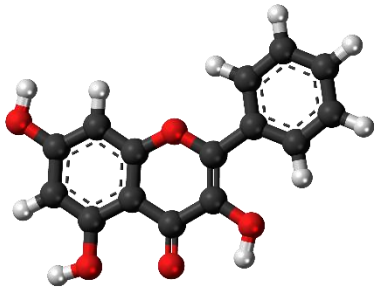
CHAPTER 07



Polyphenols: Multitargeted Therapeutics in Human Health

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Abstract: Polyphenols (PPs) are a broad class of naturally occurring plant chemicals known for their strong antioxidant capabilities and possible health advantages. There are more than 8,000 secondary metabolites which are found in a wide variety of foods, such as fruits, vegetables, tea, coffee, and spices. They have a crucial role in the defense system of plants. The four primary categories of PPs are phenolic acids, flavonoids, stilbenes, and lignans. PPs have excellent ability to affect a number of physiological functions, which may help control obesity, regulate glucose metabolism, and enhance insulin sensitivity. They accomplish this by lowering inflammation, adjusting glucose metabolism, and shielding insulin-secreting cells. Additionally, PPs have neuroprotective properties and may help prevent neurodegenerative illnesses by altering neurotransmitter pathways and lowering inflammation as well as oxidative stress. Despite these encouraging results, polyphenols' poor bioavailability remains a problem. To improve their absorption and effectiveness, future studies should concentrate on creating novel delivery mechanisms. Moreover, extensive and meticulously designed clinical studies are necessary to validate the health benefits of polyphenols, create dietary guidelines, and identify the best dosages.

Keywords: Polyphenols, Antioxidant activity, Metabolic disorders, Neuroprotection, Cardiovascular health.

Plants are the major source of naturally occurring chemicals called polyphenols (PPs). These substances demonstrate strong antioxidant properties and possess chemical characteristics that resemble phenolic compounds (Singla et al., 2019). Plants generate natural secondary metabolites, which include PPs that serve valuable industrial and medicinal functions. These molecules have the ability to move through cell membranes so they can accumulate inside cells as pigments or phytochemicals. The basic structure of these compounds consists of hydroxyl groups (-OH), which connect to single or multiple aromatic rings in various combinations; scientists have identified this structure in more than 8,000 different types. The human body requires specific foods to sustain itself, which are vegetables like broccoli, carrots, legumes, cereals and tea, coffee, herbs, spices, as well as fruits including apples, citrus, berries and grapes. The levels of these compounds are influenced by storage conditions, fruit maturity, farming methods and geographical location (Abbas et al., 2017).

Plants produce PPs as secondary metabolites, typically as defense mechanisms against infections and other stresses. Based on the number of phenolic rings and the structural element that binds them together, PPs are classified into four groups: lignans, stilbenes, flavonoids, and phenolic acids

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(Prabhu et al., 2021). Flavonols, flavones, isoflavones, flavanones, anthocyanidins, and flavonols are the six subgroups into which the flavonoids are further separated. Stilbenes, such as resveratrol and piceatannol, have been discovered to have antioxidant properties, while lignans, such as sesamol, pinoresinol, sinol, and enterodiol, are primarily found in seeds and grains (Oluwole et al., 2022). Moreover, lignins, xanthones, chromones, anthraquinones, hydrolyzable and non-hydrolyzable tannins, and condensed tannins are categorized as PPs. Due to their anti-inflammatory, antioxidant, and disease-preventive properties, dietary PPs which are mostly found in flavones, isoflavones, catechins, and phenolic acids are vital for human health (Kandar, 2020).

