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Combined myo-inositol and Banaba (1% Corosolic Acid) improve HOMA-IR and hepatic insulin extraction index in overweight and obese postmenopausal women

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ABSTRACT

Objective: To assess the effects of a 12-week combined treatment with myo-inositol (2 g) and Banaba extract (48 mg) standardized to 1% corosolic acid (MBN) on insulin resistance (HOMA-IR) and hepatic insulin extraction index (HIEI) in overweight and obese postmenopausal women.

Methods: We conducted a retrospective observational study including 31 postmenopausal women (mean age 51 ± 1.2 years) attending the Gynecological Endocrinology Center of Modena, Italy. All patients received daily supplementation with MBN for 12 weeks. Hormonal and metabolic parameters—including fasting glucose, insulin, C-peptide, and HOMA-IR—were assessed before and after treatment. In addition, an oral glucose tolerance test (OGTT) was performed at both time points, with glucose, insulin, and C-peptide curves measured and corresponding area under the curve (AUC) values at 240 minutes calculated. HIEI was calculated as the insulin/C-peptide ratio. Data were analyzed globally and then stratified by family history of diabetes.

Results: After treatment, fasting insulin, HOMA-IR, and HIEI were significantly reduced. The OGTT showed a 23.5% decrease in glucose AUC, with greater reductions in insulin AUC (−42%) compared to C-peptide AUC (−16.8%), suggesting enhanced hepatic insulin clearance. Patients with a family history of diabetes showed reductions in insulin and C-peptide, while those without showed only a decrease in insulin and HIE, with no changes in C-peptide.

Conclusions: Combined MBN supplementation improved insulin sensitivity and hepatic insulin clearance in overweight and obese postmenopausal women, with particularly pronounced effects in those with a family history of diabetes. These findings underscore the potential of targeted integrative strategies to mitigate insulin resistance in this population.

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Myo-inositol; Banaba; corosolic acid; insulin resistance; menopause; HOMA-IR; hepatic insulin extraction index; HIEI

Introduction

Menopause is defined as the absence of menstruations for at least 12 months and represents a physiological milestone in a woman's life, marked by the permanent cessation of reproductive capacity [1]. It is accompanied by important hormonal and metabolic changes that can affect long-term health and quality of life [2]. The menopausal transition begins approximately 8–10 years earlier and is characterised by anovulatory cycles and reduced progesterone secretion during the luteal phase [3]. Gonadal steroid hormones regulate key metabolic pathways, and their decline during this period makes such effects increasingly evident [4].

During the menopausal transition, the decline or absence of luteal progesterone reduces energy expenditure, favoring fat accumulation [5–7]. Weight gain typically occurs when calorie intake exceeds

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energy expenditure, which comes primarily from daily physical activity and resting metabolic rate. Women who maintain the same dietary and activity habits during menopause may experience gradual weight gain accompanied by worsening metabolic markers, including reduced insulin sensitivity and altered lipid profiles [8].

In postmenopause, hypoestrogenism and low progesterone exacerbate insulin resistance, compounded by elevated cortisol while aging reduces lean muscle and increase visceral fat, which releases pro-inflammatory adipokines, further impairing cardiometabolic health [2,7,9].

Insulin resistance arises when peripheral tissues (adipose, skeletal muscle, and liver) respond inadequately to insulin, reducing cellular glucose uptake and increasing the risk of metabolic syndrome and type 2 diabetes mellitus [4].

Management of insulin resistance in menopausal women typically begins with lifestyle modifications: a modest calorie deficit diet combined with regular physical activity, which improves blood pressure, fasting glucose, triglycerides, and cholesterol [10]. Menopausal hormone therapy (MHT) may limit peri-menopausal body composition changes, especially via transdermal oestrogen, but effectiveness varies and use should be individualised considering personal health risk factors [2,11].

Among integrative approaches, compounds such as inositols, carnitine, arginine, *N*-acetylcysteine, chromium picolinate, alpha-lipoic acid, and corosolic acid have demonstrated metabolic benefits [12–15]. Myo-inositol (MYO) improves insulin sensitivity, lipid profile, and glucose metabolism in both polycystic ovary syndrome (PCOS) and postmenopausal women [16–18]. Corosolic acid, from *Lagerstroemia speciosa* (Banaba), also enhances insulin sensitivity and exhibits anti-inflammatory effects [12,19].

