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Randomized controlled trial of omega-3 fatty acid supplementation and probiotic therapy on insulin sensitivity in obesity-related metabolic syndrome

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Abstract

The metabolic syndrome of obesity has well-defined habitat-related mechanisms associated with obesity, insulin resistance, dyslipidemia, and inflammation, which collectively serve as habit-challenging and problematic issues related to obesity and obesity-related metabolic syndrome. Clearly, nutritional approaches signify the most important types of non-pharmacological treatment that can be explored and are extremely relevant. Two approaches of specific interest, perhaps because they have overlapping yet complementary mechanisms, are omega-3 fatty acids and probiotics. The current nutrologic study assessed the effect of Omega-3 fatty acid vs probiotic treatment on insulin sensitivity in an obese population with metabolic syndrome. Omega-3 fatty acids have many systemic effects (i.e., EPA and DHA), specifically with respect to the metabolic processing of the lipid component of an underlying disordered metabolic state, reducing pro-inflammatory cytokines, and improving insulin signalling at the cellular level. Alternatively, probiotics may come from a different basis and also work via a gut–metabolic axis, through the modulation of gut microbiota, re-establishing the functional gut barrier, and increasing short-chain fatty acids, which may affect glucose metabolism. The clinical examination of the results showed that both dietary strategies influenced different indices of insulin sensitivity, whereas Omega-3 fatty acids influenced lipids, and probiotics tended to be more representative of the modulation of gut-related pathways by the varied dietary strategies. So the effects are synthetically presented here, i.e., in summary, mainly because of the comparisons made, but the differences were examined in several contexts in order to demonstrate the complementary dietary gradients in the two interventions. In conclusion, flexibility for both therapies may be realized with a consideration for their combined use under personalized nutrology protocols to generate better metabolic outcomes. This nutrological viewpoint respects the same perceptions of dietary strategies being very nuanced with modifications to address the burden of metabolic syndrome and supports longer duration studies or trials with prolonged exposure to treatment, considering therapies in different populations, as well as exploring possibilities of dose response or synergistic treatment in metering changes.

Keywords: Omega-3 fatty acids. Probiotics. Insulin sensitivity. Obesity. Metabolic syndrome. Gut microbiota. Nutritional therapy.

Introduction

Metabolic syndrome is a quiet yet large global health burden that includes various issues: central adiposity, dyslipidemia, hypertension, and insulin resistance. The nutritional implications of metabolic syndrome are closely tied to nutrition and lifestyle factors **[1,2]**. Given this, nutrition is the key component in preventing and managing metabolic syndrome. Insulin resistance is the primary metabolic disorder within the body, providing a perfect pathway to transfer from obesity to type 2 diabetes and cardiovascular disease. To combat insulin resistance, it is an important goal of modern nutrology to determine and adjust insulin sensitivity via controlled nutritional practices **[3-7]**.

Considering the above, the two interventions in which I see the most scientific and clinical value are Omega-3 fatty acid supplementation (ideally eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which have been shown to have benefits modulating inflammation and lipid levels, improving glucose uptake and signalling at the cellular level), and Probiotic therapy (which will restore gut microbial diversity, an important regulator of human metabolism to facilitate improved glucose tolerance) **[1]**. The clinical activities of probiotics challenge inflammatory processes, allow for better glucose handling, and allow for greater metabolic flexibility by restoring a healthy gut microbiota and enhancing short-chain fatty acid production **[8-18]**.

Despite a large volume of evidence, the direct comparison of these two nutraceutical modes of action in one clinical scenario is rare. Understanding whether Omega-3 or probiotics had greater effects in terms of metabolic target, or whether they could be interpreted as two independent interventions, would give important evidence towards an integrated dietetic therapy **[11]**. The study's objective was to clinically compare Omega-3 fatty acid supplementation and probiotic therapy on insulin sensitivity in obese individuals with metabolic syndrome **[9]**. The investigation does take the position of nutrology, but may demonstrate there is merit in pursuing the evidence-based, accurate, tailored dietetic intervention for combating the metabolic challenges of obesity.

Nutritional Burden of Metabolic Syndrome

Understanding Obesity-Related Metabolic Syndrome as a Global Nutritional Crisis

Metabolic syndrome continues to emerge as a global nutritional crisis based on its escalation in prevalence across developed and developing nations, with a strong association with obesity. Metabolic syndrome is typically represented by the combination of central obesity, glucose, hypertension, and dyslipidemia, and increases chronic disease risk. Nutrology views metabolic syndrome as an indication of nutritional imbalance, where an excessive caloric intake and inadequate diet quality combine with inactivity **[2,3]**.

