



Phytochemicals and Their Usefulness in the Maintenance of Health

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Abstract:

Inflammation is the immune system's first biological response to infection, injury, or irritation. Evidence suggests that the anti-inflammatory effect is mediated by the regulation of various inflammatory cytokines, such as nitric oxide, interleukins, tumor necrosis factor alpha- α , interferon gamma- γ , as well as the non-cytokine mediator, prostaglandin E2. Currently, the mechanism of action and clinical usefulness of phytochemicals is known; their action on the activity of cytokines, free radicals, and oxidative stress. The latter are of great relevance in the development of diseases, such that the evidence collected demonstrates the beneficial effects of phytochemicals in maintaining health. Epidemiological evidence indicates that regular consumption of fruits and vegetables is related to a low risk of developing cancer and other chronic diseases.

Keywords: Phytochemicals; Health; Disease; Oxidative Stress

Introduction:

Redox homeostasis is a vital process that maintains the equilibrium of radical oxygen species (ROS) and radical nitrogen species (RNS), thus ensuring the normal functioning of the cells. The superoxide radicals ($\bullet\text{O}_2$), hydrogen peroxide (H_2O_2), hydroxyl radical ($\bullet\text{OH}$), and nitric oxide (NO) are the most common free radicals, which are formed as byproducts of cellular metabolism under normal physiological conditions and in response to pathological conditions [1]. The accumulation of ROS gives rise to oxidative stress in the cells, damaging extracellular components such as proteins, lipids, and nucleic acids. In Mexican traditional medicine, the use of

plants and plant products goes back several thousand years, when the extracts of some medicinal plants were utilized against diverse types of illnesses. Plants are a rich source of secondary metabolites, commonly denominated phytochemicals; these are grouped as alkaloids, polyphenols, flavonoids, saponins, carotenoids, and terpenes, with diverse structural and functional properties that have been proven in animal and human cells [2,3]. Phytonutrients are natural substances; however, they are not called nutrients in the traditional sense because plants do not synthesize them; instead, they are produced by specific cellular types; they carry out important functions in the secondary metabolism of plants, as

insect repellents and sun blockers, as well as growth-regulators, and their effects can be beneficial or damaging to health, depending on the dose [2].

Phytochemicals are low-molecular-weight (LMW) secondary metabolites found naturally in plants; they are biologically active molecules that play a significant role in the normal cellular metabolic process and promote health and disease prevention [3]. The difference between primary and secondary metabolites lies in the fact that the former contributes to the energy metabolism and to the structure of the plant cells, examples of which are proteins, fats, carbohydrates, and dietary fiber; the secondary metabolites comprise non-nutritive dietary components that are essential for the interactions of plants with the environment, and they protect these against insects and fungi (Figure 1). Despite their benefits, phytochemicals can be harmful because they can restrict the availability of nutrients and increase the permeability of the intestinal wall [2]; clinical tests indicate that high doses of antioxidants increase mortality [2]. The exact amount of phytochemicals is unknown; however, it is estimated that this number exceeds 100,000 substances [5].

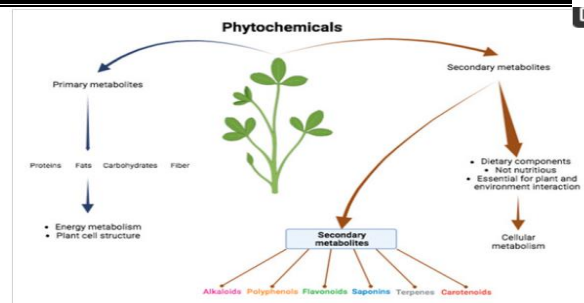


Figure 1. The difference between primary and secondary metabolites.

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Discussion:

Food composition is important for human health and aging; studies have demonstrated that the amount and quality of nutrients we consume daily are fundamental for changing the conditions of health and disease [2]. In a typical human diet, 1.5 g of phytochemicals is ingested each day, while vegans and vegetarians can exhibit much greater ingestion of secondary metabolites; notwithstanding this, there are no recommended ingestion levels for phytochemicals [4].

