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Bioactive compounds in peanuts (*Arachis hypogaea L.*): A review of their anti-inflammatory and antioxidant effects

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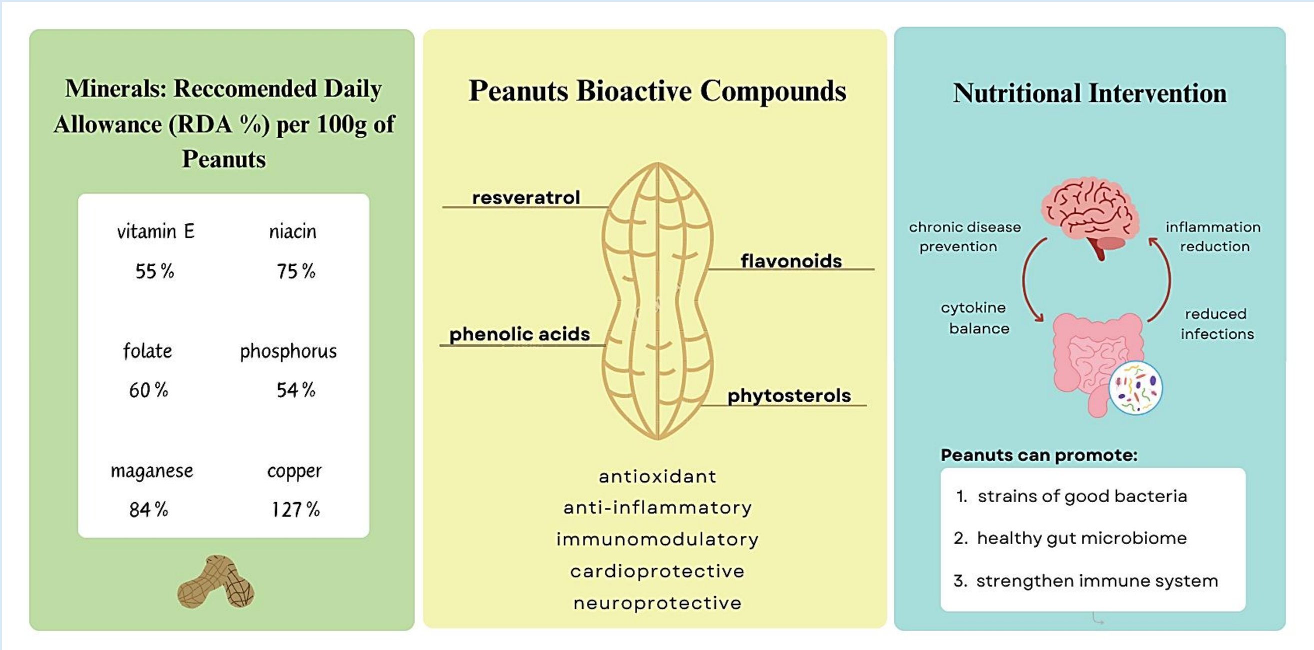
ABSTRACT:

Peanuts (*Arachis hypogaea L.)* are a widely consumed legume globally, particularly in traditional cuisine. Research highlights peanuts' antioxidants and anti-inflammatory properties, contributing to growing interest in the Mediterranean diet. This eating pattern emphasizes whole, minimally processed foods like fruits, vegetables, whole grains, legumes, and healthy fats. Recent research associates the Mediterranean diet with improved management of coronary heart disease, hypercholesterolemia, type 2 diabetes, and other illnesses. This review aims to overview the efficacy of peanuts' phytochemical profile, including resveratrol, flavonoids, phytosterols, essential amino acids and vital micronutrients like folate, niacin, vitamin E, manganese and phosphorus. Studies indicate peanuts' phytochemical profile serves as a primary source of essential micronutrients due to its abundance of biologically active agents. The functional properties of proteins depend on factors such as amino acid composition, protein structure, temperature, and processing.

Understanding these variables is crucial for utilizing peanut proteins effectively and maximizing their nutritional value. The incorporation of peanuts into a balanced diet may also support health weight management and improve overall nutritional status. The rich nutrient profile of peanuts makes them an excellent addition to meals and snacks, particularly for individuals with dietary restrictions or preferences. To fully harness the benefits of peanuts, further clinical research is necessary to explain their impact on human biology and determine recommended dietary allowances. Educational initiatives for better agricultural practices and storage are essential for safe peanut production, protecting public health, and supporting peanuts as a wholesome food source. Additional studies are required to confirm long-term benefits and explore potential synergies with other bioactive food sources. As research continues to uncover the benefits of peanut consumption, it is essential to promote sustainable peanut production practices and support local peanut farmers.

Novelty: This review uniquely examines the integration of peanuts (Arachis hypogaea L.) into the Mediterranean diet, focusing on their rich phytochemical profile, including resveratrol, flavonoids, and phytosterols—and their potential health benefits. It also addresses the functional properties of peanut proteins and their implications for nutritional optimization, areas that have received limited attention in existing literature.

