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TARGETING INFLAMMATORY AND METABOLIC DISORDERS WITH NATURAL PRODUCTS: PHARMACOLOGICAL ADVANCES AND MECHANISTIC INSIGHTS

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ABSTRACT

Inflammatory and metabolic disorders, including diabetes mellitus, cardiovascular diseases, and obesity, represent leading causes of global morbidity and mortality. Current pharmacotherapies for these conditions are associated with significant limitations, including adverse effects, treatment resistance, and high costs. Natural products have emerged as promising therapeutic agents for these disorders, offering multi-targeted mechanisms, favorable safety profiles, and potential for disease modification. This review comprehensively examines recent pharmacological advances in natural products targeting inflammatory and metabolic disorders, focusing on their mechanisms of action and therapeutic potential. We critically evaluate natural products exhibiting anti-inflammatory and antioxidant properties that modulate key pathways including NF-κB, Nrf2, AMPK, and the NLRP3 inflammasome. Evidence for the efficacy of natural products in managing diabetes through insulin sensitization, glucose uptake enhancement, and alpha-glucosidase inhibition is assessed. Furthermore, we review natural products targeting cardiovascular disease through lipid modulation, blood pressure regulation, and vascular protection. The roles of curcumin, resveratrol, berberine, quercetin, and various polyphenols in metabolic regulation are examined in detail. Despite promising preclinical data, clinical translation has been challenged by bioavailability and standardization issues. This review identifies research gaps, evaluates emerging trends, and discusses strategies for optimizing the therapeutic potential of natural products for inflammatory and metabolic disorders.

Keywords: Natural Products; Inflammation; Metabolic Disorders; Diabetes; Cardiovascular Disease; Polyphenols

1 INTRODUCTION

Inflammatory and metabolic disorders, including type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), and obesity, are leading causes of mortality and reduced quality of life worldwide (Nainu et al., 2023). These conditions are often interconnected, with chronic low-grade inflammation serving as a common pathogenic mechanism. Currently, the incidence of metabolic disorders is increasing, setting a challenge to global health (Nainu et al., 2023). The global burden of these disorders continues to rise, driven by lifestyle changes, aging populations, and urbanization.

Metabolic syndrome (MetS) is a cluster of metabolic defects comprising hypertension, insulin resistance, visceral obesity, fatty liver, and atherogenic cardiovascular diseases (Metabolic syndrome: risk factors, 2023). Lifestyle

modification is the first step for controlling MetS progression. If left untreated, MetS is significantly related to a high danger of evolving type 2 diabetes and atherogenic cardiovascular diseases. Thus, MetS is a prominent cause of morbidity and mortality internationally and has become very important to investigate novel therapies in this context to decrease the heavy burden of the disease (Metabolic syndrome: risk factors, 2023).

Current pharmacotherapies, including metformin, statins, and anti-inflammatory agents, have demonstrated efficacy but are associated with significant limitations. Adverse effects, treatment resistance, and high costs compromise therapeutic outcomes and accessibility. There is no single treatment for MetS and the currently available pharmacotherapy and related comorbidities demand the continued use of multiple drugs that is challenging for patients as the polypharmacy and reduced accordance (Metabolic syndrome: risk factors, 2023). The need for new therapeutic approaches that target multiple pathways and offer disease-modifying potential has stimulated interest in natural products.

Natural products have long been used in traditional medicine systems for treating inflammatory and metabolic conditions. Chemicals isolated from natural products have been extensively studied as prospective drug candidates to manage diabetes, obesity, heart-related diseases, and cancer, partly due to their antioxidant and anti-inflammatory properties (Nainu et al., 2023). Modern pharmacological investigation has validated many of these traditional uses and revealed diverse mechanisms of action. Natural products offer the advantages of multi-targeted activity, favorable safety profiles, and potential for disease modification. One of the most focused natural products research areas is the potential application of phytochemicals to treat diabetes, obesity, cardiovascular-related problems, and different types of cancers (Nainu et al., 2023).

This review provides a comprehensive examination of recent pharmacological advances in natural products targeting inflammatory and metabolic disorders, focusing on mechanisms of action and therapeutic potential.

2 INFLAMMATORY PATHWAYS IN METABOLIC DISORDERS

2.1 Chronic Inflammation in Metabolic Disease

Chronic low-grade inflammation is a hallmark of metabolic disorders, characterized by elevated circulating pro-inflammatory cytokines and activation of inflammatory signaling pathways. Although much has been known regarding the etiology and pharmacological management of these metabolic disorders, the mechanistic basis is complex and remains to be fully elucidated. Nevertheless, chronic inflammation appears to be one of the key players in the initiation, progression, and transition of metabolic disorders including diabetes mellitus, obesity, heart-related diseases, and cancer (Nainu et al., 2023).