The classification of phytochemicals is based on their chemical structure and their functional characteristics [2], and the phytochemical groups include carotenoids, common in vegetables and fruits, containing 50 of the 700 natural carotenoids important in human nutrition [1]; beta carotene represents up to 30% of total serum carotenoids. The total daily ingestion of carotenoids reaches 6 mg in the Western diet; phytosterols are closely related to

cholesterol due to their chemical structure and are found principally in dried fruits, legumes (alfalfa, peas, beans, white Navy beans, chickpeas, lima beans, green beans, lentils, peanuts, and soy), in seeds and oils, in which daily ingestion ranges on average from 100 to 500 mg [1], while their absorption is less (10%) on comparison with that of cholesterol (40%). This low availability of phytosterols is because they are absorbed in the enterocytes and are actively transported toward the intestinal lumen [2]. The saponins are surfactant compounds that form complexes with proteins and lipids; they are abundant in leguminous plants, their average daily ingestion is 15 mg, and they have a low absorption rate, which confers upon them greater intestinal tract activity [2]. The glucosinolates are present in members of the cabbage family, providing radishes, mustard, and broccoli with their typical flavor; their daily ingestion is between 10 and 50 mg, and this can be duplicated in vegetarians and vegans [1]; polyphenols include phenolic acids and flavonoids (quercetin is the most frequent flavonoid) [4]; flavonoids have many properties, which include antioxidant, anti-inflammatory, analgesic, anti-proliferative, anti-cancer, anti-angiogenic, anti-microbial, and anti-viral [13], they inhibit the production of NO, one of the principal mediators of inflammation, as well as of interleukin-1 β (IL-1 β), tumor necrosis factor alpha (TNF- α), and prostaglandin E2

(PGE2) [2]; they are present in red wine, dark chocolate, and are found nearly exclusively in the external layer of vegetables (onions, lettuce, tomatoes, asparagus, cabbage, artichokes, and celery) and fruits (apples, grapes, citrus fruits, cranberries, strawberries, and raspberries), tea, and olive oil. Monoterpenes such as menthol (mint), caraway seeds, and citric oil are active substances in herbs and spices, with daily ingestion of up to 200 mg, and they possess a high grade of biodiversity in humans due to their liposoluble capacity. The phytoestrogens have similar effects to the endogenous estrogens; the two main groups include isoflavones and ligands that can act as estrogens and antiestrogens. The isoflavones are nearly exclusively found in soy and its products, and Western diets provide less than 2 mg/day compared to the Asian and vegetarian diets, which can be from 15 to 40 mg/day. The sulfides include all of the organosulfur compounds of plants, such as garlic, with allicin as the main active principle of the latter.

Materials and Methods:

Phytochemicals include alkaloids, polysaccharides, and terpenoid polyphenols, which possess low availability because, despite humans consuming various grams of phytochemicals in their daily diet, only a fraction of these compounds is absorbed in the circulation. The phenolic

compounds play an important beneficial role in health due to their high antioxidant capacity, entertaining as they do the advantage of escaping from upper digestive tract digestion, allowing them to be absorbed into the plasma during digestion. The polysaccharides exert an anti-inflammatory and analgesic effect, which can be related to the diminution of RNS and associated with the increase in the antioxidant enzymes [catalase [CAT], superoxide dismutase [SOD], and glutathione peroxidase [GPx]. For example, only 16% of resveratrol consumed orally is absorbed in the blood and excreted in the urine 24 h after its consumption, while the levels of catechin and quercetin are even lower (2% and 5%, respectively). Ninety percent of the polyphenols in a cup of green tea are eliminated from circulation at 8 h, and this can vary between individuals. The non-absorbed fraction of phytochemicals promotes intestinal functions and acts as a prebiotic, while the absorbed part induces mechanisms of resistance to stress, which improves cellular and organic functions. The flavonoids are metabolized in the small intestine and the liver; the properties that they possess include antioxidant, anti-inflammatory, analgesic, antiproliferative, anticancer, anti-angiogenic, antimicrobial, antiviral, and neuroprotective activity [18]. The soy saponins significantly inhibit the release of PGE₂, NO, TNF- α , and of the monocyte

chemoattractant protein 1 (MCP-1) in a dose-dependent manner and are similarly useful for suppressing the activity of the nuclear factor of the activated kappa beta-cell light chains (NF- κ B), increasing the activity of glutathione, SOD, and CAT.

