher temperatures compared to 13X-FAU/OMC. This shift can be ascribed in the first instance to the chelating properties of the OO donor group of the β -keto-enol moiety of AVO that can form stronger interactions with the cations of the zeolite than the weak coordination bond of the carbonyl oxygen in the ester moiety of OCM as depicted in Fig. 7.

Pristine LTL zeolite loses all water molecules below 250 $^{\circ}\text{C}$, with a total weight loss of 11.2% (Fig. 6). We observe a comparable weight loss of ~ 9 wt% below 220 $^{\circ}\text{C}$ for both LTL ZEOfilters, possibly due to rehydration of the zeolite after loading. It is difficult to univocally assign this weight loss to structural water or rather to physisorbed surface H_2O since LTL hosts a large number of weakly bonded H_2O molecules that can be released below 150 $^{\circ}\text{C}$ [34]. Interestingly, the hybrids show a lower temperature for water release compared to the pristine zeolite, possibly due to the higher amount of physisorbed H_2O molecules. For the sake of brevity, in the following discussion, we discuss the results only to the more interesting optimized hybrid LTL systems since the considerations made for the unoptimized FAU13X hybrids apply also to the unoptimized LTL hybrids.

The DTG curve of the LTL/OMC sample (Fig. 6a) shows three peaks at 280, 315, and 360 $^{\circ}\text{C}$, accounting for a total weight loss of 5.9%. These peaks can be attributed to OMC molecules differently bonded to the zeolite. The data are in good agreement with the 5.60 wt% calculated by elemental analyses. LTL hybrids can hence host 0.5 OMC molecules p.u.c. and this corresponds nicely with the maximum loading predictable by structural considerations. In fact, the 12 MR channel can host, compatibly with its size, only one OMC molecule elongated along the c axis of LTL unit cell, which has a length of about half of the OMC molecule.

The LTL/AVO hybrid DTG curve shows a broad peak, with a shoulder, between 300 and 650 $^{\circ}\text{C}$, accounting for a total weight loss of 5.3 wt %, in good agreement with the 5.71 wt% of AVO measured by EA. This value corresponds to 0.5 AVO molecules p.u.c. compatible with the LTL structure as above reported for OMC hybrid.

For LTL hybrids the temperature shift between OMC and AVO loss is more marked than that observed for 13X-FAU. This could be ascribed to

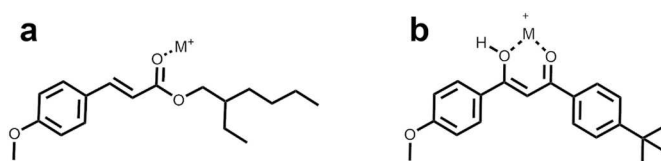


Fig. 7. Molecular scheme of the possible interaction between OMC (a) and AVO (b) with cations.

the stronger interactions between the UVfs and the extraframework cations in LTL, which presents more accessible cation sites compared to FAU. The broader DTG peak widths of the FAU ZEOfilters could be ascribed to the presence of many different Na sites in the large Y cage. In this case, UVf molecules interact with cations at different crystallographic sites and with different bond strengths, thus the molecule release occurs in a wide range of temperatures broadening the DTG peaks.

Based on the EA and TGA results obtained for FAU- and LTL-based ZEOfilters, it can be concluded that the encapsulation process is effective.

3.3. ZEOfilters efficacy in UV-light absorption

The second important goal of this paper is the assessment of ZEOfilters UV filtering power, which will enable their future exploitation. The UV-filtrating power of ZEOfilters should be comparable or better than that of the pure UVfs (Fig. 1Sa,b). UV-Vis spectra of bare UVfs in ethanol (EtOH), ethyl acetate (EtOAc), and vaseline oil (v.o.) were collected to compare their absorption capacity in different media. The AVO and OMC filters show minor solvatochromic effects since insignificant differences in transmittance are observed when the solvent is changed. OMC and AVO filters display full transmittance in the visible light range (400–700 nm), together with a neat absorption peak in the UV-A (AVO) or UV-B (OMC) range. This feature is maintained also at a high UVf concentration (data not shown), with a consequent total absorption of UV light. In addition, UVfs maintain their transparency also at high concentration, a feature mostly desired for cosmetic formulations. The anomalous behavior of EtOAc solutions below 250 nm corresponds to the solvent UV-cutoff.

To evaluate the effect of the zeolite scaffold on the UV absorption, pristine zeolites dispersed at 25 wt% in v.o. were analyzed. As shown in Fig. 1Sc, the spectra do not show absorption bands in the visible nor the UV range. HS-MOR and ZSM5-398, however, show a very low transmittance in the whole region at 25 wt%, mainly linked to particle scattering. With increasing concentration of zeolite into v.o. (data not shown), the transmittance profile lowers steadily in the whole UV-Vis range, increasing the sample opacity.