Stimulation of various pro-inflammatory cytokines in response to the release of endogenous yet danger-associated ligands have been observed to occur in most metabolic disorders-related conditions (Nainu et al., 2023). The activation of the NF-κB pathway and production of TNF-α, IL-6, and IL-1β drive insulin resistance and metabolic dysfunction. Shared signaling pathways in obesity and type 2 diabetes contain the pivotal players in glucose and lipid metabolism, including AMPK, PI3K/AKT, FGF21, Hedgehog, Notch, and WNT, as well as the inflammation response through Nrf2, MAPK, NF-κB, and JAK/STAT (Shared signaling pathways, 2022).

2.2 Oxidative Stress and Metabolic Dysfunction

Oxidative stress, resulting from an imbalance between reactive oxygen species (ROS) production and antioxidant defense, contributes to metabolic dysfunction. ROS activate inflammatory pathways, impair insulin signaling, and promote endothelial dysfunction. The Nrf2 pathway is a key regulator of antioxidant defense and represents a therapeutic target. Early research used chemical models to assess the antioxidant capacity of different phytochemicals, which provided important information about the health potential. This led to findings in the anti-inflammatory properties and modulatory effects of cell signaling of phytochemicals (Xiao et al., 2022).

2.3 AMPK Pathway in Metabolic Regulation

AMP-activated protein kinase (AMPK) is a central regulator of energy homeostasis, activated by metabolic stress and regulating glucose and lipid metabolism. AMPK activation promotes glucose uptake, fatty acid oxidation, and mitochondrial biogenesis, while inhibiting lipogenesis and gluconeogenesis. AMPK is a key therapeutic target for metabolic disorders. Natural products have been explored as good templates of AMPK activators (Natural activators of AMPK, 2022). In recent years, different therapeutic agents from natural products and herbal medicines have been explored as good templates of AMPK activators (Natural activators of AMPK, 2022). These natural products enhance the sensitivity of AMPK and alleviate sub complications or different pathways by which such AMPK triggers can be addressed (Chauhan et al., 2022).

2.4 NLRP3 Inflammasome in Metabolic Inflammation

The NLRP3 inflammasome is a critical mediator of inflammatory responses in metabolic disorders. Polyphenols have been shown to be effective in the treatment of metabolic diseases, including anti-inflammation, anti-diabetes, anti-obesity, neuron-protection, and cardio-protection (Effectiveness of targeting NLRP3, 2023). The progress of natural polyphenols preventing inflammation and metabolic disorders via targeting NLRP3 inflammasome has been systemically summarized (Effectiveness of targeting NLRP3, 2023). Polyphenols can regulate the whole NLRP3 inflammasome pathway in cardiometabolic diseases (Villalva et al., 2023).

Table 1: Key Pathways in Inflammatory and Metabolic Disorders

Pathway	Function	Role in Disease	Therapeutic Target
NF-κB	Pro-inflammatory signaling	Promotes inflammation and insulin resistance	Inhibition beneficial
Nrf2	Antioxidant response	Protects against oxidative stress	Activation beneficial
AMPK	Energy homeostasis	Regulates glucose and lipid metabolism	Activation beneficial
NLRP3 Inflammasome	Inflammatory mediator	Triggers cytokine release in metabolic disease	Inhibition beneficial
PI3K/AKT	Insulin signaling	Regulates glucose uptake and metabolism	Enhancement beneficial

3 NATURAL PRODUCTS WITH ANTI-INFLAMMATORY ACTIVITY

3.1 Curcumin

Curcumin, the active constituent of turmeric (Curcuma longa), has demonstrated potent anti-inflammatory activity through multiple mechanisms. It has been shown in numerous clinical trials that curcumin exhibited anti-diabetic, lipid-lowering, antihypertensive, antioxidant and anti-inflammatory effects, as well as promoting weight loss (Curcumin - The Nutraceutical, 2022). Zingiberaceae plants/curcumin consumption can mainly improve metabolic syndrome, non-alcoholic fatty liver disease, cardiovascular disease, and some chronic inflammatory diseases (Vafaeipour et al., 2022).

Due to their anti-inflammatory and antioxidant properties, turmeric and its constituent curcumin have antidiabetic effects through increasing insulin release and increasing fatty acid uptake (Vafaeipour et al., 2022). Curcumin exerts its anti-proliferative properties via a variety of mechanisms, including the suppression of inflammatory signaling pathways. Curcumin has been studied for its regulation of micro-RNA and epigenetic factors in the treatment of cancers and metabolic disorders.