Keywords: peanuts, resveratrol, phytosterols, flavonoids, arginine, antioxidant, anti-inflammatory, Novel bioactive compounds



INTRODUCTION

Chronic diseases pose a significant threat to the public health of the United States and are responsible for more than 70% of deaths [1]. The U.S. has very high rates of multiple chronic conditions such as cancer, diabetes, heart disease, stroke, depression, arthritis, etc. Coupled with increasing healthcare costs and long-standing health disparities, more than two-thirds of Americans suffer from at least one chronic disease and live in an environment conducive to poor socioeconomic factors [2]. Diagnosis of a chronic disease involves a complex, patient-centered collaborative discussion, given that daily dietary choices, physical inactivity, genes, and environmental factors mainly influence the root cause of chronic diseases. Pathologically, a disruption in mitochondrial function leads to an inability to produce enough adenosine triphosphate (ATP), affecting every organ in the human body and leading to oxidative stress [3]. As noted above, the goal is to improve the diagnostic criteria and advance the understanding of how the onset of symptoms manifest in patients in the first place.

Lifestyle intervention is required to invest in primary prevention and management of chronic disease effectively. It can significantly reduce the likelihood of disease progression and help reverse the pathology of the disease [4]. This comprehensive review highlights the integral role of nutrition therapy in shaping our physical and mental wellbeing and explores how informed dietary choices can drive optimal health outcomes. The Mediterranean diet serves as a prime example, characterized by an abundance of whole foods, fruits, vegetables, and healthy fats, and has been consistently shown to lower the risk of chronic disease [5]. Legumes are a fundamental component of this diet, with peanuts being a rich and nutritious option. As a snack rich in monounsaturated and polyunsaturated fats, peanuts provide a wealth of health benefits. (6). Notably, these unsaturated fats are essential to the human body, as they cannot by produced internally and must be obtained through the diet. Unlike saturated fats, which can increase levels of low-density lipoprotein (LDL) cholesterol, unsaturated fats have been shown to have a beneficial effect on cholesterol levels by elevating high-density lipoprotein (HDL) cholesterol [6]. As a result, the HDL cholesterol will take up surplus LDL found in the bloodstream and transport it back to the liver to be excreted from the body via bile [7]. In contrast, LDL cholesterol can be stored and transported to other parts of the body, causing a buildup in the arteries, where plaque can form, narrowing the vessels and increasing the risk of heart disease [8]. Therefore, this review highlights the nutritional benefits of peanuts, including their phytochemical constituents and essential micronutrients, and their potential to support improved health outcomes.

METHODOLOGY

An article search was conducted in PubMed and ScienceDirect databases concerning the positive effect of peanuts bioactive compounds on human health and wellbeing. Results were limited to articles published between 1983 and 2023. Six hundred fifty-eight articles were retrieved and screened for relevance based on their titles and abstracts. After excluding irrelevant articles and duplicates, 94 full-text articles were assessed. Of these, 52 articles were included in the final review, including 14 human studies, 22 animal studies, and 16 in vitro studies. The common reasons for exclusion were a lack of peanut-specific data (e.g., combined data for peanuts and tree nuts) and the absence of a health outcome.

Peanut consumption and cholesterol management: Peanut consumption can help manage cholesterol better by regulating lipid metabolism and reducing triglyceride blood levels, leading to cardiovascular risk reduction, as shown in Table 1 [9-10].

Table 1. The effect of peanuts on lipids and lipoprotein

Study Design and	Sample Size "N"	Findings
Randomized, controlled intervention study	**N = 1041**	A 6–52-week study involving participants with type 2 diabetes found that consuming >45g/d of peanuts resulted in significant reductions in total cholesterol (-0.14 mmol/L; 95% Confidence Interval [CI]: -0.26, -0.02; p=0.024) and triglycerides (-0.10 mmol/L; 95% CI: -0.17, -0.02; p=0.010) [11].
Randomized controlled intervention study, parallel or crossover design	**N = 711**	A 4–72-week study involving participants with a body mass index (BMI) of 25-40 kg/m^2 found that consuming $\geq$45g/d of peanuts significantly decreased serum triglycerides, with a weight mean difference (WMD) of -13.19 mg/dL (95% Confidence Interval [CI]: -25.90, -0.48) [12].
Randomized controlled intervention study	**N = 643**	A 24-week study involving healthy participants or those with metabolic syndrome (MetS) or at high risk of MetS found that consuming 25-200g/d of peanuts significantly reduced triglycerides by -0.13 mmol/L (95% Confidence Interval [CI]: -0.20, -0.07) [13].

Peanuts as a source of protein, vitamins and minerals: Additionally, peanuts are high in protein, supporting satiety and weight management, and are a good source of fiber, vitamins, and minerals, specifically potassium, magnesium, and vitamin E. Generally, a one-ounce serving of peanuts is around 7 grams of protein, which accounts to be the highest protein content among most nuts. The exceptional yield and nutritional value of peanuts have driven a significant increase in global production, reaching 45 million metric tons annually [14], accounting for a substantial 11% of the world's total protein supply. Peanuts originated in South America, however as demand surged, peanut production expanded globally, with China, India, the United States, and Nigeria being the top producers [15]. Peanuts have gained popularity in the food industry because of their enhanced bioavailability and a broader range of products, including peanut butter, roasted peanuts, peanut oil, and various snacks [14-15].

As peanuts are free from dairy or animal-derived ingredients in their production, they have emerged as a dependable nutritional option for individuals following a plant-based diet. Nevertheless, excluding animal-based proteins from one's diet may result in a deficiency of essential vitamins and minerals needed by the body, including omega-3, iron, vitamin B_{12}, vitamin D, and iodine [16-17]. Fortunately, peanut plant protein presents a viable option, as shown by the Protein Digestibility Corrected Amino Acid Score (PDCAAS), a commonly utilized test for assessing protein quality. Peanut plant protein serves as a great alternative for vegans and vegetarians because it provides comparable levels of protein fortification and distinct bioactive compounds [18].