Although PPs were originally thought to serve mainly as antioxidants, their *in vivo* significance is now being questioned because of their low tissue concentrations. They influence fat metabolism, transcription factors, inflammatory mediator production, and cellular signaling (Boccellino & Angelo, 2020). Certain flavonoids improve insulin secretion, decrease inflammation and insulin resistance, and diminish apoptosis which assist in glucoregulation. A dihydrochalcone found in apples called phenolizin, inhibits sodium-glucose transporters (SGLTs), which may help with hyperglycemia. The amount consumed determines the health advantages of PPs. They are not hazardous when consumed in conventional diets and the increase in their intake at a moderate level is advantageous (Ren et al., 2019). The current chapter discusses the therapeutic potential of PPs and their effects against various disorders.

ROLE OF POLYPHENOLS IN METABOLIC DISORDERS

Impact on obesity and weight management

One of the main issues faced by the younger generation and society is obesity, which is defined as a body weight that is higher than normal according to the BMI index. Obesity affects more than one-third of people worldwide. Obesity is closely linked to a number of illnesses, such as adipocyte hypertrophy, insulin resistance, diabetes mellitus, intracellular inflammation, non-alcoholic fatty liver disease, coronary heart disease, cardiovascular disease, and cancer (Niewiadomska et al., 2022). PPs may help manage obesity, particularly in metabolic syndrome-related disorders like diabetes and intestinal problems. The body mass index must stay within healthy limits by achieving calorie expenditure through natural processes or supplement usage. The natural fat-burning properties of PPs present in apples, pears and leafy greens support weight loss when consumed as part of a regular diet (Capomolla et al., 2019). PPs help control obesity by lowering inflammation and oxidative stress, two major components of metabolic syndrome (MS). Research indicates that substances like epigallocatechin gallate (EGCG) in combination with caffeine promote fat burning. Moreover, sustained consumption of PPs aids in weight loss and prevents heart diseases (Erpel et al.,2020). The Mediterranean diet, along with other diets which are high in PPs, enhances metabolic health. Blueberries and other fruits, as well as substances like resveratrol and curcumin, have anti-obesity qualities. PPs isolated from seaweed may increase calorie expenditure by turning white fat into brown fat. To ascertain whether PPs consumption is safe and effective for treating obesity, more clinical trials are necessary (Chen et al., 2022).

Regulation of glucose metabolism and insulin sensitivity

A potential strategy for lowering blood glucose levels after meals is the inhibition of glucose transport by PPs (Gauer et al., 2018). By preventing intestinal absorption and promoting tissue uptake, PPs may help control blood sugar levels. Green tea catechins and quercetin are examples of compounds that inhibit intestinal glucose transport, whereas their microbial metabolites promote uptake through the GLUT4 and PI3K pathways (Pico & Martínez,

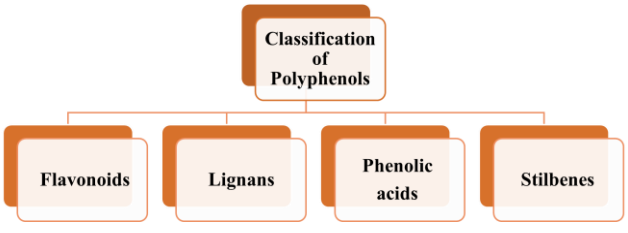

Fig 1. Classification of polyphenols

2019). Adipose and muscle tissues, which are responsible for removing glucose from the blood, exhibit insulin resistance (IR) when they fail to react appropriately to signals. Insulin and fasting blood glucose levels are used to estimate IR, although some tests additionally include an oral glucose challenge test. Epicatechin and anthocyanin-rich foods are the most promising options for reducing IR (Lee et al., 2022). Certain PPs, whether in the form of foods or supplements, have shown in intervention studies on volunteers to improve IR through a number of mechanisms, including lowering postprandial glucose, modifying glucose transport, influencing insulin signaling pathways, and preventing damage to insulin-secreting pancreatic β-cells (Williamson & Sheedy, 2020).