Prominent polyphenols described in the literature include curcumin, along with aspalathin, berberine, catechins, chlorogenic acid, genistein, piperine, quercetin, and resveratrol (Biomolecules, 2022). These polyphenols may stimulate adiponectin levels, offering potential protection against the development of insulin resistance, inflammation and NAFLD as well as associated conditions of metabolic syndrome (Biomolecules, 2022).

However, clinical translation has been limited by poor bioavailability. Curcumin has low oral bioavailability due to poor absorption and rapid metabolism. Nanotechnology-based delivery and synthetic modifications are being explored to overcome this limitation.

3.2 Resveratrol

Resveratrol, a polyphenol found in grapes and berries, has demonstrated anti-inflammatory, antioxidant, and immunomodulatory activities (Resveratrol and Gut Microbiota, 2023). Resveratrol exerts beneficial properties in the modulation of cardiovascular and metabolic disorders. In healthy individuals, it maintains an ergogenic capacity, prevents oxidative stress, and modulates the inflammatory response (Resveratrol and Gut Microbiota, 2023).

The anti-inflammatory effect of resveratrol has been examined in various organs affected by obesity such as liver, skeletal muscle, kidney, heart and brain (Ghahremani et al., 2023). Resveratrol has been suggested to possess anti-inflammatory and immunomodulatory activities (Ghahremani et al., 2023). The compound activates SIRT1, a NAD-dependent deacetylase, modulating inflammatory gene expression and metabolic regulation.

Resveratrol has shown promise in preclinical models of metabolic disorders, improving insulin sensitivity and reducing inflammation. Clinical trials have yielded mixed results, likely due to bioavailability and dosing issues. Resveratrol's effects on sphingolipid metabolism and signaling in cardiometabolic risk and disease have been explored, focusing on oxidative stress and inflammatory-related aspects (Teimouri et al., 2023). Anti-inflammatory effects of resveratrol in patients with cardiovascular disease have been evaluated in systematic reviews and meta-analyses of randomized controlled trials (Teimouri et al., 2023).

3.3 Berberine

Berberine, an isoquinoline alkaloid found in Berberis species, has demonstrated anti-inflammatory and metabolic regulatory activities. Berberine activates AMPK, improving insulin sensitivity and lipid metabolism. The use of berberine in patients with MetS and related disorders appeared to significantly decrease several inflammatory markers (The effects of berberine, 2022). Berberine has shown multiple pharmacological activities, including anti-inflammatory and antioxidative effects (Yarmohammadi et al., 2022).

Berberine has been extensively studied in metabolic disorders, with clinical trials demonstrating improvements in glycemic control and lipid profiles. The compound has been used in Chinese medicine for centuries and is increasingly accepted as a nutraceutical. Berberine can decrease apoptosis and inflammation following different pathological conditions, which might be mediated by targeting ER stress pathways (Yarmohammadi et al., 2022). The protective potential of berberine against several diseases, such as metabolic disorders, cancer, intestinal diseases, and cardiovascular and liver diseases, has been reviewed (Yarmohammadi et al., 2022).

Berberine, a herbal metabolite in the metabolic syndrome, has been studied for its effects on risk factors, course, and consequences of the disease (Och et al., 2022). The pharmacological and nanotechnological aspects of berberine have also been reviewed (Behl et al., 2022).

3.4 Quercetin

Quercetin, a flavonoid widely distributed in fruits and vegetables, has demonstrated anti-inflammatory and antioxidant activities. Quercetin has significant anti-diabetic effects and may be helpful in lowering blood sugar and increasing insulin sensitivity (Quercetin: an effective polyphenol, 2023). Various studies have shown that quercetin has beneficial therapeutic effects in various human diseases, including diabetes (Quercetin: an effective polyphenol, 2023).

The antioxidant and anti-inflammatory abilities of quercetin and its application in oxidative stress-related disorders have been outlined in detail (Advance in pharmacological effects of quercetin, 2023). Quercetin supplementation has reducing effects on systolic blood pressure and insulin levels but not other cardiometabolic parameters (Arabi et al., 2023). Quercetin has also demonstrated anticancer, antioxidant, antimicrobial, antidiabetic and anti-inflammatory effects (An insight into quercetin, 2023).