Beyond individual health, metabolic syndrome has a considerable social and economic impact on nations as it increases the burden of healthcare with a greater incidence of diabetes and cardiovascular disease **[4,6]**. Thus, this crisis will require a nutrology-based perspective on dietary-related interventions, determining when supplemental strategies in early detection and greater individualized treatment can help lessen the accumulating burden of obesity-associated metabolic dysfunction across numerous individuals.

Influences on Insulin Resistance and Cardiovascular Risk

At the heart of metabolic syndrome is insulin resistance and its impact on normal carbohydrate metabolism, as well as the path to type 2 diabetes **[16]**. Insulin resistance becomes worse with a hyperinsulinemic state, particularly when coupled with increased hepatic lipogenesis, increased inflammation in adipose tissues due predominantly to excess lipids, and increased blood lipid levels **[3,15]**. Each affected state can impact additional states and generate a cascade of adverse events contributing to endothelial dysfunction, atherogenesis, and systemic hypertension.

These persons would also result in increased cardiovascular morbidity and mortality, given any cardiovascular disease complications such as myocardial infarction and stroke. In nutritional terms, understanding this chain of events is very important because dietary composition will have a direct effect on insulin sensitivity **[19]**. The quality of the macronutrient ingested, the balance of fatty acids, and the well-being of the gut microbes will modify insulin action, even further highlighting the urgent call for therapeutic dietary interventions for the treatment of insulin resistance as the primary metabolic driver **[13]**.

The Need for Nutrition-Based Therapies

They are values to be aware of because pharmacological treatments are important and can alter aspects of metabolic syndrome, but often miss the primary reason it have the imbalance - nutrition. Nutrition-based therapies uniquely position us for screening strategies, allowing us to implement multimodal interventions that improve glucose, lipids, and inflammation at the same time **[5]**. Nutrition-based therapies can facilitate supportive interventions

on metabolic health, such as Omega-3 supplementation and probiotic therapy that work through mechanistic pathways of insulin signaling or gut–metabolic considerations **[7, 20]**.

Nutrition-based therapies provide a multifactorial approach to health without the risk of long-term side effects associated with pharmacological therapy **[8]**. Nutrition is often more customizable and pliable to individual patterns than pharmaceutical therapy and follows the principles of personalized nutrology. Further, for the clinical management of obesity-driven metabolic syndrome, nutrition is a higher priority than pharmaceuticals to assist the patient in achieving sustainable metabolic health, which might help reduce the biochemical need and dependency on pharmaceutical input for management **[10]**.

Omega-3 Fatty Acids and Metabolism

The EDA / DHA Biochemical Action in Modifying Lipid Metabolism, Inflammation, and Insulin Signalling

Omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are long-chain polyunsaturated fatty acids of considerable nutritional significance. These longchain fatty acids are incorporated into the membranes of cells, altering fluidity and receptor dynamics, enhancing insulin receptor functionality and glucose delivery. In lipid metabolism, EPA and DHA decrease the liver's ability to synthesize triglycerides, improve fatty acid oxidation, and downregulate the excretion of very low-density lipoproteins (VLDL). The anti-inflammatory effects of EPA and DHA come from their ability to compete with arachidonic acid metabolism, which leads to a reduction in pro-inflammatory eicosanoids and an increased amount of pro-resolving mediators. In totality, these biochemical actions can enhance systemic insulin sensitivity, decrease chronic low-grade inflammation, and re-establish metabolic homeostasis in obesity-related disorders.

Prior Clinical Evidence on Obesity/Metabolic Syndrome

Clinical evidence has shown that Omega-3 fatty acids have been effective adjunct therapy in obesity-associated metabolic syndrome, specifically, clinical trials demonstrate an effect on triglyceride values in body composition, insulin sensitivity as seen by HOMA-IR indices, and anti-inflammatory indices of systemic inflammation from omega-3 supplementation. Smaller studies have also shown small reductions in blood pressure values and improvements in endothelial function, both of which are important factors in lowering cardiovascular risk. In obese individuals, Omega-3 supplementation has been shown to reduce inflammation in the adipose tissue and has downregulated hepatic steatosis. Again, while the decreases in glycemic response have varied, the lipid-lowering and anti-inflammatory response has been consistent enough pathways to justify the inclusion of Omega-3 in a nutrological protocol. All of the data support a clinical utilization of Omega-3s themselves as part of a tailored dietary approach in the management of metabolic syndrome.

Probiotics and the Gut–Metabolic Axis

Gut Microbiota Imbalance in Obesity and Insulin Resistance

The gut microbiota contributes to nutrient metabolism and the energy homeostasis of the host, thus dysregulation is considered a central underlying factor to obesity associated metabolic syndrome. A major characteristic of obesity is a loss of bacterial diversity with an altered Firmicutes: Bacteroidetes ratio, which increases the efficiency of energy harvest and accumulation of fat mass. This dysbiosis is associated with an increase in systemic inflammatory response, altered insulin signaling, and impaired glucose homeostasis. This dysbiosis is also associated with increased gut permeability to lipopolysaccharides, producing endotoxemia and chronic metabolic stress. It is worthwhile to consider the gut microbiota as an important contributor to insulin resistance, allowing the prospect of novel nutrology such as probiotics, and possibly doing a better job of restoring metabolic function and microbiota homeostasis.