Anti-inflammatory and antioxidant properties in diabetes prevention

The health-promoting qualities of PPs like quercetin, naringenin, hesperetin, and polydatin are well known (Rathod et al., 2023). The strong antioxidant, anti-inflammatory, chemopreventive, anti-insulin resistance, and pro-osteogenic qualities of PPs are supported by data from preclinical and clinical studies. There is growing evidence that diets high in PPs are linked to a decreased risk of aging-related chronic illnesses. The growing need for natural, high-value bioactive components has spurred the development of innovative nutraceuticals (Stromsnes et al., 2021). The PPs including Curcumin, polydatin, and quercetin demonstrate the anti-inflammatory effects (Debelo et al., 2020).

Curcumin exists as a yellow-orange pigment within Curcuma longa while Polydatin functions as a natural precursor to resveratrol which exhibits strong anti-inflammatory properties. The research conducted by Ruan et al. (2022) shows that curcumin reduces inflammation in patients who have type 2 diabetes and multiple health conditions. Animal experiments show that polydatin reduces inflammation in fat tissue while it also shows therapeutic effects for treating colitis and diabetes. Quercetin functions as a bioactive flavonoid which slows down cell aging while enhancing overall wellness under various conditions and protects cells from high glucose damage through its antioxidant and anti-inflammatory effects (Zheng et al., 2019).

Effects on gut microbiota and metabolic homeostasis

The human gastrointestinal tract hosts a wide variety of bacteria, which form the microbiota. Each person's digestive system contains distinct bacterial communities that change throughout their lifespan and respond to various internal and external elements. The gut microbiota functions as a vital health determinant for hosts because this complex bacterial community maintains homeostasis through its interactions with the immune system and internal species relationships (Gowd et al., 2019). One of the most important factors in controlling the makeup, stability, and functionality of the gut microbiota is nutrition, as the gastrointestinal tract is the first organ exposed to food components (Zhang et al., 2018). Therefore, one strategy to influence the gut microbiota and enhance gut health is to change one's diet. By encouraging the creation of a healthy microbiota and preventing the proliferation of pathogenic bacteria, phenolic substances and their metabolites have been shown to have a positive impact in maintaining gut health (Cardona et al., 2013). However, low bioavailability limits their efficacy only 5-10% are absorbed in the small intestine, primarily because of their intricate sugar conjugates and structures. The gut bacteria convert the majority of PPs into low-molecular-weight, bioactive molecules once they reach the colon. It is thought that the health effects of PPs are due to these metabolites and their impact on the composition of the gut flora (Del Bo et al., 2019).

NEUROPROTECTIVE POTENTIAL OF POLYPHENOLS

Role in cognitive function and neurodegenerative diseases (Alzheimer's, Parkinson's)

Globally, neurodegenerative disorders impose an enormous economic impact. Their primary characteristic is the accumulation of altered proteins, which may set off an array of biological reactions, such as excitotoxicity, inflammation, oxidative stress, and signaling pathway regulation. The last ten years have seen an enormous amount of research on these conditions in an effort to create symptom-oriented treatments (Afzal et al., 2022).

Dementia, Parkinson's disease, and Alzheimer's disease are the three primary neurodegenerative diseases that threaten the world's aging population. Even though the pathophysiology of each disease varies, disease prevention strategies are similar. One of the changes that a person can do on their own is to make eating a diet rich in antioxidants a habit (Franco et al., 2023). Numerous studies have demonstrated that neurodegenerative diseases can be avoided by consuming phytochemicals with antioxidant properties. In numerous *in vitro* and *in vivo* studies, phytochemicals are shown to have neuroprotective effects via improving cognitive performance (Pohl & Kong, 2018). Figure 2 demonstrates different PPs with neuroprotective effects.