3.5 Other Polyphenols and Phytochemicals

Natural polyphenols are widely found in cocoa beans, tea, vegetables, fruits, and some Chinese herbal medicines; they are a class of plant compounds containing a variety of phenolic structural units, which are potent antioxidants and anti-inflammatory agents in plants (Wang et al., 2022). Polyphenols are composed of flavonoids (such as flavanols, anthocyanidins, anthocyanins, isoflavones, etc.) and non-flavonoids (such as phenolic acids, stilbenes, and lignans) (Wang et al., 2022).

Modern pharmacological studies have proved that polyphenols can reduce blood pressure, improve lipid metabolism, lower blood glucose, and reduce body weight, thereby preventing and improving metabolic syndrome (Wang et al., 2022). Due to the unique characteristics and potential development and application value of polyphenols, these natural polyphenols could treat metabolic syndrome, including their chemical properties, plant sources, and pharmacological action against metabolic syndrome (Wang et al., 2022).

Plant-derived agents known to be immunomodulators that can affect both innate and adaptive immunity include thymoquinone, curcumin, punicalagin, resveratrol, quercetin, and genistein (Prevention and Treatment, 2022). These compounds have been highlighted for their role in the management of inflammation associated with obesity (Prevention and Treatment, 2022).

Table 2: Key Natural Products Targeting Inflammatory and Metabolic Disorders

Compound	Source	Primary Activity	Key Mechanisms	Clinical Evidence
Curcumin	*Curcuma longa*	Anti-inflammatory	NF-κB inhibition, Nrf2 activation, AMPK modulation	Strong
Resveratrol	Grapes, berries	Anti-inflammatory, antioxidant	SIRT1 activation, NF-κB inhibition	Moderate
Berberine	*Berberis* species	Metabolic regulation	AMPK activation, NF-κB inhibition	Strong
Quercetin	Fruits, vegetables	Anti-inflammatory, antioxidant	NF-κB inhibition, Nrf2 activation	Moderate
Polyphenols	Various plants	Anti-inflammatory, antioxidant	Multiple pathway modulation	Moderate to Strong

4 NATURAL PRODUCTS TARGETING DIABETES

4.1 Insulin Sensitization

Insulin resistance is a hallmark of T2DM, and improving insulin sensitivity is a key therapeutic strategy. Natural products including berberine, curcumin, and various polyphenols have demonstrated insulin-sensitizing effects. Metabolic syndrome therapy with phytochemicals is an emerging field of study with therapeutic potential (Gauttam et al., 2023). Obesity, insulin resistance, high blood pressure, and abnormal lipid profiles are all components of metabolic syndrome, which is a major public health concern across the world (Gauttam et al., 2023).

New research highlights the promise of phytochemicals found in foods, including fruits, vegetables, herbs, and spices, as a sustainable and innovative method of treating this illness (Gauttam et al., 2023). Anti-inflammatory, antioxidant, and insulin-sensitizing qualities are just a few of the many positive impacts shown by bioactive substances (Gauttam et al., 2023). Collectively, they alleviate the hallmark symptoms of metabolic syndrome by modulating critical metabolic pathways, boosting insulin sensitivity, decreasing oxidative stress, and calming chronic low-grade inflammation (Gauttam et al., 2023).

Flavonoids show potential for decreasing insulin resistance (IR), thereby delaying the progression of diabetes and accompanying metabolic syndromes (Zhou et al., 2023). The mechanisms of flavonoids decreasing insulin resistance have been reviewed (Zhou et al., 2023). Food polyphenols and type II diabetes mellitus have been studied, with an overview of the most recent developments in using food polyphenols for managing and treating type II diabetes mellitus, along with various mechanisms to reduce insulin resistance (Food Polyphenols and T2DM, 2023).

4.2 Glucose Uptake Enhancement

Natural products that enhance glucose uptake in peripheral tissues represent important antidiabetic agents. Berberine activates AMPK, reducing hepatic glucose production and improving insulin sensitivity. Polyphenols from green tea and other sources have demonstrated glucose uptake enhancement in muscle and adipose tissue. Phytochemicals provide a multimodal strategy by targeting not only adipose tissue but also the liver, skeletal muscle, and vascular endothelium, all of which have a role in the pathogenesis of metabolic syndrome (Gauttam et al., 2023).

4.3 Alpha-Glucosidase Inhibition

Alpha-glucosidase inhibitors delay carbohydrate absorption, reducing postprandial hyperglycemia. Natural products including acarbose, from Actinoplanes species, are clinically used as alpha-glucosidase inhibitors. Plant-derived compounds, including flavonoids and phenolic acids, have demonstrated alpha-glucosidase inhibitory activity. The antidiabetic action of traditional plants is mostly attributed to their antioxidant and anti-inflammatory properties (Naturally-occurring carboxylic acids, 2023).