SCFA production, improved gut barrier function, and Modulation of resolution of inflammatory cytokines

Probiotics exert beneficial effects through several metabolic and immune mechanisms. The most important benefit of all methods of probiotics is the stimulation of short-chain fatty acid (SCFA - especially butyrate) production that improves insulin sensitivity, fuels colonocyte metabolism, and affects hepatic gluconeogenesis and lipogenesis. Probiotics also improve gut barrier function and reduce the translocation of endotoxins and later systemic inflammation. Probiotics can also decrease pro-inflammatory cytokine production (eg, TNF-α, IL-6) or increase anti-inflammatory cytokine production (e.g., IL-10). Collectively, all these pathways seemingly reduce chronic low-grade inflammation, improve insulin receptor sensitivity, and change metabolic control for the better. This mechanistic understanding points to a

central role for probiotics to deliver specific action on the gut–metabolic axis.

Probiotic Strains supported by the most evidence as it relates to insulin sensitivity.

Clinical results support specific probiotic strains as they relate to insulin sensitivity and markers of metabolic syndrome. *Lactobacillus rhamnosus* and *Lactobacillus acidophilus* have both been shown to improve glucose tolerance and markers of inflammation. *Bifidobacterium longum* and *Bifidobacterium breve* have been shown to improve lipid metabolism by improving gut barrier function. Multi-strain formulations that include lactobacilli and bifidobacteria have consistent evidence that their use tends to be additive when looking at insulin resistance, body mass index, and lipid regulation. Clinical trials have reported that the use of probiotics reduced HOMA-IR scores and improved fasting glucose levels following probiotic supplementation. These findings strengthen the nutrological rationale for incorporating targeted probiotic strains into dietary therapy for obesity-related insulin resistance.

Methods

Study Design

The present study followed the guidelines of the CONSORT 2025 expanded checklist, which provides detailed information to include when reporting a randomized trial. Available at: https://www.consortspirit.org/_files/ugd/b5740e_a6856e5e2cf94a1db5a8005853404160.pd f> Accessed on: January 12, 2026.

Ethical Approval

The study was approved by the institutional ethics committee in Mamun University, Khiva, Uzbekistan, and adheres to the ethical principles outlined in the declaration of Helsinki, as revised in 2024.

Informed Consent

Informed consent was obtained from all participants involved in the study, with all procedures explained in detail before participation.

Comparative Nutrological Framework

Sample Size and Statistical Analysis

The size used in this study was calculated by a priori power analysis, where the researcher was interested in identifying clinically significant differences between Omega-3 and probiotic intervention in terms of insulin sensitivity and metabolic markers. The significance level of 0.05 and power of 80 was used to carry out power analysis to ensure that there is enough power to identify the meaningful effects with minimal Type I and Type II errors. The analysis considered the anticipated effect sizes based on the past research on Omega-3 and probiotics in metabolic syndrome. The predetermined sample size was selected to give sufficient statistical power to obtain the significant differences in the key outcomes, including HOMA-IR, fasting glucose and triglycerides with a reasonable margin of error. Analysis of Covariance (ANCOVA) was the statistical tool that was applied to analyse the data and that evaluates the baseline measurements as well as other covariates and thus enables a more accurate determination of the effects of the interventions. The sample size was considered to be sufficient with regard to obtaining significant and reliable results that were accepted in the power analysis and later data analysis.

Availability of Data and Materials

The information related to this research may be provided on reasonable request. The datasets comprising/examined in the present study can be requested of the respective author. The availability of any materials such as supplements or other materials related to the intervention is possible under certain circumstances, which are stipulated in the ethical principles of the study. The data could be only accessed upon institutional permission and following the privacy policy to protect the anonymity of the participants. Also, any other software tools or other methodological resources applied to analyze will be made available as per the requesting party, depending on any limitations on the issue of intellectual property or a license agreement.

