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Review Article

Herbal medicines and dietary supplements in clinical nutrition & metabolism

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Abstract

Herbal medicines and dietary supplements have emerged as pivotal adjuncts in clinical nutrition and metabolic health, offering bioactive compounds that modulate physiological pathways beyond basic nourishment. Unlike conventional pharmaceuticals, these agents often exert multi-targeted actions through phytochemicals, polyphenols, flavonoids, and micronutrient synergies, thereby influencing oxidative stress, inflammatory cascades, endocrine regulation, and mitochondrial bioenergetics. Contemporary evidence underscores their role in managing metabolic syndrome, diabetes mellitus, obesity, and dyslipidemia by enhancing insulin sensitivity, lipid metabolism, and gut–microbiome interactions. Moreover, nutraceutical interventions such as curcumin, omega-3 fatty acids, resveratrol, and ginseng demonstrate significant potential in attenuating chronic low-grade inflammation and promoting metabolic homeostasis. However, their integration into clinical practice remains constrained by heterogeneity in phytochemical standardization, dosage optimization, bioavailability, and inter-individual variability. Rigorous clinical trials, mechanistic investigations, and advanced pharmacokinetic modeling are essential to establish therapeutic efficacy and safety profiles. Furthermore, the interplay between herbal bioactives and conventional drugs necessitates critical evaluation to prevent adverse interactions. A translational approach linking molecular insights with evidence-based dietary strategies can refine personalized nutrition and metabolic interventions. This paradigm shift advocates for the incorporation of validated herbal medicines and dietary supplements into preventive and therapeutic frameworks, bridging the gap between traditional knowledge and modern clinical nutrition. Ultimately, leveraging these bio-resources may significantly contribute to global strategies aimed at reducing the burden of non-communicable metabolic diseases.

Keywords: Phytotherapeutics, Nutraceuticals, Metabolic Homeostasis, Bioavailability, Clinical Nutrition

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1. Introduction

Metabolic disorders constitute a major public health concern and are increasingly recognized as a global epidemic with significant morbidity, mortality, and socioeconomic impact. Conditions such as obesity, type 2 diabetes mellitus (T2DM), dyslipidemia, cardiovascular diseases (CVDs), and non-alcoholic fatty liver disease (NAFLD) share overlapping pathophysiological underpinnings including insulin resistance, systemic oxidative stress, mitochondrial dysfunction, dysregulated adipokine signaling, and chronic low-grade inflammation. These disorders not only predispose individuals to life-threatening complications such as atherosclerosis, myocardial infarction, stroke, and hepatic fibrosis but also impose substantial healthcare costs due to their progressive, relapsing nature.[1,2]

Although conventional pharmacological therapies such as antihyperglycemics, statins, antihypertensives, and lipid-lowering agents have transformed disease management, they present considerable limitations. Long-term drug administration is often associated with iatrogenic complications, hepatotoxicity, nephrotoxicity, and gastrointestinal disturbances, in addition to issues of polypharmacy and drug–drug interactions in multimorbid patients.[4] Moreover, the cost of lifelong medication regimens, coupled with reduced patient compliance, underscores the need for safer, sustainable, and more accessible alternatives. Importantly, pharmacotherapy frequently targets isolated biochemical pathways rather than addressing the multifactorial and interconnected nature of metabolic dysregulation.[5]

In this context, herbal medicines and dietary supplements have gained increasing attention as adjunctive

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or integrative interventions in clinical nutrition and metabolism. Herbal formulations, enriched with bioactive phytochemicals such as polyphenols, flavonoids, alkaloids, terpenoids, and saponins, exert pleiotropic effects by modulating key metabolic pathways. These include the activation of AMP-activated protein kinase (AMPK), enhancement of insulin receptor signaling, suppression of nuclear factor-kappa B (NF-κB)-mediated inflammatory cascades, and restoration of redox balance through antioxidant enzyme upregulation. Likewise, dietary supplements including omega-3 polyunsaturated fatty acids, probiotics, prebiotics, vitamins, and trace minerals contribute to lipid remodeling, glucose homeostasis, mitochondrial biogenesis, and gut–microbiota-derived metabolite regulation, collectively reinforcing metabolic equilibrium.[6,7]

Unlike conventional pharmacological agents that typically act on singular targets, herbal medicines and nutraceuticals often demonstrate multi-targeted and synergistic bioactivities, potentially reducing adverse outcomes and improving therapeutic compliance. However, challenges such as heterogeneity in phytochemical composition, variable bioavailability, dosage standardization, and lack of rigorous clinical validation necessitate critical scientific evaluation. Therefore, the present review aims to provide a comprehensive appraisal of herbal medicines and dietary supplements within the domain of clinical nutrition and metabolism. It will explore their molecular mechanisms of action, experimental and clinical evidence, safety considerations, and translational applicability, with the overarching goal of assessing their role as viable integrative strategies in the prevention and management of metabolic disorders.[8]