Mechanisms: oxidative stress reduction, anti-inflammatory effects, and neurogenesis promotion

Excess ROS results in oxidative stress by disrupting the cellular redox balance. Chronic illness is brought about by both inflammation and oxidative stress. Systemic inflammation is brought on by excess mitochondrial ROS activating the NLRP3 inflammasome, which in turn promotes the production of IL-1β and downstream TLR-1/NF-κB/MAPK signaling (Dominic et al., 2022). This is rebutted by phenolic substances, especially dietary PPs, which activate the Nrf2-Keap1 and AhR pathways to enhance antioxidant enzymes (SOD, CAT, GPx, and GR). These substances strengthen redox equilibrium and encourage the production of antioxidant genes, providing defense against oxidative damage and inflammation (Zhang et al., 2016). Because neurological disorders are primarily caused by damage to neurons, treatments that target neural regeneration must control neurogenesis and neuronal differentiation.

Neurogenesis occurs when particular natural substances lead to the formation of new neurons, which then connect with established neural networks. The plant-based phenolic acids, alkaloids, flavonoids and terpenoids stimulate neurogenesis through their effects on neuronal differentiation genes, proteins and signaling molecules, including MAP-2, β-tubulin III and BDNF, as well as the JAK/STAT, Wnt/β-catenin and PI3K/Akt signaling