To meet the functional needs of skeletal protein accretion, an individual should consume about 1.6 to 2.2 grams of protein per kilogram of body weight daily for optimal growth and development [19]. This protein intake provides the essential amino acids that serve as the building blocks for new muscle tissue. Peanuts offer a complete amino acid profile comprising 20 essential amino acids, with arginine being the most abundant [20]. Legos serve as a great analogy for understanding the function of amino acids, as amino acids are present in different shapes and sequences and ultimately are pieced together to create different structures. Every specific chain of amino acids will then be assigned to a specific application in the body, such as digesting food, immune response, hormone production, and tissue growth and repair [21]. Studies indicate that there are around 500 amino acids in nature, but the human body requires 20 specific amino acids to operate at its best [22, 23]. The human body cannot produce 9 essential amino acids: histidine, lysine, methionine, leucine, isoleucine, tryptophan, threonine, phenylalanine and valine [23]. These essential amino acids must be obtained through food, specifically complete proteins include all 9 essential amino acids, such as eggs, meat, dairy products, and hemp seeds [23]. Peanuts are classified as an incomplete protein, supplying 8 of the 9 required amino acids, as illustrated in Table 2 [24, 25]. This emphasizes the necessity of combining peanuts with additional complete protein sources to guarantee a well-rounded amino acid intake.

Table 2. Total amino acids available in a serving of dry roasted peanuts (Table from Reference 20)

Amino acid		Function	Amino acid		Function
Arginine	[26]	170 mg; precursor for urea, creatine, nitric oxide (NO) and protein synthesis	**Hydroxyprolin e**	[35]	10 mg; structural strength of bone and in bone regeneration
Lysine	[27]	241 mg; protein synthesis, supports immune system, improve use of calcium	**Histidine**	[36]	170 mg; repair damaged tissues, and protects nerve cells
Glutamic Acid	[28]	1406 mg; helps metabolism, messages between brain cells and cognitive function.	**Tyrosine**	[30]	273 mg; precursor for the catecholamines adrenaline, noradrenaline, and dopamine
Serine	[29]	331 mg; vital to metabolism, and important cell signaling molecule	**Glycine**	[37]	405 mg; most abundant amino acid in collagens, synthesis of serine and glutathione
Proline	[30]	297 mg; used for protein synthesis, precursor for glutamate synthesis, abundant in collagen	**Valine**	[38]	282 mg; promotes muscle growth and tissue repair, improves mitochondrial function
Alanine	[29]	267 mg; precursor for urea, creatine, and nitric oxide (NO)	**Threonine**	[39]	230 mg; synthesis of glycine and acetyl-CoA
Aspartic acid	[31]	820 mg; precursor for pyrimidine synthesis	**Methionine**	[40]	83 mg; regulates metabolic processes, and digestive functioning
Tryptophan	[32]	65 mg; precursor for neurotransmitters serotonin, the hormone melatonin	**Cystine**	[41]	86 mg; precursor to glutathione and plays essential role in protein structure
Isoleucine	[33]	237 mg; helps make hemoglobin, and detoxification of nitrogenous waste	**Leucine**	[29]	436 mg; helps regulate tissue regeneration, and possibly increase production of human growth hormone
Phenylalanine	[34]	348 mg; precursor of tyrosine and acetyl CoA	**Betaine**	[35]	0 mg; cellular reproduction and helps make carnitine

Unlike other diets, the Mediterranean dietary pattern (MDP) ensures an adequate intake of these nine vital nutrients [42] through moderate intake of meat, fish, legumes, and nuts. The abundance of vitamins E and C, coupled with essential minerals like magnesium and iron, which collectively help mitigate the risk of micronutrient deficiencies [43]. For example, anemia is the result of an iron deficiency, where the body fails to produce enough hemoglobin for red blood cells. This condition can manifest at different stages of life, such as early childhood, during adolescent growth spurt, and throughout pregnancy, impacting around 24 % of the worldwide population [44]. Moreover, studies indicate that vitamin D deficiency (VDD) is a widespread health concern, particularly affecting individuals with gastrointestinal conditions. VDD impacts around 1 billion people globally [45]. For instance, individuals diagnosed with coeliac disease are particularly susceptible to VDD, with a prevalence rate of 55.5%, largely due to reduced absorption or insufficient intake from gluten-free products [45]. Micronutrient deficiencies can be prevented by intentional dietary choices and the inclusion of nutrient-rich foods such as peanuts, which can aid in filling nutritional voids and lower the likelihood of metabolic or chronic diseases.

According to the USDA National Nutrient Database (Table 3), peanuts are a rich source of essential nutrients, including protein, dietary fiber, vitamins (folate, niacin, thiamin, and vitamin E), and minerals (copper, iron, magnesium, manganese, phosphorus and zinc).