2. Herbal Medicines: Phytochemicals and Mechanisms

Herbal medicines exert therapeutic potential through a broad spectrum of phytochemicals that act on multiple molecular targets simultaneously. Unlike single-target pharmaceuticals, these compounds display pleiotropic effects, influencing redox balance, inflammatory cascades, energy metabolism, and endocrine regulation. The key classes of phytochemicals with relevance to clinical nutrition and metabolism include polyphenols, flavonoids, alkaloids, terpenoids, curcuminoids, and other specialized metabolites.[9]

2.1. Polyphenols and flavonoids

Polyphenolic compounds such as resveratrol and quercetin are well-characterized for their antioxidant and anti-inflammatory functions. Resveratrol enhances mitochondrial biogenesis through SIRT1 activation and improves insulin sensitivity, while quercetin modulates NF-κB signaling and reduces oxidative stress. Other flavonoids like catechins (from green tea) and hesperidin (from citrus fruits) improve endothelial function and lipid metabolism, contributing to cardiovascular and metabolic health.[10]

2.2. Alkaloids and terpenoids

Berberine, a protoberberine alkaloid, is recognized as an AMP-activated protein kinase (AMPK) activator, leading to improved glucose uptake and reduced hepatic gluconeogenesis, showing efficacy comparable to metformin in some clinical studies. Ginsenosides (triterpenoid saponins from Panax ginseng) enhance glucose regulation by modulating insulin signaling and promoting nitric oxide synthesis. Other notable terpenoids such as ursolic acid and oleanolic acid influence lipid metabolism and adipogenesis, thereby contributing to weight regulation.[11]

Table 1: Major Phytochemicals in herbal medicines: Sources, mechanisms, & clinical outcomes[8-11]

Phytochemical/Class	Source (Plant/Food)	Mechanism of Action	Clinical Outcomes/Findings	Source / Reference
Curcumin (Polyphenol)	*Curcuma longa* (Turmeric)	Inhibits NF-κB activation, reduces inflammatory cytokines, enhances antioxidant enzymes	Improved glycemic control, lipid profile, and reduced inflammatory markers in metabolic syndrome	[9,10]
Resveratrol (Polyphenol)	Grapes, red wine, berries	Activates SIRT1 and AMPK; enhances mitochondrial biogenesis and insulin sensitivity	Decreased fasting glucose, improved insulin resistance, and vascular function	[11,12]
Epigallocatechin gallate (EGCG)	Green tea (*Camellia sinensis*)	Antioxidant and anti-inflammatory; modulates lipid metabolism via AMPK activation	Reduction in body fat, improved LDL/HDL ratio, decreased oxidative stress	[13]
Quercetin (Flavonoid)	Onions, apples, citrus fruits	Inhibits lipid peroxidation and NF-κB; improves glucose uptake in muscle tissue	Decreased fasting glucose and oxidative biomarkers	[14]
Anthocyanins	Berries, black rice, red cabbage	Upregulates GLUT-4 expression; antioxidant and anti-obesity effects	Improved insulin sensitivity, lower triglycerides and total cholesterol	[15]

Catechins	Tea, cocoa	Enhances fat oxidation, inhibits digestive lipases	Reduced body weight, improved lipid metabolism	[15]
Lycopene (Carotenoid)	Tomatoes, watermelon	Scavenges reactive oxygen species; reduces LDL oxidation	Improved endothelial function, reduced lipid peroxidation	[16]
Omega-3 Fatty Acids (PUFAs)	Fish oil, flaxseed, chia	Anti-inflammatory, reduces hepatic triglyceride synthesis	Improved triglyceride profile, reduced inflammatory markers (CRP, IL-6)	[17]
Berberine (Isoquinoline Alkaloid)	*Berberis aristata*, *Coptis chinensis*	Activates AMPK pathway; inhibits intestinal glucose absorption	Reduced $HbA_{1}c$, fasting glucose, and LDL cholesterol similar to metformin	[17]
Ginsenosides	*Panax ginseng*	Modulates PPARγ and AMPK signaling; improves mitochondrial function	Enhanced insulin secretion and sensitivity, reduced oxidative stress	[17]
Garlic-Derived Sulfur Compounds (Allicin, S-allyl cysteine)	*Allium sativum* (Garlic)	Enhances antioxidant defense, inhibits hepatic lipid synthesis	Lowered cholesterol, improved endothelial function and insulin sensitivity	[17]
Gingerols and Shogaols	*Zingiber officinale* (Ginger)	Anti-inflammatory via COX-2 inhibition and NF-κB suppression	Improved glycemic indices and lipid parameters	[17]
Isoflavones (Genistein, Daidzein)	Soybeans, legumes	Estrogen receptor agonists; modulate lipid metabolism and insulin signaling	Improved lipid profile and endothelial function in postmenopausal women	[17]