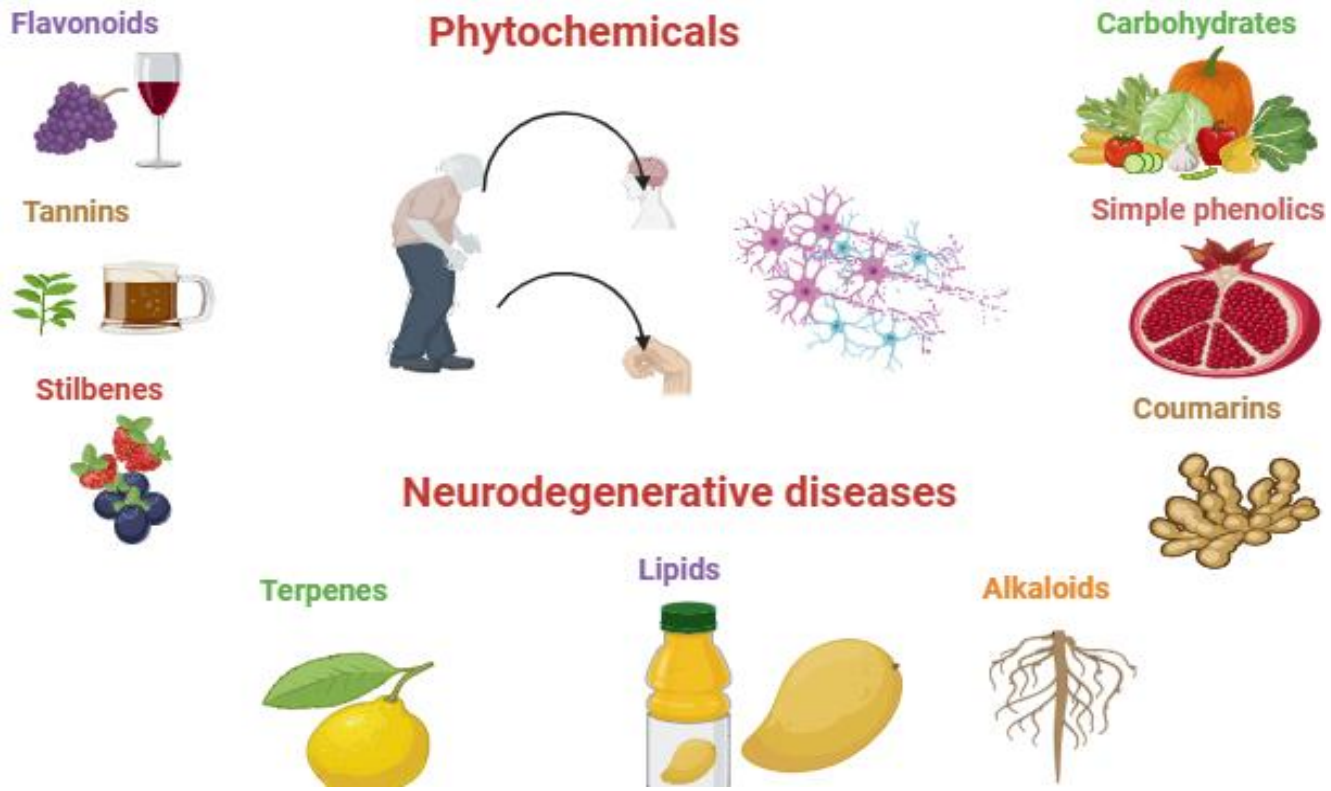

Fig 2. Polyphenols with protective effects against neurodegenerative diseases

pathways. The compounds demonstrate potential for neural regeneration therapy and function as therapeutic agents to treat neurological disorders (An et al., 2022).

Influence on neurotransmitter pathways and synaptic plasticity

Neurotransmission balance is essential for nervous system function, and even little disruptions over time may build up negative feedback loops that result in a variety of neuropathologies. Mood disorders and neurological diseases like Parkinson's and Alzheimer's are becoming more common (Rebas et al., 2020). Oxidative stress and aberrant neurotransmitter metabolism, including those of acetylcholine, GABA, glutamate, serotonin, and dopamine, are major contributors to these illnesses. Plant PPs with biological activity have shown promising potentials in controlling neurotransmitter activity and metabolism, which will enhance central nervous system function (Yang et al., 2022).

CARDIOVASCULAR BENEFITS OF POLYPHENOLS

One of the leading causes of death worldwide, cardiovascular diseases (CVDs) accounted for 17.9 million deaths in 2019, roughly 32% of all fatalities. Nearly 85% of these fatalities were caused by heart attacks and strokes. 6.7 million people die from strokes and 7.4 million from coronary heart disease each year (Li et al., 2023). Research indicates that eating a balanced diet lowers the risk of CVDs (Santhakumar et al., 2018). A long lifespan is strongly associated with a diet that includes a high percentage of fruits and vegetables, such as the vegan diet. The research by Malekmohammad et al. (2019) demonstrates that this treatment method leads to decreased rates of heart-related medical conditions. Research conducted through epidemiological studies demonstrates that high PP food consumption results in a 46% decrease in cardiovascular disease risk (Sanches-Silva et al., 2020). PPs exist in vegetables along with numerous fruits and seeds that people consume in their daily diet. The consumption of fruits together with vegetables, seeds and nuts results in reduced occurrences of chronic diseases and age-related degenerative conditions (Nayak et al., 2015).

Modulation of blood pressure and vascular health

In the human body, blood circulation carries out the transportation of oxygen and nutrients, while the cardiovascular system (CVS) removes carbon dioxide and metabolic waste products. Heart and blood artery disorders include hypertension, heart failure, stroke, peripheral artery disease (PAD), coronary artery disease (CAD), cerebrovascular disease, and congenital heart disease (CHD) (Alam, 2019). The incidence of atherothrombotic diseases and high blood pressure has increased due to increased salt intake from processed meals. In animal models of hypertension, flavonoid supplementation has been demonstrated to lower blood pressure by inhibiting ACE and producing nitric oxide (NO). With luteolin and galloylated catechins showing the highest effects, a variety of flavonoids, including flavones, catechins, and flavonols, reduce ACE activity in a dose-dependent manner. Furthermore, flavonoids boost vascular function by increasing endothelial NO generation (DiNatale & Crowe-White, 2022). Vascular health is further enhanced by flavonoid metabolites, such as short-chain fatty acids (propionic and butyric acids), which alter blood flow and epithelium function. These PPs have anti-hypertensive, vasoprotective, and vasorelaxant properties that support vascular homeostasis and lower the risk of atherothrombosis and chronic inflammation in Mediterranean diets (Reis et al., 2021).