Table 3. USDA National Nutrient database (Table from Reference 19)

Principle	Nutrient value	Percentage of RDA
Energy	567 Kcal	29
Carbohydrates	16.13 g	12
Protein	25.80 g	46
Total Fat	49.24 g	165
Cholesterol	0 mg	0
Dietary Fiber	8.5 g	22
Vitamins		
Folates	240 µg	60
Niacin	12.066 mg	75
Pantothenic acid	1.767 mg	35
Pyridoxine	0.348 mg	27
Riboflavin	0.135 mg	10
Thiamin	0.640 mg	53
Vitamin A	0 IU	0
Vitamin C	0	0
Vitamin E	8.33 mg	55.5
Electrolytes		
Sodium	18 mg	1
Potassium	705 mg	15
Minerals		
Calcium	92 mg	9
Copper	1.144 mg	127
Iron	4.58 mg	57
Magnesium	168 mg	42
Manganese	1.934 mg	84
Phosphorus	76 mg	54
Selenium	7.2 µg	13
Zinc	3.27 mg	30

BIOACTIVE COMPOUNDS IN PEANUTS

Dietary fiber and niacin: Peanuts are a nutrient-dense food, rich in bioactive compounds and functional ingredients. Their chemical makeup includes a significant proportion of healthy fats, with monounsaturated making up 50% and polyunsaturated fatty acids comprising 28% [46]. This fatty acid composition lowers LDL cholesterol levels by both soluble and insoluble fiber Epidemiological studies have shown that eating peanuts is associated with a lower risk of coronary heart disease and gallstones in both men and women, as well as in individuals with diabetes [48]. In addition, peanuts notably possess a low glycemic index (GI) of 14, signifying along with niacin (vitamin B_3) to support blood pressure regulation and promote cardiovascular health [47]. that they are broken down and absorbed gradually [49]. This slow digestion helps avoid a quick spike in blood sugar, unlike refined grains like white bread, which may lead to a rapid increase in glucose levels.

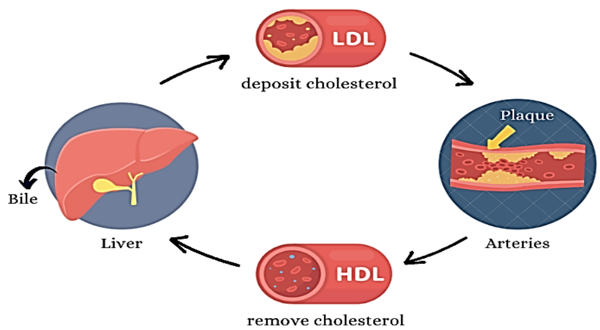


Figure 1: The impact of cholesterol on liver and artery health

Several clinical trials have indicated that peanut consumption can improve blood lipid levels, which is a significant factor in cardiovascular disease (CVD) risk. A study involving 63 healthy subjects found that consuming either skin-roasted peanuts (SRP) or peanut butter, or a control butter made from peanut oil, reduced triglycerides and lowered cholesterol ratios [10]. The decrease in cholesterol is believed to be partially mediated by phytosterols, which lessen the gut's absorption of cholesterol. The peanut treatments did not increase body fat or body mass index, but they did increase body weight in those at high cardiometabolic risk. According to dose-response studies, higher dosages of peanuts caused a slight rise in body weight. Overall, the study suggests that healthy consumers should consume peanuts in moderation to maintain a healthy diet and reduce their cholesterol levels [9].

Arginine and magnesium: Research suggests that peanuts and their bioactive compounds may have a beneficial impact on cardiovascular health by influencing blood pressure and endothelial function, two critical factors closely tied to the risk of cardiovascular disease (CVD). Notably, a 4-week intervention study found that consuming 56g of peanuts daily significantly lowered diastolic blood pressure in 45 overweight and obese males, compared to a control diet [36]. This result may be due to peanuts' high arginine and magnesium content and antioxidant properties that increase nitric oxide production and improve vasodilation [29]. Several randomized crossover trials have also shown acute or chronic patient consumption or small peanut amounts to increased flow-mediated dilation (a marker of endothelial function) [49,50].

Resveratrol and phytosterols: Peanuts are a notable source of resveratrol, a stilbene compound, with concentrations ranging from 0.03-0.14 mg/100g. Interestingly, boiled peanuts contain higher levels of resveratrol compared to their raw or roasted counterparts [51]. Resveratrol has gained attention for its antioxidant, anti-inflammatory, and chemo preventative effects [34]. Whereas phytosterols are plant-based compounds that are structurally similar to cholesterol. The main phytosterols in peanuts are campestral, β-sitosterol, and stigmasterol, which collectively account for 180-230 mg/100g [12]. Phytosterols can reduce cholesterol absorption in the small intestine, lowering healthy dietary patterns for heart health if well monitored by health specialists since regulated quantities have been known to decrease the total cholesterol by about 10% and the LDL or "bad" cholesterol by around 14%. Several scientific reports

CAPACITY OF PEANUTS

Recent studies have shown polyphenol antioxidant, like resveratrol, has been discovered to help fend off heart ailments, degenerative neural disease, Alzheimer's, cancerous tumors and inflammation [44]. Oxidation results in the production of "free radicals", which are known to be unstable substances that could harm the cells and lead to chronic diseases. The origin of free radicals is said to be neutralized by antioxidants, helping to balance the quantity of oxidants and antioxidants. In vitro experiments have confirmed that peanuts extracts exhibit anti-linoleic acid peroxidation, possess a high radical absorbance capacity (ORAC) value, and demonstrate other antioxidant constituent activity. For example, research has established that a methanolic extract of peanut skins had an IC_{50} (50 percent inhibitory concentration) of 26.9 mg/mL in a DPPH assay, indicating vigorous antiradical activity [53]. Sources of the antioxidant effects of peanuts have been found partly to be phenolics, where the antioxidant capacity is positively proportional to total phenolic content [39].