2.3. Curcuminoids

Curcumin, derived from Curcuma longa, acts as a potent regulator of metabolic inflammation. By suppressing pro-inflammatory cytokines (TNF-α, IL-6) and enhancing adiponectin expression, curcumin improves insulin sensitivity. Its antioxidant capacity also protects pancreatic β-cells from oxidative injury, thereby supporting glucose homeostasis.[12,13]

2.4. Other Phytochemicals of relevance

Isoflavones (from soy) exert phytoestrogenic activity, beneficial for metabolic and cardiovascular regulation in postmenopausal women. Lignans (flaxseed-derived) improve lipid metabolism through modulation of hepatic enzymes. Saponins from fenugreek exhibit hypoglycemic and hypolipidemic effects, while allicin (from garlic) supports cholesterol reduction and vascular health. Carotenoids such as lycopene and β-carotene contribute to antioxidant defense and modulation of oxidative stress in metabolic syndrome.[14]

2.5. Mechanistic insights

Across phytochemical classes, converging mechanisms include:

1. Redox modulation: neutralization of reactive oxygen species (ROS), upregulation of endogenous antioxidant enzymes (SOD, catalase, glutathione peroxidase).
2. Mitochondrial bioenergetics: activation of AMPK, PGC-1α, and sirtuin pathways leading to improved oxidative phosphorylation and energy efficiency.
3. Gut–microbiota crosstalk: reshaping of microbial composition, enhancement of short-chain fatty acid production, and improvement of intestinal barrier function.
4. Hormonal and metabolic signaling: regulation of insulin, adipokines, leptin, and glucagon-like peptide-1 (GLP-1), thereby influencing glucose and lipid metabolism.

These are as indicated in Figure 1. Together, these phytochemicals provide a mechanistic basis for the clinical benefits of herbal medicines in managing metabolic disorders such as obesity, type 2 diabetes, dyslipidemia, and cardiovascular risk. The **Table 1** gives Major Phytochemicals in Herbal Medicines: Sources, Mechanisms, & Clinical Outcomes.[15-17]

3. Dietary Supplements and Clinical Nutrition

Dietary supplements constitute an evolving domain in clinical nutrition, providing concentrated sources of bioactive compounds that complement conventional diets and pharmacotherapies. Their functional role extends beyond mere nutrient replacement, as many supplements exert modulatory effects on lipid metabolism, endocrine signaling, mitochondrial bioenergetics, and the gut–organ axis. The following subsections highlight major categories of dietary supplements with established or emerging relevance in metabolic health.[18]

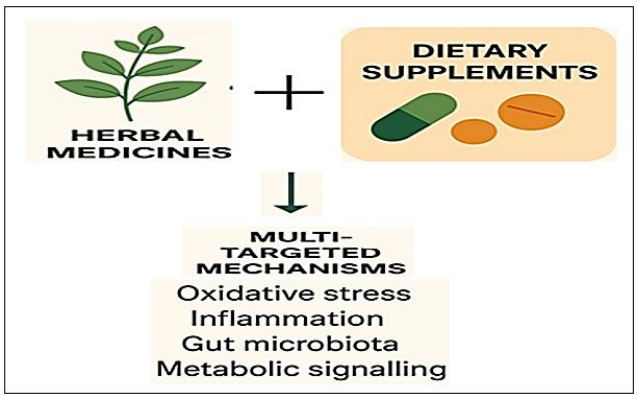

Figure 1: Mechanistic insights of herbal medicine & dietary supplements

3.1. Omega-3 fatty acids

Omega-3 polyunsaturated fatty acids (PUFAs), particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have demonstrated profound impacts on cardiometabolic health. They lower circulating triglyceride concentrations by reducing hepatic very-low-density lipoprotein (VLDL) synthesis and enhancing β-oxidation. Beyond lipid regulation, omega-3s attenuate systemic inflammation through modulation of nuclear factor-κB (NF-κB) signaling and production of specialized pro-resolving mediators such as resolvins and protectins. Furthermore, they improve endothelial function by enhancing nitric oxide bioavailability and reducing vascular oxidative stress, thereby lowering the risk of atherosclerotic progression.[19]

3.2. Probiotics and prebiotics

Probiotics (live beneficial microorganisms) and prebiotics (non-digestible substrates promoting beneficial bacterial growth) play an integral role in the gut–brain–liver metabolic axis. Clinical evidence indicates that probiotic supplementation improves insulin sensitivity by modulating short-chain fatty acid production, bile acid metabolism, and incretin release. Prebiotics such as inulin and fructo-oligosaccharides selectively enhance commensal populations, counteracting dysbiosis associated with obesity and metabolic syndrome. The combined administration as synbiotics has shown synergistic effects, particularly in reducing hepatic steatosis, chronic inflammation, and endotoxemia.[20]

3.3. Micronutrients

Micronutrients—comprising essential vitamins and trace elements—play indispensable roles in maintaining cellular metabolism, enzymatic regulation, and hormonal balance. Their deficiencies or suboptimal levels contribute significantly to metabolic dysfunctions such as insulin resistance, dyslipidemia, and chronic inflammation. The synergistic interactions between vitamins and minerals often determine the efficiency of metabolic pathways, energy utilization, and redox stability.[21]