Effects on cholesterol metabolism and lipid profile

Risk factors for CVDs encompass both physiological (high blood pressure, diabetes, high cholesterol, obesity) and behavioral (smoking, inactivity, bad nutrition) components (Nedkoff et al., 2023). Low-density lipoprotein cholesterol (LDL-C) elevation in the blood is the main cause of atherosclerosis. LDL builds up in the vessel wall, particularly in cases of hypercholesterolemia, and this is the first sign of atherosclerosis. Partially oxidized LDL attracts monocytes, which develop into macrophages, and causes inflammation. These have scavenger receptors (like SR-A and CD36) that absorb modified LDL and create foam cells that are high in cholesterol. As lesions worsen, LDL gets

more oxidized, which promotes the absorption of foam cells (Jin et al., 2022). Even while cells have the ability to efflux cholesterol to HDL (starting reverse cholesterol transport), this is frequently not enough. The condition gets worse when accumulation persists because it causes necrotic core development and macrophage mortality (Durrington et al., 2025). Clinical research shows that foods high in PPs, such as nuts, coffee, chocolate, grapes, berries, pomegranates, and olive oil, lower cardiovascular risks (Rana et al., 2022).

Anti-atherosclerotic and anti-thrombotic properties

PPs were widely recognized for their antioxidant properties, and recent research shows they also have an impact on lipid metabolism and cardiac wellness. Key atherogenesis processes such as LDL oxidation, aggregation, and foam cell formation are less likely to occur as they modify lipid-metabolizing enzymes and change the composition of lipoproteins. By preventing platelet activation, aggregation, and clot formation, flavonoids also have anti-thrombotic properties. Metabolites like protocatechuic acid prevent high shear stress-induced platelet aggregation, compounds like epicatechin, quercetin, and grape seed extract decrease platelet reactivity and thrombin production (Harishkumar et al., 2022). Furthermore, by suppressing adhesion molecules (VCAM-1, ICAM-1, and MCP-1) and cytokines (IL-6), flavonoids and their gut metabolites reduce inflammation by restricting monocyte adherence and endothelial activation. In general, consuming PPs lowers the risk of thrombosis, improves lipid profiles, and reduces inflammation, all of which help to avoid vascular and thrombotic disorders (Ebrahimi et al., 2023).

Role in endothelial function and nitric oxide bioavailability

The primary cause of death worldwide, CVDs, is partly caused by endothelial dysfunction, which is characterized by a decreased capacity of endothelial cells to combat oxidative stress, inflammation, and thrombosis. This dysfunction is a direct and early predictor of atherosclerosis and is frequently quantified by decreased endothelium-dependent vasodilation. Endothelial nitric oxide synthase (eNOS), which transforms L-arginine into NO and L-citrulline, is essential for the adequate synthesis of nitric oxide (NO) in a healthy endothelium (Oyovwi & Atere 2024). NO is a diffusible gas that plays important vasoprotective functions, including reducing LDL oxidation, preventing platelet aggregation, inhibiting inflammatory signaling (e.g., NF-κB), relaxing vascular smooth muscle through guanylate cyclase activation, and limiting aberrant smooth muscle proliferation. Decreased NO bioavailability aids in the advancement of vascular disease. Therefore, increasing NO production has emerged as a key goal in the prevention of CVD. Diet plays a big part by raising NO bioavailability, many natural substances in meals or phytomedicines have been proven to improve endothelial function, providing new methods to treat CVD (Hesari et al., 2021).

CLINICAL PERSPECTIVES ON POLYPHENOL-BASED THERAPEUTICS

The health-promoting qualities of PPs, such as their anti-inflammatory, cardioprotective, and antioxidant activities, are the subject of much research. Their ability to lower the risk of chronic illnesses like cancer, diabetes, and cardiovascular disease has been supported by their associations with better blood pressure, lipid profiles, glucose management, and gut microbial balance (Rana et al., 2022). Growing interest in healthy aging and good nutrition is reflected in an upsurge in PP research. Although the results are encouraging, observational and *in vitro* research still provide the majority of the evidence (Luo et al., 2021). The medical community now focuses more clinical trial research on PP supplementation, yet results show inconsistent findings because of different study designs and participant groups and their personal responses to treatment. The main challenges stem from missing standardized procedures, differences in bioavailability and varying PP content levels in different food items. Scientists need to conduct properly designed clinical studies to confirm the health advantages of PP intake while establishing suitable dietary guidelines for its consumption (Salehi et al., 2022).