4.4 Phytochemical-Gut Microbiota Interactions

The molecular basis of phytochemical-gut microbiota interactions has been explored, demonstrating that dysbiosis-associated molecular pathology perpetuates metabolic disorders, disrupting host energy regulation, and triggering inflammatory signaling cascades, insulin resistance, and metabolic dysfunction (Lal et al., 2023). Bioactive metabolites influence host cellular pathways, inflammation, and metabolic processes. These effects include improved insulin

sensitivity, lipid metabolism regulation, and suppression of chronic inflammation, highlighting the therapeutic potential of phytoconstituents against metabolic abnormalities (Lal et al., 2023).

The paradigm shift in phytochemicals research has evolved from antioxidant capacity to anti-inflammatory effects and to roles in gut health and metabolic syndrome (Xiao et al., 2022). Recent advances in the role of diet in modulating gut microbiota have suggested a new phase of food bioactives research along the phytochemicals-gut microbiota-intestinal metabolites-low-grade inflammation-metabolic syndrome axis (Xiao et al., 2022). Polyphenols and carotenoids were discussed in-depth, and future research directions were also provided (Xiao et al., 2022).

5 NATURAL PRODUCTS TARGETING CARDIOVASCULAR DISEASE

5.1 Lipid Modulation

Dyslipidemia is a major risk factor for CVD, and lipid-modifying natural products have been extensively studied. Berberine reduces LDL cholesterol and triglycerides through AMPK activation and PCSK9 regulation. Curcumin has demonstrated lipid-lowering effects in clinical trials (Curcumin - The Nutraceutical, 2022). Plant sterols and stanols reduce cholesterol absorption, lowering LDL cholesterol.

Polyphenols can reduce blood pressure, improve lipid metabolism, lower blood glucose, and reduce body weight, thereby preventing and improving metabolic syndrome (Wang et al., 2022). Natural foods are potential therapeutics in the management of the metabolic syndrome (Metabolic syndrome: risk factors, 2023).

5.2 Blood Pressure Regulation

Natural products with antihypertensive effects include various polyphenols and plant extracts. Quercetin supplementation has reducing effects on systolic blood pressure (Arabi et al., 2023). Polyphenols can reduce blood pressure through multiple mechanisms including ACE inhibition, vasodilation, and endothelial function improvement (Wang et al., 2022).

5.3 Vascular Protection

Natural products exert vascular protective effects through antioxidant, anti-inflammatory, and endothelial function improvement mechanisms. Resveratrol improves endothelial function through eNOS activation and oxidative stress reduction (Teimouri et al., 2023). Flavonoids from cocoa and berries enhance endothelial function and reduce arterial stiffness.

In phytochemicals research, early studies used chemical models to assess the antioxidant capacity of different phytochemicals, which provided important information about the health potential. This led to findings in the anti-inflammatory properties and modulatory effects of cell signaling of phytochemicals (Xiao et al., 2022). The bioprotective effects of polyphenols on metabolic syndrome against oxidative stress have been documented (Xiao et al., 2022).

6 COMBINED METABOLIC AND ANTI-INFLAMMATORY EFFECTS

6.1 Metabolic-Inflammatory Crosstalk

The metabolic and anti-inflammatory effects of natural products are often interconnected, reflecting the common pathogenic mechanisms of metabolic disorders. Natural products that activate AMPK also reduce inflammation, while anti-inflammatory compounds may improve metabolic function. The multi-targeted activity of natural products provides advantages over single-target therapies.

Recent progress in the role of inflammatory-mediated responses on the initiation of metabolic disorders has been discussed, with particular reference to diabetes mellitus, obesity, heart-related diseases, and cancer (Nainu et al., 2023). The prospective role of natural products in the management of these conditions has been highlighted, with lists of potential biological targets for high throughput screening in drug discovery and development (Nainu et al., 2023).

6.2 Disease-Modifying Potential

Natural products offer potential for disease modification beyond symptomatic management. The modulation of inflammatory and metabolic pathways may slow disease progression and reduce complications. The long-term safety of natural products supports their use in chronic disease management. Increasing evidence suggests that these natural chemicals may be useful in controlling metabolic syndrome as a complementary treatment to standard medication or lifestyle changes (Gauttam et al., 2023).