Vitamin D acts beyond calcium regulation, exerting pleiotropic effects on insulin secretion, adipogenesis, and immune modulation. It enhances pancreatic β-cell function and increases insulin sensitivity in peripheral tissues via vitamin D receptor (VDR)-mediated transcriptional regulation. Deficiency of vitamin D has been correlated with higher risk of type 2 diabetes, metabolic syndrome, and cardiovascular morbidity. Magnesium serves as a cofactor for more than 300 enzymes involved in ATP generation, glucose transport, and insulin receptor phosphorylation. Low magnesium status impairs tyrosine kinase activity of the insulin receptor and augments oxidative stress, promoting insulin resistance and endothelial dysfunction. Chromium, in its trivalent form, potentiates insulin signaling by enhancing insulin receptor kinase activity and facilitating glucose uptake via GLUT-4 translocation. Clinical studies show that chromium supplementation improves glucose tolerance and glycated hemoglobin in insulin-resistant subjects. Among trace elements, zinc is crucial for insulin synthesis, storage, and secretion. It stabilizes insulin hexamers in pancreatic β-cells and protects them from oxidative injury. Zinc deficiency leads to altered lipid metabolism and impaired antioxidant defense. Selenium, incorporated into selenoproteins such as glutathione peroxidase, regulates redox homeostasis and thyroid hormone metabolism, thereby influencing energy expenditure and lipid oxidation.[21-22]

Iron, though vital for oxygen transport and mitochondrial respiration, requires tight regulation; iron overload can catalyze reactive oxygen species formation, contributing to insulin resistance and hepatic steatosis. Collectively, these micronutrients function as integral cofactors in glucose and lipid metabolism, antioxidant defense, and endocrine regulation. Optimal intake through diet or supplementation—guided by metabolic profiling—is essential for restoring homeostasis and reducing the burden of metabolic diseases.

Table 2 integrates these micronutrients under the broader category of dietary supplements influencing clinical nutrition and metabolism.[22]

3.4. Protein and amino acid supplements

Protein supplementation, particularly in the form of whey and soy isolates, improves muscle protein synthesis and enhances satiety, thereby contributing to weight management. Branched-chain amino acids (BCAAs; leucine, isoleucine, valine) directly activate the mammalian target of rapamycin (mTOR) pathway, promoting anabolic responses in skeletal muscle and modulating glucose uptake. L-carnitine facilitates the transport of long-chain fatty acids into mitochondria for β-oxidation, improving energy metabolism and potentially ameliorating fatigue and sarcopenia in metabolic disease states.[23]

3.5. Fiber supplements

Dietary fiber supplementation, including psyllium husk and β-glucans, exerts hypoglycemic and hypocholesterolemic

effects by delaying gastric emptying, enhancing satiety, and promoting colonic fermentation to yield short-chain fatty acids. These metabolites improve gut barrier function, modulate lipid metabolism, and reduce systemic inflammation.[24]

3.6. Antioxidant and polyphenol supplements

Compounds such as coenzyme Q10, α-lipoic acid, and green tea catechins act as potent antioxidants that reduce mitochondrial oxidative stress and improve endothelial health. Resveratrol supplementation has been associated with activation of sirtuin-1 (SIRT1), enhancing mitochondrial function and mimicking caloric restriction effects in metabolic regulation.[24]

3.7. Emerging supplements

Novel dietary interventions include collagen peptides for joint and muscle health, betaine for homocysteine regulation, and plant sterols/stanols for cholesterol reduction. Additionally, adaptogenic botanicals such as ashwagandha and rhodiola are gaining recognition for their roles in stress resilience and metabolic balance, though rigorous clinical evidence is still evolving.[26]

Dietary supplements represent a diverse group of bioactives that influence metabolism through multiple biochemical and physiological mechanisms. While omega-3 fatty acids, probiotics, vitamin D, and protein supplements are supported by substantial clinical evidence, other agents such as polyphenols, trace minerals, and adaptogens are emerging candidates requiring further exploration. Their integration into clinical nutrition should be guided by individualized metabolic profiling, safety considerations, and robust clinical validation.