Studies on animal feeding have demonstrated the antioxidant and bioactive properties of peanuts. Higher oxidation stability, longer shelf life, and nutritional advantages are all features of high oleic acid peanuts (HOPO). Therefore, compared to olive oil, HOPO has higher quantities of monounsaturated fatty acids (MUFA) and lower levels of minor bioactive components including phytosterols and polyphenols. HOPO improved the serum lipid levels of induced rats compared to the olive oils. This makes HOPO a more attractive option for the consumers [54].

cholesterol levels [35]. Some phytosterols are recommended in

suggest that incorporating plant foods containing phytosterols into the current diet could help enhance serum lipid (cholesterol) concentrations and positively affect the course of CVD [52].

THE ANTIOXIDANT

Although there is little human research on peanuts antioxidant properties, it mostly corroborates the results from in vitro and animal studies. Consumption of peanuts significantly increased plasma's ORAC (oxygen radical and absorbance capacity), indicating an improved antioxidant status. Another study found that consuming peanuts with their skins for 4 weeks increased the total antioxidant capacity of serum compared to consuming peanuts without skin or a control diet [55].

CARDIOVASCULAR HEALTH BENEFITS

Global data reveals that cardiovascular diseases contribute to 30% prevalence and cause about 17.9 million fatalities annually [39]. Peanuts are an excellent source of resveratrol. This bioflavonoid is known to affect the brain's blood flow with an increase of 30% which cuts the risk of a stroke by half. In addition to its role as an antioxidant that offers a shield against cardiovascular diseases, including arteriosclerosis, resveratrol has been shown to have chemo-venture properties against several types of cancer through its actions on the tumor initiation, promotion, and progression phases. Furthermore, resveratrol appears to increase the life span of various species such as *Saccharomyces cerevisiae, Drosophila melanogaster,* and mouse [54]. A randomized control clinical trial of 12 weeks with 151 participants revealed that moderate peanut intake of 42 g/day positively affected participants with high serum lipids and elevated blood cholesterol levels, and pressure. The study found that diastolic cholesterol, blood pressure, and triglyceride concentrations decreased more often in individuals with high-risk CVD than in those with reduced risk. The mean reductions were (-12.1 ± 8.5 mg/dL0, (-5.0 ± 1.7 mm Hg), and (-31.7 ± 15.8mg/dL) [56]. There is ample evidence of direct and inverse relationships between peanuts and other nuts consumption and the risk of CVD from prospective cohort investigations [40]. A cohort study of 13 trials showed that high intake of peanuts reduced the occurrence of stroke by 22% and CVD risk by 44% [57]. Peanuts are more likely to exert most of this effect due to their high magnesium levels and favorable fatty acid profile, through bioactive substances might contribute as well.

Phenolic acids, flavonoids and phytates: Phenolic acids are a major class of polyphenols characterized by a phenol ring and at least one organic acid group. Peanuts' total phenolic acid content is approximately 65 mg Gallic Acid Equivalents (GAE) per 100g [61]. Out of all phenolic acids present in peanuts, the most dominant amount of p-coumaric acid and protocatechuic acid is reported [62]. Flavonoids are polyphenols with a three-ring structure and various substitution patterns. Peanuts contain flavonoids such as catechins, epicatechins, and proanthocyanidins at levels of 1.2-2.3 mg/g [63]. Peanut skins are a particularly concentrated source of proanthocyanidins. Many flavonoids are potent antioxidants that neutralize reactive oxygen species and reduce oxidative stress [60]. Emerging evidence suggests that flavanols possess remarkable bioactive properties, include antioxidant and anti-inflammatory activities [87]. These attributes may contribute significantly to promoting cardiovascular wellness and cognitive vitality [88]. Additionally, research proposes that flavanols' ability to induce vasodilation through enhanced nitric oxide production may be a key mechanism underlying their beneficial effects [87, 89]. Phytates (phytic acid) are the principal storage form of phosphorus in peanuts and other seeds. Although they are known to chelate minerals and are highly regarded as anti-nutrients, phytates still demonstrate antioxidant and anticancer properties.

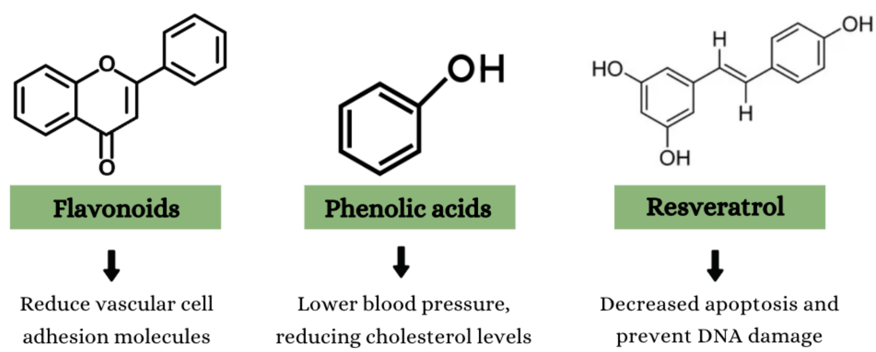


Figure 2. Polyphenol trio: flavonoids, phenolic acids, and resveratrol for optimal health