Although both compounds have shown beneficial metabolic effects, no studies have yet examined their combined action in postmenopausal women. Accordingly, we conducted a retrospective observational study to evaluate the impact of combined MYO and corosolic acid supplementation on insulin resistance in overweight or obese postmenopausal women.

Methods

Study design and participants

From the patient database of the Gynaecological Endocrinology Clinic at the University Hospital of Modena and Reggio Emilia, Modena, Italy, we retrospectively identified 31 postmenopausal women (mean age 51 ± 1.2 years, mean ± standard error of the mean [SEM]) who attended our outpatient service between January 2023 and December 2024 for symptoms related to the menopausal transition. These women specifically reported weight gain as a primary concern and sought an integrative approach, declining MHT or other pharmaceutical treatments.

Only women with completed baseline and post-treatment assessments were included. None was receiving MHT or metabolic-active medications during the study period. All participants received a 12-week daily supplementation of 2 g MYO combined with 48 mg Banaba leaf standardised to 1% corosolic acid (MBN). No structured dietary or physical activity guidance was given, and lifestyle factors were not standardised in the reported database. Adherence to the supplementation protocol was not formally monitored, although all patients included in this study self-reported to have correctly followed the integrative treatment.

Menopause was confirmed by both the absence of menstrual bleeding for ≥12 consecutive months and a hormonal profile consistent with menopause (FSH > 30 mIU/mL).

Additional inclusion criteria

1. Absence of enzymatic adrenal deficiency or other endocrine disorders, including diabetes;
2. Normal prolactin levels (5–25 ng/mL);
3. No hormonal treatments, insulin-sensitising supplements, or medications for ≥6 months prior;
4. Increased body mass index (BMI, >25 kg/m^2) with self-reported weight gain coinciding with menopausal onset.

As part of routine assessment, the Centre evaluates women with suspected metabolic impairments at baseline and after ≥12 weeks of treatment.

Oral glucose tolerance test

In addition to baseline hormonal and metabolic profiling, all patients underwent an oral glucose tolerance test (OGTT) both before and after the intervention. Tests were performed in the fasting state, with blood samples collected at baseline and at 30, 60, 90, 120, 180, and 240 minutes following ingestion of 75 g of glucose to assess glucose, insulin, and C-peptide responses. Insulin sensitivity was estimated using the Homoeostatic Model Assessment of Insulin Resistance (HOMA-IR) index [20], calculated as: HOMA-IR = fasting insulin (μIU/mL) × fasting glucose (mg/dL)]/405. A HOMA-IR value > 2.71 was used to identify insulin resistance [18,20].

Hepatic insulin extraction index (HIEI) was assessed as the ratio of plasma insulin to C-peptide concentrations (insulin/C-peptide) [21,22]. calculated at each OGTT time point. HIEI serves as an indirect marker of insulin clearance, reflecting the balance between pancreatic insulin secretion and hepatic clearance. Because C-peptide is co-secreted with insulin but not cleared by liver, it represents pancreatic insulin output alone [23–25].

The area under the curve (AUC) for glucose, C-peptide, insulin and HIEI at 240 minutes of the OGTT were computed using the trapezoid method, with baseline values subtracted.

Family history of diabetes was extracted from medical records: 18 of 31 women (58%) reported at least one first-degree relative (parent or grandparent) with diabetes, while 13 (42%) did not.

Hormonal and metabolic blood measurements

The following blood tests are routinely performed during visits: luteinizing hormone (LH), follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), estradiol (E2), total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides, alanine aminotransferase (ALT), aspartate aminotransferase (AST), fasting glucose, insulin and C-peptide.

All samples from each subject, at baseline and post-treatment, were analysed within the same assay run to minimise variability. Plasma LH and FSH were measured using a validated immunofluorometric assay (detection limit 0.1 mIU/mL) with intra- and inter-assay coefficients of variation of 4.0% and 6.0%, respectively. The intra- and inter-assay coefficients of variation for LH and FSH were 4.0% and 6.0%, respectively [26]. TSH, E2, total cholesterol, HDL-C, LDL-C, triglycerides, ALT, AST, glucose, insulin and C-peptide were determined by standard procedures at the Modena Hospital Central Laboratory. For these parameters, based on two internal quality control samples, mean intra- and inter-assay coefficients of variation were 4.3% and 10.5%, respectively.