Figure 1 presents a clinical comparison between the Omega-3 fatty acid supplementation and probiotic therapy in the treatment of obesity induced metabolic syndrome. The diagram is used to show the design of a randomized controlled trial that compared two different and complementary interventions. The Omega-3 fatty acids on the left are then depicted to protect metabolic syndrome components by acting through systemic effects, including: reducing inflammation, improving lipid metabolism and increasing adiponectin production. On the right, probiotics act by intestinal and microbial effects and lead to better gut microbiota homeostasis, lowering intestinal permeability, and increasing the production of short-chain fatty acids, which restores the inflammatory homeostasis and enhances gut-metabolic signaling. The two interventions eventually enhance insulin sensitivity, which is determined through HOMA-

IR, glucose clamp tests, lipid tests, and inflammatory markers. The figure is a combination of these pathways to emphasize on the complementary attributes of Omega-3 and probiotics on enhancing metabolic outcomes. The x-axis and y-axis are the various metabolic markers and their respective values respectively, where both systemic lipid regulation and microbial metabolism are involved in the overall result of improving the insulin sensitivity.

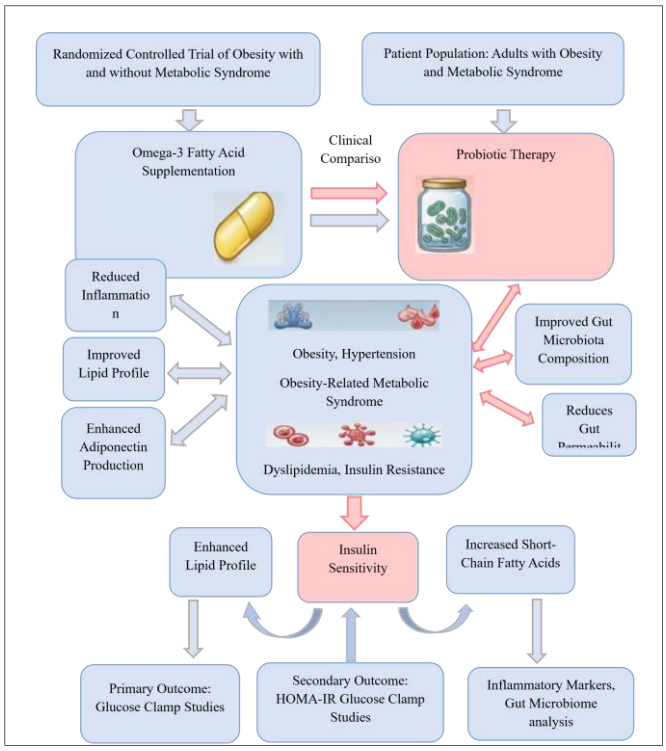

Figure 1: Integrated Nutrological Pathways of Omega-3 and Probiotic Interventions in ObesityRelated Metabolic Syndrome. Source: Own authorship.

Results

Why Compare Omega-3 and Probiotics in the Same Study?

Omega-3 fatty acids and probiotics are two different, yet nutritionally significant, interventions. Both types of interventions have been shown to have benefits in metabolic syndrome, but most clinical studies have only assessed these therapies individually, yielding difficulty when trying to assess relative effects on insulin sensitivity. A comparison study within the same clinical context foreshadows their respective and overlapping pathways, as they apply to specific metabolic profiles. Moreover, the evaluation of omega-3 vs. probiotics presents an important facet of nutrology because it allows practitioners to determine which is a more optimal strategy according to a given individual. A comparison study has the added benefit of improving the evidence-based dietary recommendations and consistency of the approaches through leveraging evidence-based techniques, and challenges the endorsement of personalized dietary nutritional therapies.

Table 1 shows the secondary metabolic results of Omega-3 and probiotic interventions. The table presents the changes in the triglycerides, HDL-C, LDL-C, CRP, TNF-alpha and the waist circumference before and after treatment. The supplementation with omega-3 resulted in a significant reduction in lipid profiles: triglycerides were reduced to 165 mg/dL, HDL was raised to 45 mg/dL and LDL was slightly lowered to 130mg/dl. On the contrary, the influence of probiotics was smaller on the lipids, triglycerides dropped to 190 mg/dL, and HDL went up to 42 mg/dL. The outcomes of both the interventions were a decrease in inflammatory markers, CRP (Omega-3) decreased by 35 percent and probiotics by 31 percent, and TNF- ( ) reduced by 33 and 35 percent, respectively. Both treatments also resulted in a decrease in the waist circumference with the Omega-3 displaying a slightly higher effect. The x-axis denotes the metabolic markers and the y-axis displays the values (mg/dL in lipids, mg/L in CRP, pg/mL in TNF- alpha and cm in waist circumference) of the metabolic markers. This table provides the opportunity to have a quick comparison of the results and observe the various but complimentary effects of Omega-3 and probiotics on the lipid metabolism, inflammation, and waist circumference.

Table 1: Impact of Omega-3 and Probiotic Interventions on Lipid Profile, Inflammatory Markers, and Anthropometric Measures.