PEANUTS FOR WOMEN'S WELLNESS

Recent research by Chinese health practitioners has revealed how peanuts can potentially help fuel fertility, increasing a woman's chance of conception by practicing plant-forward eating [59]. Evidence suggests that integrating nutrition therapy for women is crucial and can improve the likelihood of positive fertility outcomes. Such knowledge can contribute to greater reproductive health and enhance the national nutrition guidelines similarly across all body mass index (BMI) categories [59]. Notably, women must meet unique nutritional needs during certain life stages, which can require for more calcium, to maintain bone strength, iron, due to menstrual blood loss, and folate, to support healthy fetal development. With the onset of puberty, the nutritional need of a woman evolves, especially during hormonal changes, menstruation, pregnancy, and menopause. Although there are established supplements that women can use to address dietary deficiencies, it is highly beneficial to acquire vitamins and minerals primarily from whole food sources. Around 100 grams of raw peanuts can offer up to 92 mg of calcium, 4.6 mg of iron, and 66 mg of folate [58].

Therefore, consuming peanuts daily can positively affect women's health by providing various nutrients that help address vitamin or mineral deficiencies. Peanuts are reported to have moderate amounts of phosphorus and manganese, two essential minerals important for bone development and energy production (59). According to human feeding studies, individuals who consumed ≥5 servings/wk of peanuts demonstrated a 20% reduction in frailty [59]. As people age, there is a decline in muscle mass and strength, however, combined with physical activity, adequate nutrients can prevent and manage frailty by providing the necessary amino acids the human body requires to function optimally.

Dysmenorrhea is a common menstrual disorder that affects a significant portion of women, often in the first few years of menstruation. This condition is marked by painful menstrual cramps, increasing uterine contractions and uterine pressure [60]. Research has indicated the presence of inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) stimulates production of prostaglandins, causing uterine contractions [60]. Several studies suggested that vitamin E, a powerful antioxidant, can help reduce inflammation and significantly decrease the severity and duration of menstrual pain by reducing the production of prostaglandins [60]. Given that a serving of raw peanuts contains around 2.2 mg of vitamin E, current research indicates vitamin E may act as a great alternative to nonsteroidal anti-inflammatory drugs (NSAIDs) for pain relief. Furthermore, this review encourages peanuts as a nutrient-dense option to deliver a high yield benefits for women at every stage of their life.

WEIGHT MANAGEMENT

Due to the high energy density, peanuts have been viewed as foods that can lead to weight gain. Research also established that peanut skin polyphenols have specific influences on the western-type diet-fed rats, including reduced weight gain, lesser accumulation of adiposity, and modulation of the fatty acid synthesis gene regulation [28]. However, observational studies have found that nut consumers tend to have lower body weights than non-consumers [26]. Controlled feeding trials also indicate that the body does not absorb all the energy in nuts and that nuts increase satiety and reduce appetite [64]. Several trials have investigated the use of peanuts on weight and fat-influenced outcomes as intervention treatments. Comparing the results of a two-group, 6-month, parallel-design study on 107 overweight adults it was found that consuming peanuts, 35 g/day influenced outcomes as intervention treatments [65]. Comparing the results of a two-group, 6-month, parallel-design study on 107 overweight adults, it was found that consuming peanuts, 35 g/day in the context of a low-fat nutrition plan reduced the overall weight and the quantity of body fat more effectively than a conventional, low-fat diet without peanuts. This randomized trial also revealed that incorporating peanuts into a weight loss diet produced weight loss similar to a conventional low-fat weight loss regimen, which could be a particularly beneficial approach for 5–19-year-olds, given the alarming rise in childhood obesity from 4% to 18% over the past decade [85, 86].

Nevertheless, it was found that there was a reduction in weight in patients who had a peanut-containing diet to prepare weight-loss foods compared to patients on the traditional diet by 6 months. The study found that incorporating 70g/d peanuts into a calorically restricted weight loss diet without reducing weight loss over 6 months is possible [65]. Nuts are metabolically dense and may enhance weight, so they are not recommended for weight loss diets. Participants in the peanut group received 70g/d peanuts before two main meals per day. On average, participants who followed an energy-restricted diet lost 7.5% of their initial body weight or approximately 3500 kcal/week, which is considered clinically significant weight loss. The changes in macronutrient content of the diets were consistent with the nutrient composition and portion of peanuts [64].

The potential mechanisms by which peanuts could assist with weight management include increased satiety, reduced energy absorption, and modulation of gut hormones involved in appetite regulation [65]. The protein, fiber, and healthy fats in peanuts all promote feelings of fullness that may lead to reduced energy intake [65]. The incomplete mastication and digestion of peanuts also result in metabolizable energy through fecal fat excretion [66]. Finally, bioactive compounds such as resveratrol and phenolic acids have been shown to influence energy metabolism and feeding behavior in animal studies [67].

GASTROINTESTINAL HEALTH BENEFITS

The gut microbiota is a group of bacteria that live in the human gastrointestinal system. The composition is predominantly bacterial, with Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria making up approximately 99.1% [90-91]. Smaller proportions consist of archaea, including methanogens and haloarchaea strains, at 0.8%, and a diverse array of microorganisms – such as viruses, fungi, and protozoa – accounting for the remaining 0.1% [92-95]. Digestion, nutritional absorption, immune responses, and overall health are all influenced by the composition and activities of gut microbes [68]. The gut microbiota is greatly influenced by diet; some foods may suppress dangerous bacteria or encourage the growth of healthy ones. Peanuts contain several components that could potentially modulate gut microbiota, including fiber, polyphenols, and phytosterols. Peanut peels and other parts of a peanut can facilitate the occurrence of *Lactobacillus* and *Bifidobacterium* species, which are regarded as healthy gut bacteria, according to in vitro fermentation research [69]. Short-chain fatty acids (SCFAs), such as butyrate, are produced by these bacteria and provide colonocytes with energy and anti-inflammatory properties [70].