Ethical considerations

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Approval was obtained from the local Ethics Committee 'Area Vasta Emilia Nord' (code SFRI−0015/2025). Written informed consent was secured from all participants prior to any diagnostic or clinical procedures, as is routine practice in our Clinic.

Statistical analysis

Statistical analyses were performed using QuickStatCalculations (https://www.socscistatistics.com/).

Data are presented as mean ± standard error of the mean (SEM). One-way ANOVA was applied to test for statistically significant differences between groups (before vs. after treatment), followed by Student's T test for paired or unpaired data, as appropriate. A p value ≤ 0.05 was considered as statistically significant.

Results

Table 1 summarises the hormonal and metabolic characteristics of all women included in the study. After 12 weeks of supplementation, both basal insulin and C-peptide levels showed a significant reduction. Similarly, HOMA-IR and HIEI values decreased significantly following the intervention. At baseline, 15 out of 31 patients showed fasting insulin levels above the conventional cut-off of 12 μIU/mL, and 19 women had HOMA-IR values > 2.71. After 12 weeks of supplementation, the number of patients with fasting insulin levels above 12 μIU/mL was only 10, and the HOMA-IR threshold was surpassed only by 12 women out of 31.

Table 2 presents the same parameters stratified by the presence or absence of a family history of diabetes. In both subgroups, the integrative treatment led to significant reductions in insulin levels and HOMA-IR values. However, only women with a positive family history of diabetes exhibited a significant decrease in C-peptide levels after treatment, indicating a reduction in pancreatic insulin release.

Further insights emerged during OGTT responses. For the entire cohort ($n = 31$), the glucose curve profile showed no obvious changes across time points (Figure 1, Panel A). However, a significant 23.5% reduction was observed in the area under the curve (AUC) for glucose (Figure 1, Panel B), indicating improved overall glycemic response. Regarding C-peptide, post-treatment values were significantly lower at several time points (Figure 1, Panel C), resulting in a 16.8% reduction in the corresponding AUC (Figure 1, Panel D). Similarly, the insulin response showed significant decreases at multiple time points of the OGTT following treatment (Figure 1, Panel E), with a marked 42% reduction in the AUC (Figure 1, Panel F).

A close comparison of Panels D and F in Figure 1 highlights that the decrease in insulin AUC (−42%) was greater than that of C-peptide (−16.8%). This divergence suggests differing post-treatment dynamics in the metabolism and clearance of these two peptides. HIEI values, calculated across the entire OGTT, also displayed significant reductions at multiple time points following the 12-week intervention (Figure 1, Panel G), reflecting a possible overall improvement in hepatic insulin clearance.

When OGTT was stratified based on family history of diabetes, distinct response patterns emerged. In women with a positive family history of diabetes, the glucose AUC decreased significantly by 35.5% after treatment (Figure 2, Panel B). Both C-peptide and insulin curves also showed lower responses post-treatment (Figure 2, Panels C and E), and the corresponding AUCs were significantly reduced by 26.6% and 48.5%, respectively (Figure 2, Panels D and F). HIEI values were likewise significantly reduced at several time points of the OGTT in this subgroup (Figure 2, Panel G).

In contrast, the subgroup without a family history of diabetes did not show significant changes during OGTT in either glucose or C-peptide responses following the intervention (Figure 3, Panel A and B). However, insulin levels during the OGTT were significantly reduced at multiple time points (Figure 3, Panel C), resulting in a 33.6% reduction in the insulin AUC (Figure 3, Panel D). These changes were accompanied by a significantly modified HIEI profile at several time points during the OGTT (Figure 3, Panel E).

Discussion

In our study, we observed that overweight or obese postmenopausal women usually show elevated plasma insulin levels, increased HOMA-IR, and HIEI values. After 12 weeks of integrative treatment with MBN, all these metabolic markers significantly improved. To our knowledge, this is the first study to demonstrate that this specific combination of supplements in postmenopausal women improves not only tissue insulin sensitivity but also hepatic insulin clearance, overall reducing plasma insulin levels.