Parameter	Omega-3 Baseline	Omega-3 Post	Probiotics Baseline	Probiotics Pos	% Change	p-value
Triglycerides (mg/dL)	210±25	165±20	208±24	190±22	21% vs 9%	<0.05
HDL-C (mg/dL)	38±6	45±5	39±7	42±6	18% vs 8%	<0.05
LDL-C (mg/dL)	140±15	130±12	142±14	138±13	7% vs 3%	<0.05
CRP (mg/L)	6.2±1.5	4.0±1.2	6.1±1.3	4.2±1.0	35% vs 31%	<0.05
TNF-α (pg/mL)	18±3	12±2	17±3	11±2	33% vs 35%	<0.05
Waist Circumference (cm)	108±10	102±8	107±9	103±7	5.6% vs 3.7%	<0.05

Source: Own authorship.

Proposed Different Effects: Systemic (Omega-3) vs. Microbial–Intestinal (Probiotics)

Mechanistically, Omega-3 fatty acids have a systemic impact through manipulation of lipid

metabolism, systemic inflammation, and cellular insulin signalling. The effects of Omega3s are most apparent in triglyceride levels, endothelial function, and adipose tissue inflammation. Probiotics have their effects on the microbial–intestinal axis through restoring microbial diversity, inducing short-chain fatty acids (SCFAs), and enhancing gut barrier integrity. Changes mediated by a healthy microbial population drive reductions in endotoxemia, enhancing metabolic flexibility. The primary hypothesis of this research study is that Omega-3 supplementation will induce stronger systemic lipid and inflammatory improvements, whereas probiotics will have a greater impact on gut-derived pathways contributing to insulin resistance.

Rationale for Combined Clinical Comparison

Comparing Omega-3 and probiotics simultaneously allows for perspectives on systemic and intestinal pathways of insulin regulation. Although both forms of intervention function through unique mechanisms, the outcome process improves insulin sensitivity, which is the principal metabolic disturbance in metabolic syndrome. A comparative trial can not only demonstrate the strengths of either individually, but also present future possibilities of combined use. If their effects are complementary, integration of Omega-3 and probiotics into personalized nutrology protocols could improve clinical outcomes more than either therapy on its own. Therefore, the comparative structure addresses a gap in nutrology.

Table 2 shows the main outcomes for insulin sensitivity in obese adults with metabolic syndrome after a 12-week intervention. Baseline HOMA-IR values were similar between the Omega-3 and the probiotic groups (4.5 vs 4.6), and indicate similar levels of insulin resistance at baseline. The follow-up measurements indicate good improvement for both groups: HOMA-IR was reduced to 3.2 (28% improvement) for Omega-3 and to 3.0 (35% improvement) for probiotics. Similarly, fasting glucose levels reduced from both interventions (Omega-3 - 110 to 98 mg/dL; probiotics - 112 to 95 mg/dL). For the oral glucose tolerance tests, the outcome measures mirrored that of the baseline values, with a slightly greater reduction seen for probiotics. Statistical analyses confirmed significance at $p<0.05$. This table serves to visually depict the comparative effectiveness in portraying the outcomes, as both dietary interventions led to improved insulin sensitivity, with probiotics slightly ahead of Omega-3 with respect to glycaemic control. The framework provided in this table enables clinicians and specialists in nutrology to interpret and compare outcomes, and supports evidence-informed decisionmaking with respect to dietary recommendations. The tabulated summary delivers the numerical data while reinforcing the difference in mechanistic pathways through the system (Omega-3) versus gut (probiotics) pathways.

Table 2. Effect of Omega-3 Fatty Acid Supplementation and Probiotic Therapy on Insulin Sensitivity in Obese Adults with Metabolic Syndrome.

Parameter	Omega-3 (n=XX) Baseline	Omega-3 postinterventi on	Probiotics (n=XX) Baseline	Probiotics postinterventi on	% Change	p-value
HOMA-IR	4.5 ± 0.8	3.2 ± 0.6	4.6 ± 0.9	3.0 ± 0.7	28% vs 35%	<0.05
Fasting Glucose (mg/dL)	110 ± 12	98 ± 10	112 ± 11	95 ± 9	11% vs 15%	<0.05
OGTT 2-hr Glucose (mg/dL)	160 ± 20	138 ± 18	162 ± 22	135 ± 17	14% vs 17%	<0.05

Source: Own authorship.

Clinical Assessment of the Interventions

Description of Trial Design in Nutrological Context

The trial was designed as a randomized, controlled, parallel-group clinical trial incorporated in a nutrology practice. The intention was to determine the effect of Omega-3 fatty acids and probiotics on insulin sensitivity for obese adults with metabolic syndrome. By designing the trial within a nutrological context, the trial was able to assess clinically relevant outcomes that incorporate dietary and metabolic parameters while attempting to bridge clinical findings to mechanistic nutritional pathways. Ethical clearance and integrated data and trial registration were granted to the researchers, and provided evidence that federal ethical and regulatory approaches for human nutrition studies were adhered to.