The UV-Vis measurements on ZEOfilters were performed on a suspension of the hybrid material in v.o. The final concentration of the UVf in this mixture was equal to 1 wt%. This filter concentration was chosen firstly because it allowed the observation and comparison of the UV-Vis spectral features of the investigated hybrids and secondly in view of further cosmetic applications (Fig. 8).

ZEOfilters based on HS-MOR, HS-FAU, ZSM5-30, and ZSM5-398 seem less promising since exhibit limited UV filtering properties compared to hybrids of 13X-FAU and LTL, and bare UVfs (Fig. 8). Moreover, all ZEOfilters based on acid zeolites show selective visible light absorption as apparent from the final color of the hybrid powders (Fig. 9). The absorption color of hybrids tends to change from white to violet or yellow (for OMC and AVO ZEOfilters, respectively) while

increasing the zeolite Si/Al ratio, even if for ZSM5-398/AVO and HS-FAU/OMC colors are very pale. Preliminary Infrared Spectroscopy (IR) results revealed the protonation of the UVf molecules interacting with the HS-MOR acid sites.

Fig. 10 shows the infrared spectra for OMC (a) compared to the HS-MOR/OMC ZEOfilter (b). It is noticeable that the interaction with the zeolite causes changes in the structure of the OMC. Indeed, the most characteristic signal responsible for the stretching of the carbonyl group $\nu\text{C}=\text{O}$ at 1710 cm^{-1} is dampened in the ZEOfilter as well as the signal attributed to the $\nu\text{C}=\text{C}$ at 1635 cm^{-1} . On the other hand, the signals attributed to the aromatic skeleton at 1604 cm^{-1} , 1575 cm^{-1} , 1512 cm^{-1} , and 1422 cm^{-1} stand out in the ZEOfilter spectrum having a higher relative intensity, with respect to the OMC one. A less important modification occurs for the group of signals with maximum at 1465 cm^{-1} that contain the deformation of CH_2 (δCH_2).

This behavior can be compatible with the protonation of the α,β -unsaturated ester system due to the high defectivity of the HS-MOR zeolite, which notably contains a high amount of acid sites. This protonation might explain the absorption bands in the visible light range (Fig. 8a), but a deeper IR investigation of the UVfs-zeolite interaction is needed for all ZEOfilters.

Using a mixture with 1% of UVf, ZSM5-398 hybrid samples are opaque, thus not measurable as a consequence of the high ZEOfilter amount to be used in the mixture due to the low UVf loading in this zeolite (2.53% OMC and 1.41% AVO, respectively, Table 1). The amount of UVfs for these samples was then decreased to 0.5 wt%. However, even at lower ZEOfilter content, these samples display a very low transmittance over the whole wavelength range, indicating a major contribution of zeolite particle scattering to the spectra.

Concerning the low silica ZEOfilters, 13X-FAU and LTL hybrids display an enhancement of UV filtering power even when compared to bare UVfs, and, in addition, they maintain perfect visible transparency. Conversely, ZSM5-30 hybrids display spectral features similar to HS-MOR, probably because both these zeolites are in protonic form. Both these hybrids display some absorption bands in the visible range leading to colored samples (Fig. 9) with very limited absorption in the UV region. It is worth noting that the UV absorption band of the ZSM5-30 hybrids, and, to a lesser extent, of the HS-MOR ones, is shifted towards higher wavelengths compared to the other ZEOfilters. This shift towards lower energy can be related to the acidic environment of ZSM5-30 and HS-MOR, favoring the keto-enol form for AVO, and the protonated ester form for OMC (as shown by FTIR data).

The enhancement of the UV filtering power of LTL and 13X-FAU ZEOfilters is very promising for their future development and industrial application. Indeed, the increased efficiency in UV filtering can be key to reduce the amount of UVfs employed in cosmetic formulations.

Another important point to pave the way for the use of these ZEOfilters in cosmetic formulations (and in other product categories) is to assess their photostability under protracted UV exposure. The preliminary exposure tests performed by a solar lamp (not reported here) show promising results, and high ZEOfilter stability. Indeed, the

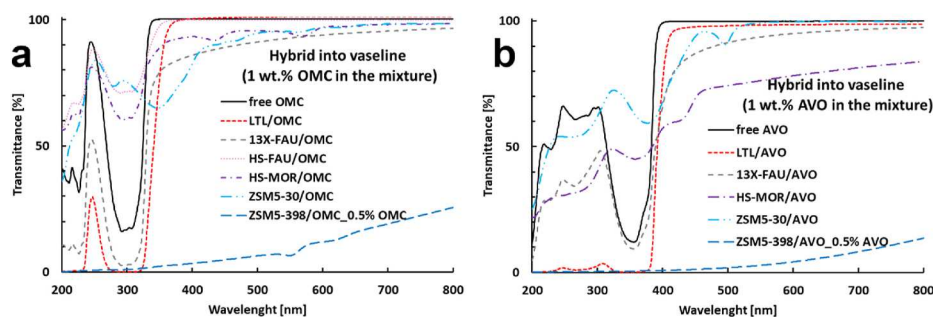


Fig. 8. UV-Vis spectra of bare UVfs, and OMC (a) and AVO (b) ZEOfilters into vaseline oil (v.o.). All spectra, except ZSM5-398 hybrids, are collected on mixtures containing 1 wt% of UVf (i.e. in the case of ZEOfilters UVf:(zeolite + v.o.) = 1:99).