Although PPs are known to have anti-inflammatory, antioxidant, and disease-preventive properties, their poor oral bioavailability presents a significant barrier to their widespread application. The absorption and activity of complex chemical structures in the digestive tract are determined by their chemical composition and many of these compounds decompose before reaching their intended targets. Scientists have researched various methods to overcome this limitation by concentrating their efforts on using bio-based nanocarriers as the main solution. Scientists have improved PP encapsulation and delivery systems by using natural proteins and polysaccharides as protective materials in their research (Sahraeian et al., 2024). The carriers function as perfect solutions for food and nutraceutical products because they biodegrade naturally while providing safe consumption and nutritional advantages. Scientists create nanoscale delivery systems through protein-based carriers, which use their emulsification and gelation and amphiphilic properties to produce nanoparticles and nanogels and nano-emulsions. The structural flexibility and safety of polysaccharide-based nanocarriers make them useful building blocks as well (Aatif, 2023).

Additionally, lipid-based carriers such as solid lipid nanoparticles, liposomes, and nano-emulsions are necessary to enhance the bioavailability of fat-soluble PPs and shield them from digestion. These novel delivery methods are opening the door to more efficient PP utilization in nutraceuticals and functional foods (Ashfaq et al., 2023).

PPs have demonstrated great potential in pharmaceutical and nutraceutical uses owing to their anti-inflammatory, disease-preventive, and antioxidant qualities (Sun & Shahrajabian, 2023). These substances help control and stop chronic diseases, including cancer, heart disease and neurological disorders through their ability to block DNA synthesis, promote cell death and their effects on cell communication as well as antioxidant defense. The substances have shown pain relief properties, fever reduction effects, nerve seizure control, cancer fighting potential and bacterial as well as fungal infection control, along with immune system regulation in laboratory and animal studies (Al-Shuhaib & Al-Shuhaib 2025). With the use of advanced analytical methods like mass spectrometry, which facilitate precise determination and use of bioactive plant ingredients, their integration into functional foods and supplements is expanding. To fully achieve their therapeutic potential in contemporary nutrition and healthcare, careful extraction and formulation are necessary (Kumar et al., 2024).

SAFETY, RECOMMENDED DOSAGES, AND REGULATORY CONSIDERATIONS

The consumption of phytochemicals, including PPs has been practiced by various civilizations throughout history. People have passed down this practice through ethno-botanical knowledge from one generation to the next. The safety of these compounds is not always assured, even when they come from natural sources. Laboratory studies have been performed by scientists but they lack sufficient information to determine both the safety and effectiveness of these substances when they interact with living organisms. PPs protect people against chronic diseases because of their antioxidant characteristics (Cladis et al., 2022). However, PPs may be hazardous when taken in excess, especially through dietary supplements. The scientific community needs additional toxicological research to comprehend the risks of caffeic acid since animal tests showed its potential to foster tumor growth even though it seems useful in other circumstances (Cortez et al., 2024).

Furthermore, substances such as isoflavones (genistein, daidzein) can alter hormones by imitating estrogen, which may have an impact on reproductive health. Quercetin and other polyphenols can affect thyroid function. Scientists need to learn about PP toxicity as well as safe dosage amounts so humans can avoid adverse health consequences (Duda-Chodak & Tarko, 2023). The ToxDP2 (Toxicology Database for Dietary Polyphenols 2) database contains toxicological profiles of over 400 PPs, which scientists use to evaluate their safety and develop regulatory measures. People usually think PPs are safe because they come from natural sources but this database provides crucial information about their safety when taken in large amounts, which helps develop safe nutraceutical products. The safe and advantageous use of PPs in dietary supplements ultimately

depends on careful supervision and appropriate dosage (Teslić et al., 2024).