Inflammation is a reaction of the body to a foreign substance (viral, bacterial, parasitic, or chemical). These substances are recognized by the immune cells through various proinflammatory pathways, leading to the production of cytokines and the activation of the immune cells, such as macrophages and lymphocytes, which will be charged with eliminating the foreign substances. However, if the organism fails in this elimination process, the inflammation increases, generating a chronic phase characterized by the overproduction of cytokines, chemokines, and inflammatory enzymes. The flavonoids, with their anti-inflammatory properties, can interact with many molecules involved in the inflammatory pathways, diminishing the activity of cytokines (NF- κ B, IL-1 β , TNF- α , IL-6, IL-8, and cyclooxygenase 2 [COX-2]), chemokines, and also of inflammatory enzymes. Catechins and quercetin could increase the production of IL-10, an anti-inflammatory compound, through the combined inhibition of IL-1 β and TNF- α ; other flavonoids inhibit arachidonic acid, phospholipase A₂, the COX, and the RNS.

Rutin, hesperidin, and quercetin reduce chronic and acute inflammation; it has been observed that diosmin and hesperidin reduce the synthesis of leukotriene B₄ (LTB₄), accompanying the improvement of inflammation of the colon. Silymarin is a flavonoid subtype that reduces the hypoxia-inducible factor 1 alpha (HIF-1 α) and the induction of nitric acid synthase (iNOS) using the inhibition of NF- κ B. The principal component of silymarin, silybinin, diminishes the epidermal growth factor receptor (EGFR), thus reducing hypertrophy. It has been demonstrated that flavonoids increase the activity of the natural killer (NK) cells and the cytotoxic C cells; they induce transcription factors such as nuclear factor erythroid 2-related-factor 2 (Nrf-2) that mediate the expression of the antioxidant proteins. Nrf-2 suppresses the expression of the monocyte MCP-1 and of the vascular cell adhesion molecule 1 (VCAM-1), which diminishes the formation of atherosclerotic lesions in rats and rabbits.

Flavonoids are exogenous antioxidants; they reduce the reactive species on inhibiting iNOS, xanthine oxidase synthase, or regulation of the ionic channels, and they reduce the oxidation of low-density lipoproteins (LDL). Apigenin diminishes the markers of oxidative stress, such as GPx, SOD, and the activation of caspase-3; another of their functions is exerting their

antibacterial action on inhibiting nucleic acid synthesis, it diminishes the energy metabolism, and it modifies the function of the cellular membrane. Some flavonoids exhibit cytotoxic and cytostatic activity in tumor cells. Metabolites extracted from the plant material are used to induce apoptosis in cancer cells. The herbal medicines are tested both in vitro and in vivo; the anticancer activities of the various medicinal plants have been tested in vivo using different animal models. Although plant-based compounds have been shown to be less toxic compared to conventional synthetic compounds, there is growing evidence of the side effects of the unregulated use of these plants against different diseases. Flavonoids act at different stages of viral infection, such as viral entry, replication, and protein translation. There are several mechanisms by which flavonoid phytochemicals inhibit and act on the viruses. They can obstruct the attachment and entrance of viruses into the cells and hamper different phases of viral DNA replication, protein translation, and poly-protein processing. They can also inhibit the release of viruses to invade other healthy host cells. Even though their mechanisms of action are not fully clarified, polyphenols seem to damage bacterial cell membranes or interfere with the production of amino acids needed for bacterial growth. Phytochemicals exert their antibacterial activity through

different mechanisms of action, such as damage to the bacterial membrane and suppression of virulence factors, including inhibiting the activity of enzymes and toxins and bacterial biofilm formation. Phytochemical investigations exhibited that *Actinidia eriantha* Benth (AE) contains rich phytochemicals, like terpenoids, alcohols, phenolics, aldehydes, organic acids, flavonoids glycosides, ketones, and glucoside. A 24 h administration of an ethyl acetate fraction from the root of *Actinidia eriantha* Benth (AE) EA-EER (100 µg/mL) significantly suppressed cell proliferation by blocking the G1 to S cell cycle progression and downregulating the VEGF-A (vascular endothelial growth factor A) and VEGFR-2 (vascular endothelial growth factor receptor 2) expression.