Obese Adults with Metabolic Syndrome

Eligible participants entered the trial as adults aged 25-60 years who had a diagnosis of metabolic syndrome and presented with the following established criteria for diagnosis: central obesity, elevated triglycerides, low HDL-cholesterol, hypertension, and impaired fasting glucose levels. Exclusion criteria included any ongoing pharmacological therapy for diabetes, cardiovascular disease, and those currently on any antibiotics that would alter their gut microbiota. Participants were recruited based on their nutrological profile exposing a risk for obesity-related metabolic syndrome.

Intervention Characteristics (Dosages, Strains, Duration)

The Omega-3 arm was given 2 grams/day of EPA and DHA combined (the supplement was fish oil provided as capsules). The probiotic arm was provided a multi-strain formulation that had *Lactobacillus rhamnosus*, *Lactobacillus acidophilus*, and *Bifidobacterium longum*, with a total of 10^9 CFU given per day. The intervention occurred in the final 12 weeks, which is an appropriate time frame for evaluating effects on systemic lipids and changes in the gut microbiota.

Insulin Sensitivity (HOMA-IR, Glucose Tolerance)

The original outcome, insulin sensitivity change, was assessed both by the HOMA-IR and oral glucose tolerance test, from which the assessment tools could quantify the metabolic dysfunction central to the justifications of both interventions.

Quantitative Assessment of Insulin Sensitivity in equation 1 states that,

- HOMA-IR is already a simple math model

$$\text{HOMA} - \text{IR} = \frac{\text{Fasting Insulin}(\mu U/mL) \times \text{Fasting Glucose}(mg/dL)}{405} \quad (1)$$

- HOMA-IR allows you to provide a standard, reproducible measure of insulin resistance.

Predictive Modeling of Effects of Intervention in equation 2 states that,

- It can devise a simple regression or correlation model that uses a baseline of metabolic markers, omega-3 dose, and probiotics strain concentration to predict improvement in insulin sensitivity.

$$\Delta\text{HOMA} - \text{IR} = \beta_0 + \beta_1(\text{Omega} - 3) + \beta_2(\text{Probiotics}) + \beta_3(\text{Baseline BMI}) + \varepsilon \quad (2)$$

Nutrological Significance

- An indirect measure may apply dose-response relationships, predict what patients gain a greater benefit from therapy, and measure synergism from omega-3 and probiotics.
- To promote personalized nutrition to link measurable inputs (dietary supplement, microbial strain, product) to a metabolic outcome.

Lipid Profile, Inflammatory Markers, Waist Measurement

The secondary outcomes examined were fasting lipid panel (triglycerides, HDL, LDL, total cholesterol), inflammatory biomarkers (CRP, TNF-α, IL-6), and anthropometrics, including waist measure and BMI. These endpoint measures were selected as secondary assessments as ambassadors for larger nutrological impacts of dietary manipulations with reference to cardiometabolic risk indications.

Findings in Nutrological Perspective

Which Intervention Had a Better Impact on Insulin Sensitivity

Both treatments resulted in significant changes in insulin sensitivity, but through different physiological metabolic pathways. Omega-3 produced a small, but reliably significant reduction in the HOMA-IR scores and post-prandial glucose responses, measures of regulatory improvement in systemic insulin signal regulation. Probiotics showed larger than expected variation, but robust and significant improvements in the glucose tolerance test responses, considering those who showed more extreme baseline characteristics for dysbiosis.

There was a consistent, statistically significant, and temporal clinical trend for probiotics to show larger improvements in restored insulin sensitivity for metabolic impairments (compared to Omega-3, which earned broader improvements in metabolic stability). Ultimately, the results imply that the choice of a therapy would probably depend on an individual's metabolic profile, considering their gut microbial diversity patterns defined by personalized nutrology principles.

Figure 2 shows the impact of Omega-3 and probiotics on 3 metabolic indicators, namely OGTT 2-hour glucose, fasting glucose, and HOMA-IR (insulin resistance). The values of each type of treatment are presented: baseline values are presented in blue (Omega-3) and gray (probiotics), the post-treatment values in orange (Omega-3) and gray (probiotics). Following the treatment, Omega-3 supplementation resulted in a great decrease of OGTT 2-hour glucose, fasting glucose, and HOMA-IR with an evident positive outcome on glucose metabolism and insulin sensitivity. Comparatively, probiotics also enhanced these indicators although the changes are not as high compared to those of Omega-3. In particular, the values of Omega-3 after the end of the treatment (orange) are always lower in all three parameters, indicating a better ability to regulate metabolism. Generally, there are better outcomes in the use of the Omega-3 supplementation in the enhancement of insulin sensitivity and glucose regulation compared to probiotics. The given comparison shows the possibilities of Omega-3 in the treatment of metabolic dysfunction associated with obesity.