A few animal studies have also demonstrated the prebiotic effects of peanuts. In rates fed with a high-fat diet, supplementation with peanut skin extract significantly increased fecal counts of *Bifidobacterium* and *Lactobacillus* compared to controls [71]. Similarly, mice fed a diet containing 10% peanut oil had higher levels of Bacteroidetes and lower levels of Firmicutes in their cecal contents compared to those fed a control diet [72]. Human trials on the gut health effects of peanuts currently need to be improved. However, one study found that consuming 56 g/day of peanuts for 4 weeks increased fecal butyrate concentrations in healthy adults, suggesting a potential pre-biotic effect [73]. Peanuts could enhance gut health by inhibiting the growth of harmful bacteria and may offer potential pre-biotic advantages. Given their high phenolic content, peanut skin extracts have been demonstrated *in vitro* to suppress the development of *Salmonella typhimurium, Escherichia coli*, and *Listeria monocytogenes* [74]. However, the clinical relevance of these antimicrobial effects remains to established.

In addition to the benefits for cardiovascular, metabolic, and gastrointestinal health discussed above, peanuts and their bioactive compounds have been studied for several other potential health effects. Inflammation in the body's natural reaction to an injury or infection [75]. It has been demonstrated that peanuts and their phytochemicals have anti-inflammatory qualities. When compared to the placebo diets, diabetic individuals who ate 25g of peanuts twice a day for 12 weeks had a significant reduction in the inflammatory marker C-reactive protein in a randomized study including 48 participants. Consuming peanuts in the treatment groups was linked to decrease in body mass index (BMI) and systolic blood pressure but not insulin resistance [76]. The ability of resveratrol and other peanut polyphenols to inhibit pro-inflammatory enzymes and cytokines including *COX-2, TNF-a,* and *IL-6* has been demonstrated in both *in vitro* and *in vivo* studies [77].

Peanuts have also been investigated for potential anticancer effects, particularly in the context of colon cancer. Peanut bioactive compounds such as resveratrol, phytosterols, and flavonoids have exhibited anti-proliferative and apoptotic effects in human colon cancer cell lines [78]. In a rat model of azoxymethane-induced colon cancer, diets containing 10% or 20% peanuts significantly lowered the tumor load and tumor number compared with the control diet [79]. Additionally, epidemiological research revealed a direct link between peanut consumption and a lower incidence of colon cancer; however, the effect of peanuts has not yet been sufficiently demonstrated [80].

Finally, peanuts along with their bioactive compounds have demonstrated potential in regulating blood glucose levels and reducing the risk of diabetes. 24 weeks of peanuts (28g/day) significantly reduced fasting blood glucose and HbA1c in 60 adults with type 2 diabetes in a randomized trial comparing peanuts to a control diet [81]. Similarly, a study established that peanut polyphenols exhibit adverse effects on α-glucosidase and α-amylase, which facilitate glucose absorption and carbohydrate digestion [82]. Nevertheless, a number of studies reporting on the influence of peanuts on glucose homeostasis vary, and additional research is required on this subject.

CONCLUSION

This review provides a detailed analysis of the commonly identified bioactive compounds in peanuts and their associated health benefits. This research also showed that peanuts have moderate consumption of resveratrol, phytosterols, phenolic acids, flavonoids, and phytates which have been established to possess desirable antioxidant, anti-inflammatory and other bioactive properties as evidenced by in vitro as well as in vivo experiments. Investigative research conducted on peanut intake has indicated that a peanut-enriched diet is protective against cardiovascular diseases, can aid in weight loss, promote the growth of beneficial bacteria in the gut, and overall help reduce inflammation throughout the body. However, more human studies are required to understand the mechanism of peanut consumption and assess the potential for peanuts bioactive compounds on chronic diseases. Yet, based on current information, peanuts can be recommended as an ingredient in a healthy dietary plan and should be considered a potential functional food component. According to the Functional Food Center, functional foods are characterized as "natural or processed foods that contain biologically active compounds, which, in defined, effective, non-toxic amounts, provide a clinically proven and documented health benefit utilizing specific biomarkers, to promote optimal health and reduce the risk of chronic/viral diseases and manage their symptoms'' [83].