Table 2 gives Dietary Supplements and Their Roles in Clinical Nutrition and Metabolism.[27,28]

Table 2: Dietary supplements and their roles in clinical nutrition & metabolism[21-26]

Micronutrient / Class	Dietary Source	Mechanism of Action	Clinical Outcomes / Findings	Source / Reference
Vitamin D (Cholecalciferol)	Sunlight exposure, fortified dairy, fish liver oil	Regulates insulin secretion via VDR activation; improves β-cell function and insulin sensitivity	Improved glucose tolerance, reduced inflammatory markers, better metabolic profile in deficiency states	[21,36]
Vitamin E (Tocopherols)	Nuts, seeds, vegetable oils	Lipid-soluble antioxidant; protects membranes from peroxidation	Decreased oxidative stress and improved lipid profile in metabolic syndrome	[21]
Vitamin C (Ascorbic acid)	Citrus fruits, guava, amla, berries	Enhances collagen synthesis, regenerates vitamin E, reduces oxidative stress	Improved endothelial function, reduced inflammation and HbA_1c	[21,22]
B-Complex Vitamins (B1, B6, B12, Folate)	Whole grains, pulses, leafy vegetables, eggs	Coenzymes in carbohydrate metabolism, methylation, and red blood cell formation	Reduced homocysteine levels, improved energy metabolism, and neuroprotection	[21]
Magnesium	Whole grains, legumes, green leafy vegetables, nuts	Cofactor for >300 enzymes; improves insulin receptor phosphorylation and glucose uptake	Enhanced insulin sensitivity, reduced blood pressure and HbA_1c	[21,36]
Chromium (Cr^{3+})	Whole grains, broccoli, nuts	Potentiates insulin receptor kinase activity; enhances GLUT-4 translocation	Improved glucose tolerance and insulin sensitivity; reduced HbA_1c in type 2 diabetes	[21,36]
Zinc	Meat, fish, seeds, legumes	Essential for insulin synthesis, storage, and secretion; antioxidant function	Improved glycemic control and lipid profile; antioxidant protection to β-cells	[21,24]
Selenium	Brazil nuts, seafood, cereals	Component of selenoproteins; regulates thyroid hormones and antioxidant enzymes	Improved redox balance and reduced inflammation; dose-dependent metabolic effects	[21]

Iron	Red meat, lentils, green vegetables	Oxygen transport, mitochondrial respiration; component of cytochromes	Maintains energy metabolism; excess may induce oxidative stress and insulin resistance	[21,22]
Calcium	Dairy products, leafy greens, fortified foods	Secondary messenger in hormonal and metabolic signaling	Supports bone and metabolic health; low levels linked to obesity and insulin resistance	[21,23]
Potassium	Fruits (banana, orange), vegetables	Regulates blood pressure and electrolyte balance	Decreased risk of hypertension and cardiovascular complications	[21,25]
Iodine	Iodized salt, seafood	Required for thyroid hormone synthesis; regulates energy metabolism	Normalized thyroid function and basal metabolic rate	[21,26]

4. Evidence from Clinical Studies

Clinical investigation of herbal medicines and dietary supplements in metabolic disorders has progressed from small exploratory trials to an expanding corpus of randomized controlled trials (RCTs) and meta-analyses. Collectively, this literature signals therapeutic promise but is characterised by heterogeneity in product identity, dose, formulation, study populations and endpoints.[29]

4.1. Diabetes mellitus (type 2)

Randomized trials and pooled meta-analyses indicate that several phytotherapeutics produce clinically meaningful improvements in glycaemic indices (fasting plasma glucose, postprandial glucose, and HbA_1c) relative to placebo. Notably, berberine a plant isoquinoline alkaloid has been repeatedly evaluated in RCTs and meta-analyses showing reductions in fasting glucose and HbA_1c approaching those reported for first-line oral antidiabetics in short-term studies, with concomitant improvements in insulin sensitivity and homeostatic indices. Curcumin and polyphenol-rich extracts (e.g., green tea catechins, cinnamon polyphenols) have demonstrated moderate glycaemic benefits, often via anti-inflammatory and insulin-signalling modulation. However, trials vary in duration and baseline glycaemic control, and many exclude participants on complex polypharmacy, limiting generalisability to multimorbid clinical populations.[30]

4.2. Obesity and weight management

Interventional studies on weight outcomes reveal modest but reproducible benefits for several nutraceuticals when paired with lifestyle interventions. Mechanistic candidates include green tea extracts (thermogenic polyphenols), capsaicinoids (appetite and energy-expenditure modulators), and fiber supplements (satiety enhancers). Some RCTs report small reductions in body weight and waist circumference versus control, but effect sizes are typically modest and often transient. Trials that demonstrate larger weight loss commonly combine supplements with dietary counselling and increased physical activity, emphasising that supplements act as adjuncts rather than stand-alone anti-obesity therapies.[31]

4.3. Dyslipidemia

Omega-3 polyunsaturated fatty acids (PUFAs) show strong, consistent evidence for triglyceride lowering in meta-analyses of RCTs, with dose-responsive effects. Plant sterols/stanols reduce LDL-cholesterol when incorporated into food matrices. Red yeast rice containing monacolin K produces appreciable LDL reductions similar to low-dose statin therapy in multiple trials, though product variability and regulatory considerations complicate interpretation. Phytosterol trials typically demonstrate predictable LDL lowering, but effects on hard cardiovascular outcomes remain less well-defined in supplement-specific trials.[32,33]