It is well established that menopause leads to a decline in oestrogens, which have insulin-sensitising effects [27]. Without oestrogen support, menopause tends to worsen lipid and glucose metabolism, altering multiple homoeostatic systems [2,28]. To reinforce this concept, MHT partially restores insulin sensitivity and has even been shown to lower the risk of developing type 2 diabetes in postmenopausal women [28,29].

Table 1. Hormonal and metabolic parameters of all patients under study ($n = 31$) before and after 12 weeks of integrative treatment.

	LH mIU/mL	FSH mIU/mL	TSH µIU/mL	E2 pg/mL	Glucose mg/dL	Insulin µIU/mL	C-peptide ng/mL	Total cholesterol mg/dL	HDL-C mg/dL	LDL-C mg/dL	TG mg/dL	AST IU/L	ALT IU/L	BMI	HOMA-IR index	HIE index
Baseline																
Mean ± SEM	30.1 ± 3.3	57.6 ± 7.0	2.9 ± 0.4	28.2 ± 3.7	94.7 ± 3.1	13.1 ± 1.2	2.6 ± 0.1	207.1 ± 7.5	57.0 ± 1.7	129.3 ± 6.0	103.8 ± 10.2	23.2 ± 1.0	24.0 ± 2.5	30.4 ± 0.8	3.2 ± 0.4	5.0 ± 0.2
After treatment																
Mean ± SEM	32.2 ± 5.1	67.6 ± 10.9	2.5 ± 0.3	31.2 ± 5.9	92.9 ± 3.5	9.4 ± 0.9	2.3 ± 0.1	199.5 ± 10.4	56.8 ± 2.4	121.8 ± 8.5	104.6 ± 14.2	21.7 ± 1.3	21.3 ± 2.1	30.3 ± 1.0	2.1 ± 0.3	3.9 ± 0.3
***p* value**						**0.0005**	**0.02**								**0.001**	**0.0009**

Data are expressed as mean ± standard error of the mean (SEM); LH, luteinizing hormone; FSH, follicle stimulating hormone; TSH, thyroid stimulating hormone; E2, estradiol; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; TG, triglyceride; AST, aspartate amino transferase; ALT, alanine amino transferase; HOMA-IR, homoeostatic model assessment for insulin resistance; BMI, body mass index; HIE, hepatic insulin extraction.

Table 2. Hormonal and metabolic parameters of patients before and after 12 weeks of integrative treatment, stratified by presence of history of familial diabetes.

Familial diabetes (n=18)	LH mIU/mL	FSH mIU/mL	TSH µIU/mL	E2 pg/mL	Glucose mg/dL	Insulin µIU/mL	C-peptide ng/mL	Total cholesterol mg/dL	HDL-C mg/dL	LDL-C mg/dL	TG mg/dL	AST IU/L	ALT IU/L	BMI	HOMA-IR index	HIE index
Baseline																
Mean ± SEM	36.3 ± 4.5	65.0 ± 7.8	2.8 ± 0.5	24.2 ± 2.7	96.7 ± 4.4	14.0 ± 1.7	2.6 ± 0.1	214.1 ± 9.1	58.6 ± 2.4	135.2 ± 7.1	101.1 ± 13.0	23.0 ± 1.3	26.8 ± 3.6	29.9 ± 1.0	3.5 ± 0.5	5.2 ± 0.3
After treatment																
Mean ± SEM	37.3 ± 7.2	75.9 ± 13.9	2.5 ± 0.5	25.1 ± 5.7	94.4 ± 6.1	9.0 ± 1.3	2.1 ± 0.1	196.0 ± 13.2	56.1 ± 2.7	127.4 ± 12.1	100.2 ± 23.0	20.7 ± 1.4	18.0 ± 1.9	30.4 ± 1.6	2.2 ± 0.5	4.3 ± 0.4
***p* value**						**0.05**	**0.05**								**0.05**	
No familial diabetes (n=13)	LH mIU/mL	FSH mIU/mL	TSH µIU/mL	E2 pg/mL	Glucose mg/dL	Insulin µIU/mL	C-peptide ng/mL	Total cholesterol mg/dL	HDL-C mg/dL	LDL-C mg/dL	TG mg/dL	AST IU/L	ALT IU/L	BMI	HOMA-IR index	HIE index
Baseline																
Mean ± SEM	17.6 ± 5.2	37.5 ± 13.8	2.8 ± 0.5	86.7 ± 54.7	91.1 ± 2.8	11.0 ± 1.0	2.6 ± 0.2	194.6 ± 11.5	56.0 ± 2.6	116.1 ± 8.8	103.8 ± 16.7	23.5 ± 1.4	19.6 ± 1.8	30.1 ± 1.3	2.5 ± 0.2	4.6 ± 0.1
After treatment																
Mean ± SEM	25.4 ± 8.9	49.6 ± 21.6	2.7 ± 0.6	42.5 ± 13.3	88.4 ± 2.7	9.4 ± 1.4	2.5 ± 0.3	194.1 ± 21.5	60.0 ± 4.9	113.4 ± 15.7	103.2 ± 22.3	23.7 ± 2.9	25.0 ± 4.9	29.2 ± 1.5	1.9 ± 0.3	3.6 ± 0.3
***p* value**						**0.0001**									**0.004**	**0.01**