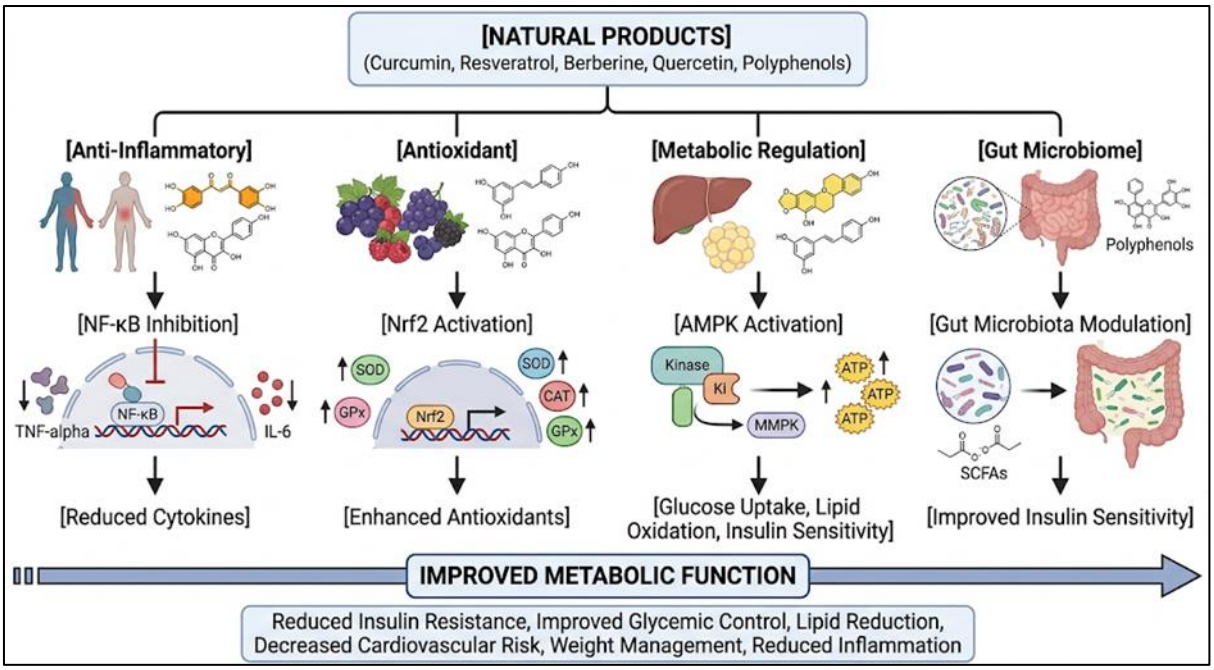

Figure 1: Natural Product Mechanisms in Inflammatory and Metabolic Disorders

7 CHALLENGES AND RESEARCH GAPS

7.1 Bioavailability

Poor bioavailability remains a significant limitation for many natural products. Curcumin and resveratrol are notable examples with low oral bioavailability. Nanotechnology-based formulations, analogs, and co-administration with absorption enhancers are being explored to address this limitation. Continuous efforts have been made in parallel to improve their bioactivity and bioavailability using selected drug delivery approaches (Nainu et al., 2023).

7.2 Standardization

The variability in natural product composition due to species, growing conditions, and processing presents standardization challenges. The lack of standardized extracts complicates clinical trial interpretation and clinical use. Analytical methods and quality control are essential for ensuring consistency.

7.3 Clinical Translation

The translation of preclinical findings to clinical practice has been challenging, with mixed results in clinical trials. The limitations of bioavailability, dosing, and trial design contribute to inconsistent results. Findings observed in preclinical and clinical studies prior to identifying suitable approaches on the phytochemical drug delivery systems that are potential to be used in the treatment of metabolic disorders have been discussed (Nainu et al., 2023). The identification of biomarkers and patient selection strategies may improve clinical outcomes.

8 FUTURE PERSPECTIVES

The future of natural products for inflammatory and metabolic disorders lies in the integration of emerging technologies and personalized approaches. The application of multi-omics and systems pharmacology will enable comprehensive characterization of natural product mechanisms and identification of therapeutic targets. The development of optimized formulations, including nanotechnology-based delivery systems, will address bioavailability limitations. The identification of predictive biomarkers will enable patient stratification and personalized therapy.

The integration of natural products with conventional pharmacotherapies, including synergistic combinations, represents a promising direction. The continued exploration of traditional medicine knowledge may reveal novel therapeutic agents and mechanisms. The role of the gut microbiota in mediating the effects of natural products on metabolic health represents an emerging frontier that warrants further investigation.