4.4. Metabolic syndrome (clustered risk factors)

Trials targeting composite metabolic syndrome endpoints are fewer; however, several nutraceuticals (berberine, omega-3, certain probiotic strains) have shown concurrent improvement across glycaemia, lipids and inflammatory biomarkers in short-to-medium term studies. Heterogeneity of diagnostic criteria and endpoint definitions across studies makes pooling difficult, but meta-analytic signals favour multi-target phytotherapeutics for partial syndrome amelioration.[34,35]

4.5. Other dietary supplements in clinical nutrition

A variety of dietary supplements beyond the principal categories of omega-3 fatty acids, probiotics, and polyphenols contribute meaningfully to metabolic regulation. These include vitamins, minerals, amino acids, and fibers that act through diverse mechanisms affecting endocrine, inflammatory, and oxidative pathways.[36]

Vitamin D supplementation has been extensively studied for its role in glucose and lipid metabolism. Randomized controlled trials reveal modest improvements in insulin sensitivity and β-cell function, particularly in individuals with baseline deficiency. Its immunomodulatory and anti-inflammatory actions help reduce low-grade systemic

inflammation that underpins metabolic syndrome. However, optimal dosing, duration, and patient stratification remain areas of active research. Magnesium plays a central role in glucose utilization and oxidative phosphorylation. Supplementation in magnesium-deficient or insulin-resistant individuals has shown improvements in fasting glucose, HbA_{1c}, and blood pressure. The effect appears greater in populations with low baseline intake or concurrent vitamin D insufficiency, suggesting nutrient interdependence. Chromium (picolinate or nicotinate forms) supplementation exerts modest but consistent improvements in glucose tolerance, insulin sensitivity, and lipid parameters, especially in type 2 diabetes and polycystic ovarian syndrome. Long-term safety and inter-individual variability warrant further exploration.[36,37]

Probiotics and Prebiotics continue to demonstrate growing clinical relevance in metabolic regulation. Their metabolic benefits stem from modulation of gut microbiota composition, increased short-chain fatty acid (SCFA) production, improved intestinal barrier function, and reduced endotoxemia. Strain-specific probiotics—such as Lactobacillus rhamnosus and Bifidobacterium longum—have been associated with reduced inflammation and improved insulin sensitivity. Prebiotics like inulin and fructo-oligosaccharides foster beneficial bacterial growth, while synbiotic combinations amplify metabolic and immunological outcomes. L-Carnitine and Branched-Chain Amino Acids (BCAAs) contribute to improved mitochondrial fatty-acid oxidation and energy metabolism. L-Carnitine facilitates the transport of long-chain fatty acids into mitochondria for β-oxidation, thereby reducing lipid accumulation in liver and muscle tissues. Although some studies show enhanced exercise tolerance and reduced fatigue, results on glycemic and lipid outcomes remain variable. BCAAs, especially leucine, stimulate the mTOR signaling pathway, supporting muscle protein synthesis and glucose uptake; however, excessive intake may aggravate insulin resistance in predisposed individuals, emphasizing dose-dependent caution.[36]

Dietary Fiber supplementation—soluble fibers such as psyllium, β-glucans, and inulin—exerts consistent hypoglycemic and hypocholesterolemic effects. Fiber delays gastric emptying, increases satiety, and undergoes fermentation in the colon to produce SCFAs, which improve insulin sensitivity and lipid metabolism. High-fiber interventions also lower postprandial glucose peaks and reduce systemic inflammation through gut-derived signaling. Antioxidant Supplements such as coenzyme Q10, α-lipoic acid, and resveratrol mitigate oxidative stress by enhancing mitochondrial integrity and redox balance. α-Lipoic acid, in particular, regenerates endogenous antioxidants (vitamin C, vitamin E, and glutathione) and improves endothelial function in diabetic neuropathy. CoQ10 supplementation supports mitochondrial ATP synthesis and may reduce statin-associated myopathy. In synthesis, these supplements address distinct yet interrelated aspects of metabolic dysfunction—oxidative stress, inflammation, dysbiosis, and insulin resistance. While evidence supports their adjunctive roles, clinical application must consider baseline nutritional status, comorbidities, and potential interactions. Integrating these agents within personalized nutrition frameworks can maximize therapeutic efficacy while minimizing risks.[36,37]

4.6. Promising interventions

1. Berberine appears to activate AMP-activated protein kinase (AMPK), improving hepatic glucose output and peripheral insulin sensitivity; head-to-head short-term trials report glycaemic effects comparable to metformin in selected cohorts, but long-term safety and interaction data remain limited.[38]

2. Curcumin exerts pleiotropic anti-inflammatory and antioxidant effects that translate into modest improvements in glycaemic control and surrogate markers of metabolic inflammation, though bioavailability constraints temper clinical potency.[39]

3. Omega-3 PUFAs are among the most robust supplements for triglyceride reduction; high-dose formulations reliably lower TG but effects on LDL and HDL are variable and depend on EPA/DHA ratio.[40]