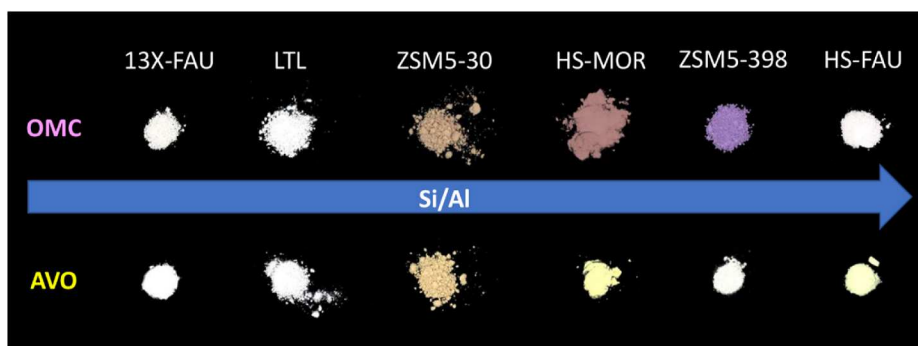


Fig. 9. ZEOfilter powders. Samples are organized as a function of the Si/Al ratio.

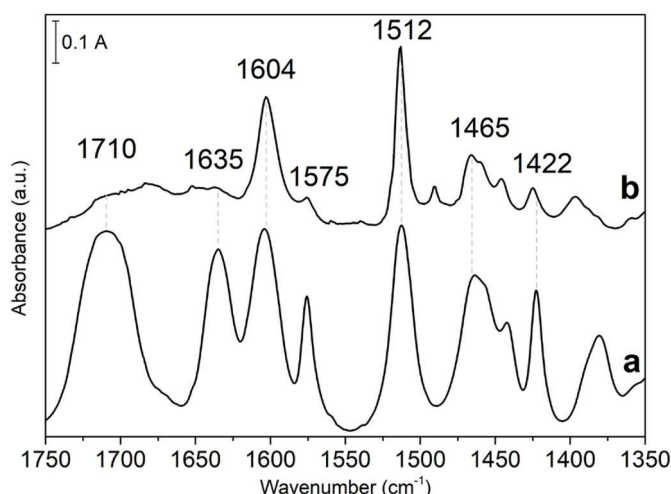


Fig. 10. FTIR spectra of OMC (a) and HS-MOR/OMC (b) subtracted for the HS-MOR spectrum.

confinement in zeolite scaffold probably prevents i) the molecules isomerization [11], and ii) the interactions among the different filters in the formulation [12].

4. Conclusions

We presented an efficient approach to the production of ZEOfilters, hybrid UV filtering materials constituted by the encapsulation of organic UV filters (avobenzone and octinoxate) into zeolites with different framework topologies (LTL, MOR, FAU, MFI) and chemistry. ZEOfilters displayed variable spectral features depending on the combination zeolite/UVf, with some of them being greatly effective in UV absorption.

Overall, the encapsulation of UV filters resulted in an enhanced UV filtering power for cationic, not protonated, zeolites (i.e. LTL and 13X-FAU) hybrids, whereas high silica zeolites (i.e. HS-MOR and HS-FAU e ZSM398) yielded materials with reduced filtering power. The protonated ZSM5-30 hybrids display spectral features in between cationic and high silica ZEOfilters. The increased UV filtering power makes LTL and 13X-FAU ZEOfilters more effective than the bare UV filters, thus requiring a lower organic filter amount in the formulations.

Compared to traditional organic UV filters, ZEOfilters are expected (also thanks to some preliminary tests here not reported) to enhance the photostability of the filters thanks to guest-host stabilization, a feature able to limit their detrimental effects on human health and the environment, particularly the direct contact of UVfs with skin is avoided. Furthermore, a sensible reduction of stabilizers in the formulations is also expected since UVfs are encapsulated separately in the zeolites, and photochemically incompatible filters can be applied simultaneously as a

mixture of different ZEOfilters, paving the way to more effective and safer formulations.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:
Patent application

Acknowledgments

Monica Malavasi, Simona Bigi, and Simona Marchetti Dori are acknowledged for EA and TGA. The master students Giulia Coppeta and Benedetta Bonini are acknowledged for their experimental contributions.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.micromeso.2021.111478>.

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