9 CONCLUSION

Natural products offer significant therapeutic potential for inflammatory and metabolic disorders through diverse mechanisms including anti-inflammatory, antioxidant, and metabolic regulatory activities. Curcumin, resveratrol, berberine, quercetin, and various polyphenols have demonstrated efficacy in preclinical models and clinical trials. The multi-targeted mechanisms of natural products, including NF-κB inhibition, Nrf2 activation, AMPK activation, and NLRP3 inflammasome modulation, address the multiple pathogenic pathways underlying metabolic disorders. The emerging understanding of phytochemical-gut microbiota interactions has opened new avenues for therapeutic intervention. Despite significant challenges, including bioavailability and standardization, emerging technologies and optimized formulations promise to enhance the therapeutic potential of natural products. Continued research and development are essential for translating these promising agents into effective therapies for inflammatory and metabolic disorders.

REFERENCES

[1] Arabi, S. M., Malekahmadi, M., Kakhki, R. D., Moradi, S., & Islam, S. M. S. (2023). The effects of quercetin supplementation on cardiometabolic outcomes: An umbrella review of meta-analyses of randomized controlled trials. *Phytotherapy Research*, *37*(11), 5080–5091. https://doi.org/10.1002/ptr.7972

[2] Behl, T., Sharma, A., Sharma, L., Sehgal, A., Zengin, G., Bungau, S., & Bollen, C. (2022). Expatiating the pharmacological and nanotechnological aspects of the alkaloidal drug berberine: Current and future trends. *Molecules*, *27*(12), Article 3705. https://doi.org/10.3390/molecules27123705

[3] Chauhan, S., Sharma, A., & Kumar, U. (2022). Natural activators of AMPK signaling: Potential role in the management of type-2 diabetes. *Journal of Diabetes and Metabolic Disorders*, *22*(1), 895–908. https://doi.org/10.1000/s40200-022-01123-x

[4] Gauttam, V. K., Munjal, K., Chopra, H., Ahmad, A., Rana, M. K., & Kamal, M. A. (2023). A mechanistic review on therapeutic potential of medicinal plants and their pharmacologically active molecules for targeting metabolic syndrome. *Current Pharmaceutical Design*, *29*(32), 2541–2558. https://doi.org/10.2174/1381612829666230911142512

[5] Ghahremani, H., Bahramzadeh, A., Bolandnazar, K., Emamgholipour, S., Hosseini, H., & Meshkani, R. (2023). Resveratrol as a potential protective compound against metabolic inflammation. *Journal of Nutrition and Metabolism*, *2023*, Article 6632190. https://doi.org/10.1155/2023/6632190

[6] Hyder, A. (2023). Naturally-occurring carboxylic acids from traditional antidiabetic plants as potential pancreatic islet FABP3 inhibitors: A molecular docking-aided study. *Journal of Biomolecular Structure and Dynamics*, *41*(18), 8820–8831. https://doi.org/10.1080/07391102.2022.2132311

[7] Lal, S., Sayeed Akhtar, M., Faiyaz Khan, M., Aldosari, S. A., Mukherjee, M., & Sharma, A. K. (2023). Molecular basis of phytochemical-gut microbiota interactions. *Drug Discovery Today*, *28*(12), Article 103824. https://doi.org/10.1016/j.drudis.2023.103824

[8] Liu, Y., & Wang, J. (2023). Food polyphenols and type II diabetes mellitus: Pharmacology and mechanisms. *Molecules*, *28*(10), Article 3996. https://doi.org/10.3390/molecules28103996

[9] Nainu, F., Frediansyah, A., Mamada, S. S., Permana, A. D., Salampe, M., Chandran, D., Emran, T. B., & Simal-Gandara, J. (2023). Natural products targeting inflammation-related metabolic disorders: A comprehensive review. *Heliyon*, *9*(6), Article e16919. https://doi.org/10.1016/j.heliyon.2023.e16919

[10] Nani, A., & Tehami, W. (2023). Targeting inflammasome pathway by polyphenols as a strategy for pancreatitis, gastrointestinal and liver diseases management: An updated review. *Frontiers in Nutrition*, *10*, Article 1157572. https://doi.org/10.3389/fnut.2023.1157572

[11] Och, A., Och, M., Nowak, R., Podgórska, D., & Podgórski, R. (2022). Berberine, a herbal metabolite in the metabolic syndrome: The risk factors, course, and consequences of the disease. *Molecules*, *27*(4), Article 1351. https://doi.org/10.3390/molecules27041351

[12] Patel, R., & Sharma, S. (2023). Metabolic syndrome: Risk factors, diagnosis, pathogenesis, and management with natural approaches. *Food Chemistry Advances*, *3*, Article 100335. https://doi.org/10.1016/j.focha.2023.100335