5. Safety, Bioavailability, and Interactions

The clinical translation of herbal medicines and dietary supplements is often constrained by issues related to pharmacokinetics, pharmacodynamics, and safety monitoring. While numerous phytochemicals and nutraceuticals demonstrate promising effects in vitro and in preclinical models, their efficacy in humans is frequently undermined by inadequate absorption, rapid metabolism, and unpredictable interactions with conventional therapies. A comprehensive understanding of these challenges is crucial to ensure their rational and safe application in clinical nutrition and metabolic health.[41]

5.1. Challenges of absorption and bioavailability

Several phytoconstituents, such as curcumin, resveratrol, and quercetin, exhibit potent bioactivity but suffer from poor oral absorption, extensive first-pass metabolism, and rapid systemic clearance. Similar challenges are observed in dietary supplements like omega-3 fatty acids (susceptible to oxidation) and fat-soluble vitamins (A, D, E, K), which require optimal dietary fat for absorption. Moreover, gastrointestinal pH, enzymatic activity, and gut microbiota composition significantly influence the pharmacokinetics of both herbal compounds and dietary nutrients. This variability contributes to inconsistent clinical outcomes and highlights the necessity for optimized formulations.[42]

5.2 Novel delivery approaches

To overcome these limitations, innovative delivery platforms have been developed. Nanoparticles, polymeric micelles, liposomes, solid lipid carriers, and phyosome complexes markedly enhance solubility, stability, and intestinal uptake of poorly bioavailable compounds. For instance, curcumin nanoparticles exhibit improved plasma concentrations and prolonged systemic retention, while omega-3 nanoemulsions enhance oxidative stability and absorption. Additionally, probiotic-engineered formulations are emerging as bioenhancers, facilitating targeted delivery and synergistic modulation of gut microbiota, which directly impacts metabolic regulation.[43]

5.3. Drug–herb and drug–nutrient interactions

Herbal medicines and dietary supplements may alter the pharmacokinetics of prescription drugs by modulating cytochrome P450 isoenzymes, transport proteins, and enterohepatic recycling. For example, ginseng can potentiate or diminish the anticoagulant effect of warfarin, whereas St. John's wort induces CYP3A4, reducing the bioavailability of drugs such as cyclosporine and certain antidiabetic agents. Similarly, high-dose vitamin K supplementation may counteract the therapeutic effect of warfarin, and excessive magnesium or calcium intake can impair antibiotic absorption. Such interactions necessitate vigilant monitoring, particularly in polypharmacy contexts common in metabolic disease management.[44]

5.4. Toxicity risks and quality concerns

Unregulated supplements pose substantial risks due to variability in botanical sourcing, adulteration with synthetic drugs, contamination with heavy metals or pesticides, and mislabeling of active ingredients. Case reports have documented hepatotoxicity from certain green tea extracts and nephrotoxicity from improperly processed aristolochic acid-containing botanicals. Similarly, excessive intake of fat-soluble vitamins or high-dose amino acid supplements may result in toxicity. The absence of globally harmonized regulations exacerbates these risks, underscoring the importance of stringent quality assurance, good manufacturing practices (GMP), and validated analytical methods for phytochemical standardization.[45,46]

5.5. Integrating safety into clinical nutrition

Safety assessment must extend beyond herbal formulations to include dietary supplement use in clinical nutrition protocols. For example, while probiotics and prebiotics are generally regarded as safe, inappropriate strains or contamination can lead to infections in immune compromised patients. Similarly, excessive protein or branched-chain amino acid supplementation may exacerbate renal dysfunction in susceptible individuals. Therefore, personalized risk–benefit evaluation, guided by metabolic profiling and clinical monitoring, should form the foundation for incorporating herbal medicines and dietary supplements into therapeutic nutrition strategies.[47]

6. Translational Perspectives

The successful incorporation of herbal medicines and dietary supplements into clinical nutrition and metabolism requires a translational framework that bridges mechanistic insights with patient-centered applications. Phytotherapeutics possess inherently complex mixtures of bioactive molecules, and their integration into personalized nutrition must move beyond generalized recommendations toward stratified approaches. Tailoring interventions according to individual genetic predispositions, metabolic phenotypes, and lifestyle determinants ensures optimized efficacy and minimizes the risk of adverse responses. The paradigm of precision medicine offers powerful tools to refine these strategies. Metabolomics enables high-resolution profiling of metabolic signatures that reflect real-time physiological states, thereby identifying responders and non-responders to specific phytochemicals. Nutrigenomics elucidates gene–nutrient interactions, providing insights into how polymorphisms in metabolic enzymes or transporters influence bioactive utilization. Simultaneously, microbiome profiling highlights the critical role of gut microbial consortia in modulating the biotransformation, absorption, and systemic effects of herbal-derived metabolites. Such multi-omics integration lays the groundwork for evidence-based personalization of nutraceutical therapies.[48,49]