Future Directions and Challenges

Advances in formulation and delivery systems (nanotechnology, encapsulation)

Although PPs exhibit remarkable medicinal properties but their bioavailability is limited after ingestion due to their low water solubility, instability at low pH levels, and difficulties with absorption in the small intestine. These issues prevent their medical and nutritional supplement applications from being approved (Stielow et al., 2023). Scientists have discovered promising methods to boost PP bioavailability through new nanotechnology advancements. The substances find protection from digestive system decomposition through their encapsulation in nano carriers which include liposomes, nanoparticles and nanoemulsions. The technique reduces systemic adverse effects while boosting treatment effectiveness through better solubility and direct delivery to specific body tissues (Adefegha et al., 2022).

Need for large-scale, long-term human trials

Research studies show that consuming polyphenol-rich foods provides various health benefits to the body. The text contains multiple essential points which need further elaboration. What amount of PPs should people consume each day according to nutritional guidelines? Moreover, scientists need to develop exact methods for detecting the levels of PPs that exist in food items. They also need to determine why substances metabolize differently in human bodies, i.e., via different metabolic pathways. It's critical to provide fresh, trustworthy techniques and resources to answer these queries. The methods enable scientists to determine the exact food intake of PPs while tracking specific biological markers that show PP consumption (Visioli et al., 2011).

Table 1. Applications of polyphenolic formulations and their therapeutic outcomes

Polyphenolic Formulation	Therapeutic Outcomes	References
Kaempferol and chrysin	Anti-inflammatory, antioxidant, neuroprotective	Khanam et al., 2025
Quercetin and resveratrol	Mitigate dyslipidemia, diabetes induced organ damage, and serum glucose dysfunction	Yang & Kang, 2018
L-carnitine, soy isoflavone and red grape extract	Reduces obesity and lowers the risk of non-alcoholic fatty liver disease and CVDs	Kang et al., 2011

Personalized medicine approach to polyphenol-based therapies

PPs have shown potential as individualized cancer treatments because of their many uses, such as immunomodulatory, anticancer, and antioxidant activities. The development of specialized drug delivery systems is made possible by their structural characteristics, such as the catechol and gallol groups, which allow for specific interactions with a range of biological targets and materials (Guo et al., 2021). It is possible to build these molecules into nanocarriers that reduce systemic toxicity while protecting therapeutic chemicals, targeting tumor locations, and controlling medication release. Their potential in precision immunotherapy is supported by the fact that PP-based carriers can be further customized by boosting local immune responses or including metal immune adjuvants. These characteristics make PPs appropriate for specific treatments meant to increase therapeutic effectiveness and lessen adverse effects in cancer treatment (Mohammed et al., 2023).

Synergistic effects with other dietary components and lifestyle interventions

Polyphenols have synergistic or additive effects that improve their anti-inflammatory, antioxidant, lipid-lowering, and metabolic advantages when paired with other bioactive dietary components (such as flavonoids, saponins, carotenoids, and metabolic cofactors) (Rane et al., 2023). At low concentrations, these actions are frequently synergistic, but at high dosages, they may become antagonistic. Table 1 shows different PP formulations and their therapeutic outcomes.

CONCLUSION

Plants are rich in biologically active PPs. These PPs exhibit promising therapeutic applications, especially in the prevention, treatment, and reduction of chronic diseases. They may also be beneficial against metabolic imbalances, cardiovascular diseases, and neurodegenerative disorders. However, their low bioavailability has prevented them from being widely used. In response, innovative delivery and absorption techniques, including encapsulation and nanotechnology, are designed and executed. Large-scale and long-term human studies should be the main focus of future research in order to confirm health consequences and create ideal usage guidelines. To optimize the therapeutic potential of polyphenols, research into synergistic interactions with other dietary components and personalized medicine strategies tailored to individual variability is also crucial.

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