Data are expressed as mean ± standard error of the mean (SEM); LH, luteinizing hormone; FSH, follicle stimulating hormone; TSH, thyroid stimulating hormone; E2, estradiol; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; TG, triglyceride; AST, aspartate amino transferase; ALT, alanine amino transferase; HOMA-IR, homoeostatic model assessment for insulin resistance; BMI, body mass index; HIE, hepatic insulin extraction.

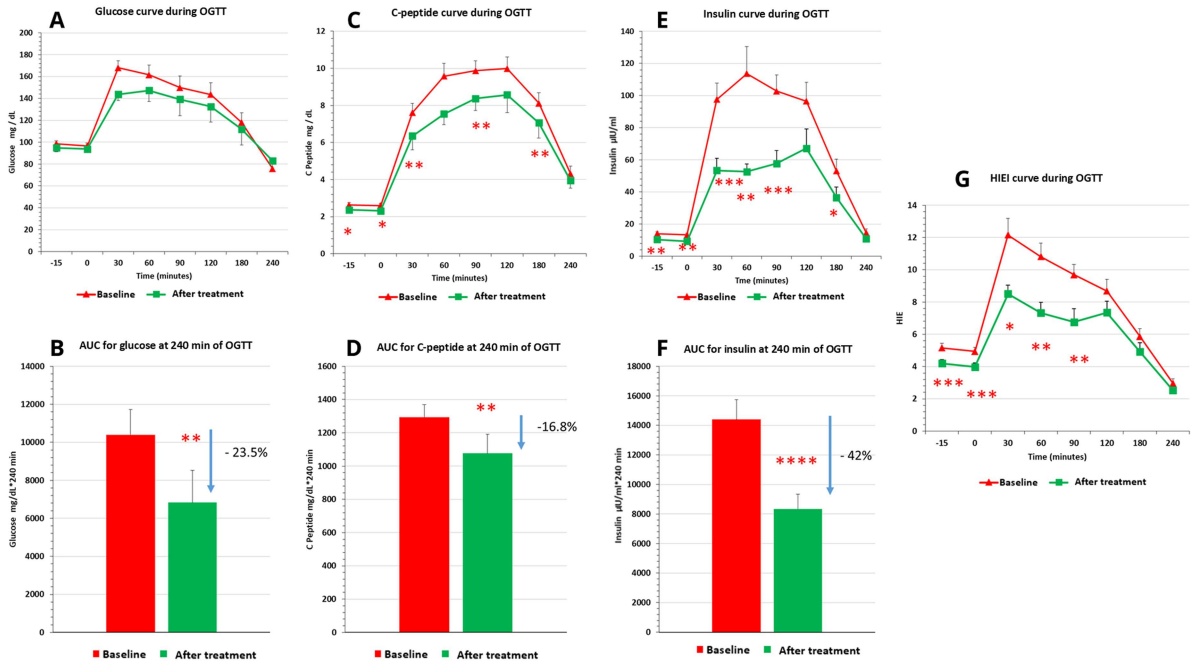

Figure 1. Glucose (Panel A), C-peptide (Panel C), and insulin (Panel E) responses during the OGTT before and after treatment, with corresponding AUCs (Panels B, D, and F), and HIEI values calculated at each OGTT time point (Panel G). *$p < 0.02$; **$p < 0.01$; ***$p < 0.001$; ****$p < 0.0001$, comparing each time point before vs. after treatment.