From a public health perspective, phytotherapeutics present opportunities for cost-effective and culturally acceptable interventions, particularly in resource-limited settings. Their accessibility and alignment with traditional practices enhance community acceptance, yet ensuring affordability without compromising quality remains a major challenge. The widespread clinical translation is constrained by regulatory bottlenecks. The absence of harmonized standards in phytochemical characterization, dosage uniformity, and bioequivalence testing undermines reproducibility. Strengthening quality assurance systems through validated analytical methodologies, establishing standardization protocols, and developing evidence-based guidelines are indispensable for mainstream clinical adoption. A globally harmonized regulatory framework can foster both innovation and patient safety, enabling phytotherapeutics and dietary supplements to evolve from complementary remedies into validated pillars of clinical nutrition and metabolic medicine.[50]

7. Future Directions

7.1 Multi-omics approaches to elucidate mechanisms

Emerging omics platforms including genomics, transcriptomics, proteomics, metabolomics, and microbiomics provide powerful tools to dissect the complex, multi-targeted actions of herbal bioactives. These approaches

can reveal how phytochemicals influence gene expression, modulate signaling pathways, and reshape host–microbiome interactions. Systems biology integration of omics datasets will enable the construction of holistic metabolic networks, clarifying the precise molecular underpinnings of nutraceutical interventions.[51]

7.2. Large-scale, multi-center randomized controlled trials (RCTs).

Despite promising preclinical and small-scale clinical studies, evidence remains fragmented due to heterogeneity in formulations, dosages, and study designs. Multi-center RCTs with robust methodological rigor are essential to validate efficacy, establish optimal dosing regimens, and define long-term safety profiles across diverse populations. Harmonized trial designs and international collaborations could accelerate the generation of high-quality evidence, facilitating regulatory approval and clinical adoption.[52]

7.3 AI-driven personalized supplement regimens.

Artificial intelligence and machine learning have the potential to transform nutritional therapeutics by integrating omics data, lifestyle factors, and clinical parameters to generate individualized supplement strategies. Predictive modeling could optimize phytochemical combinations, anticipate drug–herb interactions, and enhance adherence through precision-tailored recommendations. Such digital health platforms would align herbal and dietary supplement interventions with the paradigm of personalized medicine.[53,54]

7.4 Bridging traditional knowledge with modern evidence-based nutrition.

Traditional systems of medicine, such as Ayurveda, Traditional Chinese Medicine, and ethnobotanical practices, embody centuries of experiential insights into diet–health relationships. Scientific validation of these practices through modern pharmacological, clinical, and nutritional sciences can unlock novel bioactives and therapeutic frameworks. A bidirectional approach respecting cultural heritage while applying rigorous evidence-based methodologies will foster sustainable integration of traditional wisdom into contemporary clinical nutrition. The advancing the field demands interdisciplinary collaboration that unites omics sciences, clinical research, computational modeling, and ethnomedicine. Such integrative strategies hold the promise of redefining the role of herbal medicines and dietary supplements in promoting metabolic health at both individual and population levels.[55-57]

8. Conclusion

Herbal medicines and dietary supplements have emerged as integral adjuncts in the landscape of clinical nutrition and metabolic health. Unlike single-target pharmacological interventions, these bio-resources provide a spectrum of bioactive compounds capable of modulating multiple biochemical and physiological pathways simultaneously. Their pleiotropic effects on oxidative stress regulation, inflammatory cascades, mitochondrial dynamics, gut–microbiota composition, and hormonal signaling highlight their potential in addressing complex metabolic disorders such as diabetes, obesity, dyslipidemia, and metabolic syndrome. Despite compelling preclinical and clinical evidence, challenges remain that hinder their systematic integration into evidence-based medical practice. Variability in phytochemical composition, lack of standardized formulations, inconsistent dosing regimens, and limited bioavailability significantly restrict translational outcomes. Furthermore, the risk of herb–drug interactions and safety concerns associated with unregulated supplements demand rigorous pharmacovigilance. Establishing validated biomarkers of efficacy, advanced delivery platforms to improve bioavailability, and harmonized regulatory frameworks will be pivotal in bridging the gap between traditional knowledge and modern clinical applications. The future of these therapeutic agents lies in multidisciplinary collaboration across nutrition science, pharmacology, molecular biology, and clinical medicine. Incorporating precision tools such as metabolomics, nutrigenomics, and microbiome profiling can help personalize interventions and optimize therapeutic outcomes. Large-scale, well-designed randomized controlled trials are essential to substantiate long-term efficacy and safety, enabling healthcare professionals to recommend these interventions with confidence. Ultimately, herbal medicines and dietary supplements represent more than supportive care; they embody a paradigm shift toward integrative, sustainable, and culturally adaptable solutions for metabolic health. When validated through scientific rigor and safeguarded by regulatory oversight, these bio-resources have the potential to significantly reduce the burden of non-communicable diseases and advance global strategies for preventive and therapeutic nutrition.

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None.

10. Conflict of Interest

None.

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