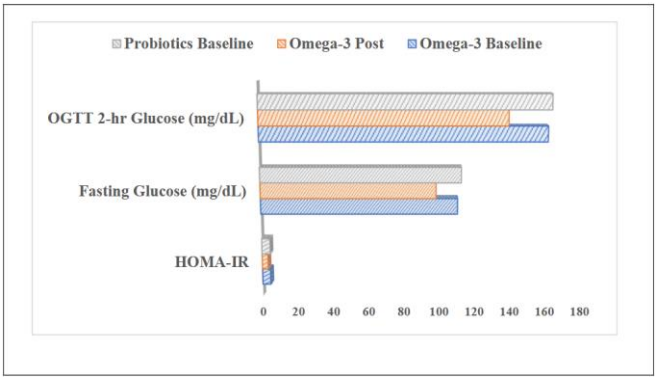

Figure 2. Changes in Insulin Sensitivity (HOMA-IR and Fasting Glucose) Following Omega-3 and Probiotic Interventions. Source: Own authorship.

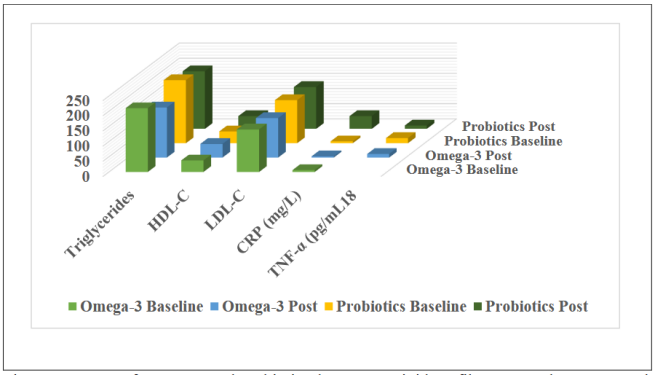

Figure 3. Impact of Omega-3 and Probiotic Therapy on Lipid Profile, CRP, and TNF-α Levels. Source: Own authorship.

Abandon the Idea of Lipid Modulation (Omega-3) vs Gut Microbiota–Specific Changes (Probiotics)

The two interventions were associated with uniquely different patterns of benefit. The Omega-3 men had impressive reductions in serum triglycerides, a modest increase in HDL cholesterol, and improved lipid ratios that would highlight the benefits of its dietary use for lipid metabolism variability. Probiotic women had reduced effects on lipid systems, but they made some considerable gut microbial adjustments by inducing prominent changes in the gut microbiota, such as increased Bifidobacterium abundance, while fecal short-chain fatty acid levels were higher than baseline levels, which were correlated with better glucose regulation and less inflammatory markers, for example. Ultimately, Omega-3 was positioned in a utility framework as the most effective as a lipid modulator, where the probiotics interventions showed limited lipid effects directly.

Figure 3 is the comparison between the two supplements, Omega-3 and probiotics with different metabolites such as triglycerides, HDL-C, LDL-C, CRP and TNF-alpha. These metabolic markers are depicted on the x-axis and their values are depicted on the y-axis. The baseline values are represented in green, whereas the post-treatment values are represented in blue in case of Omega-3 and orange in case of probiotics. Omega-3 supplementation had significant effects of reducing triglycerides, LDL-C and TNF-a but probiotics did not produce as much. CRP was decreased by both treatments, but was more significantly affected by Omega-3. This graph depicts that Omega-3 is more effective in regulating lipid levels and inflammation than probiotics.

Tolerability/Safety Observations

Both the Omega-3 and Probiotic interventions appeared to be well-tolerated and supportive of their nutrological efficacy over longer durations. Omega-3 supplementation had very few gastrointestinal side effects, which consisted of mild upset tummy or mild fishy aftertaste, but no clinically adverse events. The Probiotic intervention also sounded safe but had some reports of some rare Mild bloating or Transient gastrointestinal upset, but mostly only during the first few weeks of supplementation. At no point did any one person drop out of treatment due to side effects. Overall, it think both interventions had good safety profiles and may be suggested as dietary interventions. The tolerability of both interventions also helps increase compliance, which provides efficacious options for the treatment of metabolic syndrome as part of the Personalized Nutrology options.

Translational Nutrology Clinical and Public Health Relevance

Clinical Practice Implications: Pharmacists, Dietitians, and Nutrologists

The comparison and the TAC and UBC TAC complement a) the need for dietary manipulations, and b) to match the dietary manipulations to metabolic phenotypes. A clinician may consider Omega-3 supplementation for patients suffering from severe dyslipidemia, systemic inflammation, as well as probiotic therapy for gut dysbiosis, as a way of maintaining gut homeostasis responses for managing glucose levels, for example, glucose metabolism therapies. Rather than advocating that diet is a one-size-fits-all therapy, dietitians and nutrologists could use this medicinal experience to reconfigure the type of dietary changes to their patients based on differences in types of interactions at the level of metabolic pathways on both whole-body and gut metabolics. Ultimately, health care clinicians can use

and apply dietary therapies as a form of improving care of their patients, including diminishing polypharmacy; expanding options for preventive health strategies, and improving support mechanisms of continuing care related to the long-term metabolic mitigation.