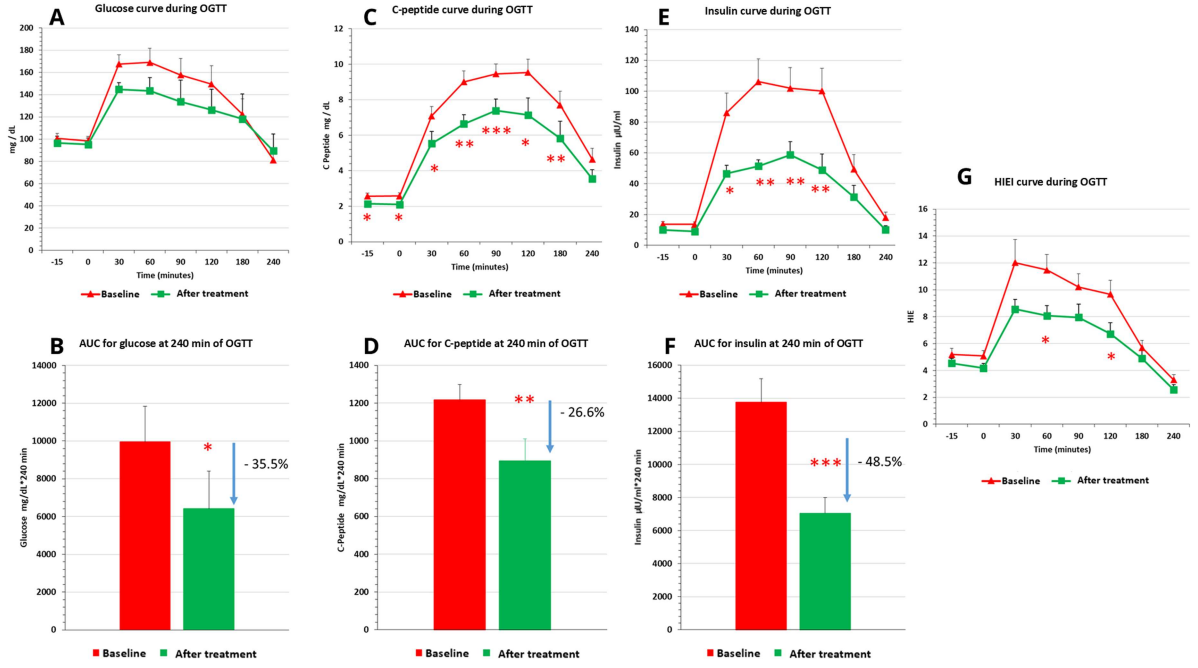

Figure 2. Glucose (Panel A), C-peptide (Panel C), and insulin (Panel E) responses during the OGTT before and after 12 weeks of treatment in patients with a family history of diabetes, with corresponding AUCs (Panels B, D, and F), and HIEI values calculated at each OGTT time point, showing marked reductions at +60 and +120 minutes (Panel G). *$p < 0.02$; **$p < 0.01$; ***$p < 0.001$, comparing each time point before vs. after treatment.

Many of the enroled patients already showed signs of early metabolic disruption at fasting: insulin levels above the conventional cut-off of 12 µIU/mL [18],considered a marker of insulin resistance in premenopausal women,were accompanied by elevated HOMA-IR indices (>2.71) [13,23].

After 3 months of treatment, fasting insulin, HOMA-IR, and HIEI values were all significantly reduced. When analysing the OGTT, glucose AUC was significantly lowered by the complementary treatment,