The functional food development process: A 17-step roadmap: The Functional Food Center outlines a comprehensive 17-step process (Table 5) for creating functional food products tailored to consumer needs [83]. The initial stages of the process, steps 1 and 2, involve defining the objectives of the functional food product and pinpointing the specific bioactive compounds that will be utilized. As resveratrol and flavonoids share the ability to mitigate inflammation and oxidative stress, this dual action suggests a potential goal of minimizing these harmful processes in the body. In Step 3, the focus is on establishing the most effective and safe dosage regimen for the bioactive compounds. A key finding from this review is the considerable variation in dosage levels across different studies [64-64,73,83]. Further research is needed to determine the precise dosage that maximizes efficacy while ensuring safety. Step 4 involves determining the most effective time of day for consumption to maximize the benefits of the bioactive compounds [83]. Previous research indicates that peanuts can be consumed at any time of day, with optimal absorption of nutrients occurring when paired with a snack or meal [18, 64]. Additionally, eating peanuts with their skins provides the highest concentration of bioactive compounds [28, 53, 55, 71-74]. Future research could provide invaluable insights by exploring ideal timing and frequency of consumption. Step 5 involves determining the detailed mechanisms of action and biological pathways through which the bioactive compounds produce their desired effects [83]. While the foundation for understanding the microbiota's interaction with the immune system has been established, additional research is required to explore the implications of this relationship for weight management [28, 64-68]. Step 6 involves identifying and validating the most relevant biomarkers [83]. Previous research has employed a core set of biomarkers to assess treatment effects, including body weight, BMI, lipid profiles (total cholesterol, LDL, HDL, and triglycerides), blood pressure (systolic and diastolic), glycemic control (HbA1c, fasting glucose and insulin sensitivity), and inflammatory markers (interleukin-6, and tumor necrosis factor-alpha) [6-8, 60, 76]. Although these biomarkers are commonly used, incorporating additional measures could provide further insights. Step 7 involves selecting a suitable food matrix to deliver the bioactive compound. Peanuts are a common ingredient in many food products, making some of these items promising starting points for further enrichment with bioactive compounds [20]. Steps 8 involve preclinical studies that will evaluate efficacy and safety, while Step 9 comprises clinical trials designed to optimize dosage, consumption timing, and assess the compound's efficacy and safety in humans [83]. Step 10 involves creating consumer-friendly labeling that provides clear guidance on optimal consumption methods, highlights the product's benefits, and specifies recommended dosages [83].

In Step 11, the research outcomes on the functional food product will be communicated to the scientific community via publications in peer-reviewed journals, with a preference for open-access platforms [83]. Step 12 focuses on promoting public awareness and education about the functional food product, ensuring consumers are well-informed and empowered to make informed decisions [83]. In Step 13, the necessary information will be forwarded relevant government authorities for review and approval, noting the specific requirements for scientific evidence may differ across countries [83]. Step 14 marks the successful development of the functional food product. Upon market release (Step 15), the product is designated as a Level C functional food. As additional epidemiological studies and post-market research becomes available, the product's classification may be revised to Level B or Level A.

Table 5: The Functional Food Center's step-by-step guide to developing and marketing Functional Food Products (Table from Reference 83)

Step number	Description of steps to create FF Products
1	Establishes a goal of the functional food product
2	Determines relevant bioactive compound(s)
3	Establishes the appropriate dosage of bioactive compound(s)
4	Establishes the appropriate time of consumption of bioactive compound(s)
5	Determines the specific pathway and mechanism of action
6	Establishes relevant biomarker(s)
7	Chooses an appropriate food vehicle for bioactive compound(s)
8	Provides preclinical studies on efficacy and safety
9	Provides clinical trials for dosage, time of consumption, efficacy, and safety
10	Creates a special label that informs the consumers of the most effective way to consume the product
11	Publications are submitted to peer-reviewed journals, preferably in open access
12	Educates the general public
13	Sends information to credible governmental agencies, such as the FDA, for approval
14	Official establishment of the accredited functional food product
15	Release the functional food product to the market. (Receive the basic category (level C)
16	Provides epidemiological studies. (Reapply for the approval for a new category (level B)
17	Provides after market research. (Reapply for the approval for a new category (level A)

The identification of functional foods involves a multifaceted and rigorous process. Nevertheless, as our understanding of the role bioactive compounds play in functional foods continues to evolve, a consensus on a formal definition of functional foods is likely to emerge, ultimately gaining widespread acceptance. A fundamental principle underlying functional foods is the presence of bioactive compounds, which can be derived from various natural sources, including plants, fungi, and animals. The comprehensive characterization of food bioactive compounds encompasses identification, bioavailability assessment, determination of safe and efficacious dosages, and biomarker validation. Through this systematic process, the precise role of specific bioactive compounds in functional foods can be clarified, thereby establishing a robust foundation for their evidence-based integration into health promotion strategies.

The Novelty of This Work: This systematic review has shown that peanuts have been composed of moderate content of resveratrol, phytosterols, phenolic acids, flavonoids and phytates which demonstrated significant antioxidant, anti-inflammatory, and bioactive properties in both in vitro and in vivo studies. Although more human research is required to ascertain the full health advantages of eating peanuts, the available evidence encourages peanuts as a valuable component of a healthy dietary regimen.

Abbreviations: Acetyl Coenzyme-Acetyl CoA, ATP-Adenosine triphosphate, BMI- Body Mass Index, CVD-cardiovascular disease, GAE- Gallic Acid Equivalents, GI-glycemic index, HDL- high-density lipoprotein, LDL- low-density lipoprotein, NO- nitric oxide, MUFA-monounsaturated fatty acids, ORAC- oxygen radical and absorbance capacity, HOPO- high oleic acid peanut, MPP Mediterranean dietary pattern, PDCAAS- Protein Digestibility Corrected Amino Acid Score, VDD- vitamin D deficiency, SRP- skin roasted peanuts, IC50- Half-maximal inhibitory concentration, *COX-2*- cyclooxygenase-2, *TNF-α*- tumor necrosis factor-alpha, *IL-6*- interleukin-6

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