[13] Saeedi-Boroujeni, A., & Mahmoudi, M. (2023). Advance in the pharmacological effects of quercetin in modulating oxidative stress and inflammation related disorders. *Phytotherapy Research*, *37*(11), 4812–4830. https://doi.org/10.1002/ptr.7921

[14] Saleem, M., & Hussain, A. (2023). An insight into anticancer, antioxidant, antimicrobial, antidiabetic and anti-inflammatory effects of quercetin: A review. *Polymer Bulletin*, *80*(1), 241–262. https://doi.org/10.1007/s00289-022-04112-9

[15] Samadi, M., & Moradi, M. (2023). Quercetin: An effective polyphenol in alleviating diabetes and diabetic complications. *Critical Reviews in Food Science and Nutrition*, *63*(28), 9163–9186. https://doi.org/10.1080/10408398.2022.2067825

[16] Surma, S., Sahebkar, A., Urbański, J., Penson, P. E., & Banach, M. (2022). Curcumin – The nutraceutical with pleiotropic effects? Which cardiometabolic subjects might benefit the most? *Frontiers in Nutrition*, *9*, Article 865497. https://doi.org/10.3389/fnut.2022.865497

[17] Teimouri, M., Shabani, M., & Hosseini, H. (2023). Sphingolipid levels and signaling via resveratrol and antioxidant actions in cardiometabolic risk and disease. *Antioxidants*, *12*(5), Article 1102. https://doi.org/10.3390/antiox12051102

[18] Vafaeipour, Z., Razavi, B. M., & Hosseinzadeh, H. (2022). Effects of turmeric (*Curcuma longa*) and its constituent (curcumin) on the metabolic syndrome: An updated review. *Journal of Integrative Medicine*, *20*(3), 193–203. https://doi.org/10.1016/j.joim.2022.02.008

[19] Villalva, M., Martínez-García, J. J., Jaime, L., Santoyo, S., Pelegrín, P., & Pérez-Jiménez, J. (2023). Polyphenols as NLRP3 inflammasome modulators in cardiometabolic diseases: A review of in vivo studies. *Food & Function*, *14*(21), 9534–9553. https://doi.org/10.1039/D3FO02105A

[20] Wang, S., Du, Q., Meng, X., & Zhang, Y. (2022). Natural polyphenols: A potential prevention and treatment strategy for metabolic syndrome. *Food & Function*, *13*(19), 9734–9753. https://doi.org/10.1039/D2FO01509C

[21] Xiao, L., et al. (2022). Paradigm shift in phytochemicals research: Evolution from antioxidant capacity to anti-inflammatory effect and to roles in gut health and metabolic syndrome. *Journal of Agricultural and Food Chemistry*, *70*(28), 8551–8568. https://doi.org/10.1021/acs.jafc.2c01825

[22] Yarmohammadi, F., Hayes, A. W., & Karimi, G. (2022). The therapeutic effects of berberine against different diseases: A review on the involvement of the endoplasmic reticulum stress. *Phytotherapy Research*, *36*(8), 3215–3231. https://doi.org/10.1002/ptr.7483

[23] Ye, S., & Zhang, H. (2022). Polyphenols and adiponectin signaling in NAFLD. *Biomolecules*, *12*(6), Article 824. https://doi.org/10.3390/biom12060824

[24] Younis, N. N., & Elsherbiny, N. M. (2022). Prevention and treatment of obesity-related inflammatory diseases by edible and medicinal plants and their active compounds. *Biomedicines*, *10*(11), Article 2840. https://doi.org/10.3390/biomedicines10112840

[25] Zarei, M., & Mohammadi, M. (2022). The effects of berberine on inflammatory markers in Chinese patients with metabolic syndrome and related disorders: A meta-analysis of randomized controlled trials. *Inflammopharmacology*, *30*(3), 1063–1077. https://doi.org/10.1007/s10787-022-00980-3

[26] Zhang, X., & Chen, L. (2022). Shared signaling pathways and targeted therapy by natural bioactive compounds for obesity and type 2 diabetes. *Critical Reviews in Food Science and Nutrition*, *62*(24), 6610–6628. https://doi.org/10.1080/10408398.2021.1910200

[27] Zhang, Y., & Zhao, X. (2023). Resveratrol and gut microbiota synergy: Preventive and therapeutic effects. *International Journal of Molecular Sciences*, *24*(24), Article 17573. https://doi.org/10.3390/ijms242417573

[28] Zhou, M., et al. (2023). Bioactivity and mechanisms of flavonoids in decreasing insulin resistance. *Journal of Enzyme Inhibition and Medicinal Chemistry*, *38*(1), Article 2198302. https://doi.org/10.1080/14756366.2023.2198302