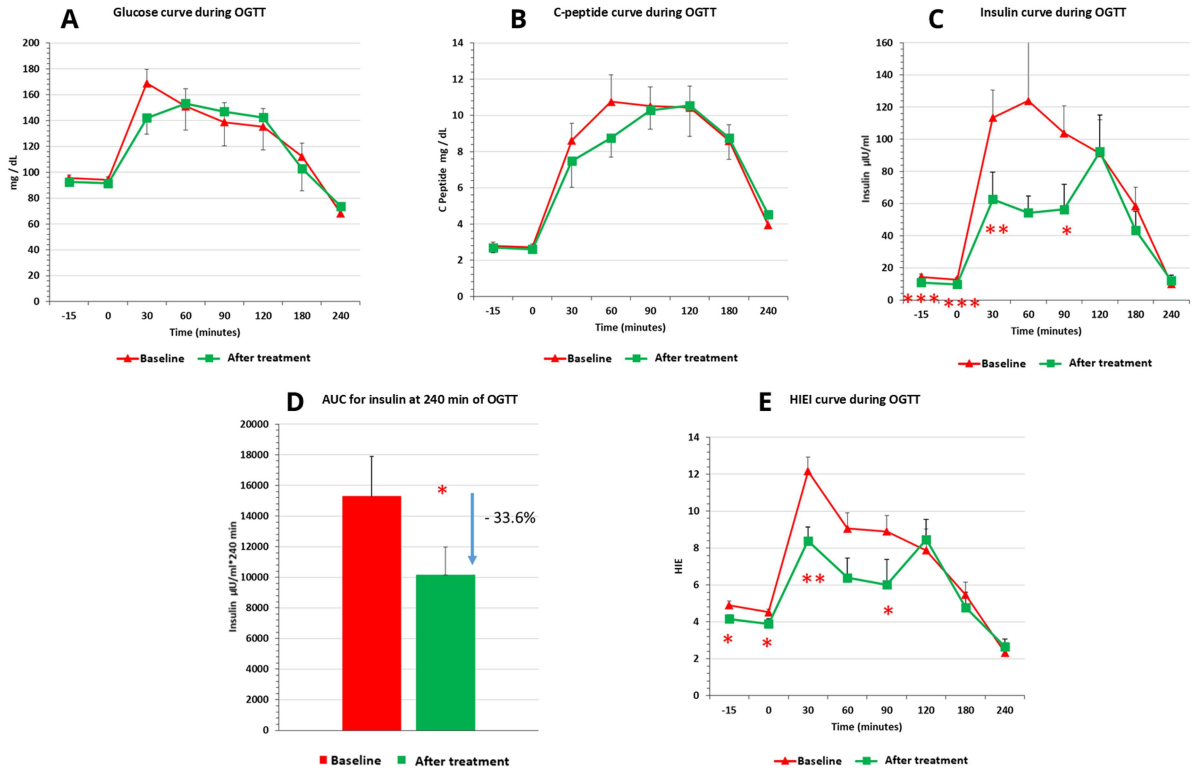

Figure 3. Glucose (Panel A), C-peptide (Panel B), and insulin (Panel C) responses during the OGTT before and after 12 weeks of treatment in patients without a family history of diabetes, with AUC calculated only for insulin (Panel D), and HIEI values determined at each OGTT time point (Panel E). *$p < 0.02$; **$p < 0.01$; ***$p < 0.001$, comparing each time point before vs. after treatment.

indicating an overall improvement in peripheral insulin sensitivity. In parallel, both insulin and C-peptide curves shifted downward, reflecting a reduction in insulin secretion. It is important to note that while insulin and C-peptide are secreted in equimolar amounts, the decline in insulin AUC was more than twice that of C-peptide. This discrepancy indicates that the insulin AUC reduction may be primarily attributed to enhanced insulin clearance rather than solely to reduced pancreatic secretion resulting from increased peripheral insulin sensitivity. Since insulin undergoes hepatic clearance while C-peptide does not, the HIEI ratio (insulin/C-peptide) serves as a reliable marker of hepatic insulin clearance and hepatocyte function. Its reduction after treatment strongly suggests that improved hepatic insulin degradation was a key contributor to the observed metabolic improvements [21].

According to our findings, myoinositol of the combined treatment improved peripheral insulin sensitivity, particularly at the skeletal muscle level, while corosolic acid likely enhanced hepatic insulin clearance [12,17]. These results for myoinositol align with prior studies in menopausal women treated with comparable doses (2 g/day), which also reported reductions in fasting insulin and HOMA-IR values [16]. Conversely, the decline in HIEI levels appears to be driven mainly by corosolic acid, consistent with its known antioxidant and anti-inflammatory actions on the liver [19].