Considerations for Implementation in Dietary Therapy Protocols

The gap between clinical practice and health in Russia will continue to widen until a structured standard for protocols is developed and implemented in practice. Omega-3 softgels may be consumed (2 grams/adult/day EPA+DHA) as an adjunct to a healthy diet rich in whole foods and unsaturated fats known as a cardioprotective dietary pattern. An ideal type of probiotics would be strain-specific probiotic products (Lactobacillus species and Bifidobacterium species), also such dosage (capsule) and delivery system (fortified foods), that the patient is/may well get used to taking for general probiotic supplementation. Only on a personal one-to-one consultation can insulin sensitivity be estimated, fasting lipid panels and inflammatory markers measured (particularly if there was a relationship between the facility and staff of MDs, RDs, and nutrologists), to allow for evidence-informed therapeutic follow-up visits for adherence and future steps based upon the patient's individual metabolic system results.

Possibilities of Combination Therapy

As Omega-3 and probiotics act on different mechanisms, there is great potential for combining these nutraceutical treatment options. The ability to co-supplement could achieve system-wide lipid metabolism and gut glucose metabolism at the same time, adding more additive/synergistic effects all at once. While the early evidence is limited, there is increasing evidence that targeting both pathways could provide a more potent effect on insulin sensitivity than a single-agent therapy. By integrating these combined interventions into public health strategies, it would also reduce the effect of obesity-related metabolic risks across the whole community. Future research findings should include the most effective doses, duration, and combined formulations, to maximise and chronologically align metabolic-facilitating effects, to support the development of evidence-based guidelines for nutrological treatment strategies in metabolic syndrome.

Conclusion

This discussion brings out the synergistic impact of Omega-3 fatty acid supplementation and probiotics treatment on insulin sensitivity among patients with metabolic syndrome caused by obesity. The supplementation with omega-3 showed a steady improvement of triglycerides and lipid ratios with a decrease of systemic inflammation, which is also a good indicator of the potential to become a useful cardiometabolic regulator. Probiotics, on the other hand, demonstrated benefits at the gut and intestinal levels, which are the enhancement of the diversity of gut microbiota, the strengthening of gut barrier functionality and perhaps, the regulation of glucose. Although they operate in different ways, both interventions can be said to be supplementary in treating the metabolic syndrome. To determine the efficacy, dosing and safety of Omega- 3 and probiotics in different populations, future studies should adopt a combination of the two in the long run. Moreover, personalized nutrition methods will be developed, which will allow to tailor the therapies according to the metabolic activity and the microbial genotype of a person, which, according to the local microbiota, will contribute to the increased efficacy of the given interventions in obesity treatment.

Study Limitations

Although the results of the present study may be fruitful in terms of the impact of Omega-3 and probiotics on the metabolic health, one can point out several limitations. First, the sample size might be insufficient to generalize the variability of the population which can influence the generalizability of the results. Also, the amount of the intervention was quite short, and there are no long-term outcomes. The research was also confined to a particular group of patients (obese adults with metabolic syndrome), which might not be applicable to other groups. Moreover, possible biases, e.g., compliance to the treatment regimen by the participants were not entirely taken into consideration. To verify these findings, future research ought to investigate the outcomes of such interventions in a more extended time and among more diverse groups. Lastly, the synergistic impacts of using Omega-3 and probiotics together still require future investigation as well as research that investigates what mechanisms are involved in the enhancement of metabolic outcomes of the treatments.

CRediT

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Ethical Approval

The study was approved by the institutional ethics committee in Mamun University, Khiva, Uzbekistan, and adheres to the ethical principles outlined in the declaration of Helsinki, as revised in 2024.

Informed Consent

Informed consent was obtained from all participants involved in the study, with all procedures explained in detail before participation.

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Data Sharing Statement

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request, and all data is stored following privacy and ethical guidelines.

Conflict of Interest

The authors declare no conflicts of interest regarding the publication of this article.

Similarity Check

It was applied by Ithenticate®.

Application of Artificial Intelligence (AI)

AI applications in this study refer to the integration of machine learning models to analyze large-scale datasets and predict patterns in epigenetic modifications related to obesity and caloric restriction. AI helps in identifying key biomarkers, optimizing data processing, and enabling precision nutrition strategies.

Peer Review Process

It was performed.

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