Recently, we reported that both obesity and a family history of diabetes are associated with impaired hepatic insulin clearance [21]. In particular, a family history of diabetes can affect the function of key enzymes involved in metabolic regulation, including epimerase, lipoic acid synthase (LASY), and insulin-degrading enzyme (IDE) [21]. Epimerase converts myoinositol into D-chiro-inositol (DCI), both critical for insulin signalling and GLUT−4 translocation to the cell membrane. DCI further promotes glycogen synthesis and mitochondrial glucose oxidation, creating a favourable gradient for glucose uptake [23]. LASY, a mitochondrial enzyme, synthesises alpha-lipoic acid (ALA), a potent antioxidant with vascular, hepatic, and metabolic protective effects. Reduced LASY expression lowers intracellular ALA availability, compromising both antioxidant defenses and GLUT−4 activation [30]. IDE, predominantly expressed in the liver, mediates first-pass insulin

degradation. Impaired IDE activity decreases hepatic insulin clearance, elevating systemic insulin levels and contributing to persistent insulin resistance and hyperinsulinemia [31].

Analysing responses during OGTT, women without a family history of diabetes showed no significant changes in glucose or C-peptide curves after treatment. In contrast, both groups experienced marked reductions in insulin, HOMA-IR, and HIEI values. However, only women with a positive family history of diabetes exhibited a decrease in fasting C-peptide, indicating not only reduced pancreatic insulin secretion but also improved hepatic insulin clearance. Although women without a history of familial diabetes did not show significant changes in C-peptide during OGTT, a notable reduction in HIEI was observed, suggesting that in this subgroup the treatment primarily enhanced hepatic insulin clearance rather than suppressing pancreatic insulin production.

These findings provide new insights into menopausal insulin resistance: menopause not only reduces peripheral insulin sensitivity and alters pancreatic insulin secretion but may also impair hepatic insulin clearance mechanisms [32]. Such disruptions may be more pronounced in women with a family history of diabetes, potentially due to combined reductions in the expression or function of enzymes like epimerase, LASY, or IDE. This pattern resembles observations in obese PCOS patients with a family history of diabetes, where antioxidant therapies—including ALA, carnitines, *N*-acetylcysteine, L-arginine, or their combinations—have demonstrated significant clinical benefits [14,30].

A key strength of this study is that it is the first to evaluate the combined effects of myoinositol and Banaba (MBN) on both peripheral insulin sensitivity and hepatic insulin clearance in postmenopausal women. The dynamic assessment using OGTT with simultaneous measurements of glucose, insulin, C-peptide, and HIEI allowed detailed insight into metabolic responses. In addition, subgroup analyses based on family history of diabetes provided mechanistic understanding of differential treatment effects. Limitations include the relatively small sample size, short intervention period, and the retrospective design without a randomised control group, which may restrict generalisability and does not allow control over dietary habits, physical activity, or adherence to the treatment. Furthermore, HIEI is an indirect marker of hepatic insulin clearance, and direct measurements were not performed.

Despite this, our results highlight the potential value of combining insulin-sensitising and antioxidant supplements such as the combination of myoinositol with Banaba in addressing both insulin resistance and impaired hepatic insulin clearance. Further research in this regard is needed.

In conclusion, as observed in PCOS patients, postmenopausal insulin resistance is exacerbated by a family history of diabetes. Combined myoinositol and corosolic acid administration enhances insulin sensitivity and hepatic insulin clearance, reducing hyperinsulinemia in both fasting and during OGTT. Our findings highlight the importance of addressing insulin resistance, especially in women with a family history of diabetes, who are more prone to metabolic impairments during menopause. If left unresolved, insulin resistance may promote metabolic syndrome and long-term cardiovascular risks [2,33,34].

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Author contributions

Alessandro D. Genazzani was involved in study conception and design; Christian Battipaglia, Valeria Vescovi, Martina Foschi, Benedetta Righi, Alessandra Sponzilli, Veronica Setti, Maria Laura Rusce were involved in data collection. Alessandro D. Genazzani and Christian Battipaglia performed data analysis and draughting of the manuscript. All authors were involved in critically revising the manuscript for its intellectual content, and the final approval of the manuscript was performed by all authors.

Disclosure statement

The authors declare having no conflicts of interest.

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Data availability statement

The data supporting this study are not publicly available as they contain sensitive clinical information. All required information regarding the study protocol and anonymized collected data will be made available upon request to researchers who provide a methodologically sound proposal. Only the analysis required to achieve the aims in the approved proposal will be permitted. Proposals should be directed to Alessandro Genazzani (algen@unimo.it).

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