There are many methods by which essential oil (EO) exposure can occur, including inhalation, ingestion, massage, and skin application. EOs are known for many of their health effects, such as their antibacterial, antibiotic, and antiviral properties. The oils are typically extracted via steam distillation of plants; most EOs are generally safe, and most adverse effects are mild. Terpenes are the biggest class of chemicals found in EOs. There are several classes of terpenes, but the most important in EO are the monoterpenes and sesquiterpenes; the distinct smell is produced from these two groups of chemicals

Several EOs have a strong interest in research for their cytotoxic capacity. The main mechanisms that mediate the cytotoxic effects of EO include the induction of cell death by activation of apoptosis and/or necrosis processes, cell cycle arrest, and loss of function of essential organelles. The effect antibacterial activity of EO may be bacteriostatic or bactericidal; the mechanism of antibacterial action is facilitated by a succession of biochemical reactions within the bacterial cell; due to lipophilic compounds, EOs easily penetrate bacterial cell membranes and have been reported to disrupt critical processes of the cell membrane like nutrient processing, synthesis of structural molecules, energy generation, emission of growth regulators, and influences on the cell-cell communication. Some of the EOs commonly used come from garlic, ginger, clove, black pepper, green chile, cinnamon, pimiento, thyme, oregano, and rosemary. The microorganisms mainly inhibited by essential oils are *S. aureus*, *V. parahemolyticus*, *C. perfringens*, polio virus, Adeno virus, *L. monocytogenes*, *Candida* spp., *Enterobacteriaceae*, *P. mirabilis*, *S. pyogenes*, and *E. coli*. EOs might interfere with virion envelopment, designed for entry into human host cells, synthesis of viral proteins, inhibition of the early gene expression process, glycosylation process of viral, and inhibition of virus

replication by hindering cellular DNA polymerase.

Essential oils, such as chamomile, eucalyptus, rosemary, lavender, and millefolia, have been found to mediate the inflammatory response; they have the ability to influence antioxidant activity, signaling cascades, cytokines, regulatory transcription factors, and the expression of pro-inflammatory genes. The three main anti-inflammation properties of EOs include inhibiting arachidonic metabolism, cytokine production, and pro-inflammatory gene expressions.

Function of the Phytochemicals in the Organism:

Intestinal Diseases:

The intestinal microbiota (IM) represents a great composition, nearly 4×10^{13} , of unique and intricate microbes that reside in the gastrointestinal tract (GI), the majority presenting in the colon and, to a lesser degree, in the upper digestive tract. Thus, it is that in the stomach, due to its acidity, we find therein approximately 10 bacteria/g, 1000 bacteria/g in the duodenum, 10,000 bacteria/g in the jejunum, 10 million bacteria/g in the ileum, and 10^{12} bacteria/g in the colon (Figure 2). The principal bacteria comprise Bacteroides, Firmicutes, Actinobacteria, Proteobacteria, and Verrucomicrobia, with the former two representing approximately 90% of the species [27,28].

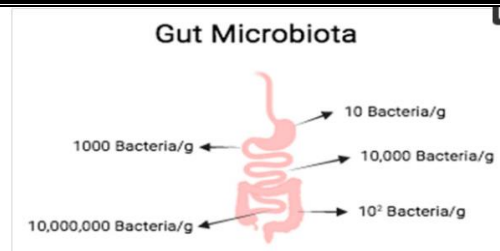
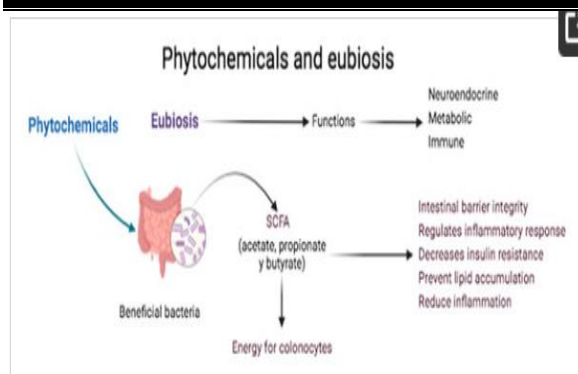


Figure 2. Normal intestinal microbiota.

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The IM depends on the host and provides benefits for the same [2] because it synthesizes certain vitamins (vitamin K, biotin, cobalamin, folates, nicotinic acid, pantothenic acid, pyridoxine, riboflavin, and thiamin), which are important for the bacterial metabolism [2]; these can provide energy (around 10% of the required daily energy) through the epithelial absorption of the bacterial products such as short-chain fatty acids (SCFA) (butyrate, propionate, and acetate). The IM plays a critical role in health, preserving the neuroendocrine, metabolic, and immune functions; therefore, dysbiosis (disequilibrium in the diversity and composition of the microbiotas) of the IM has shown a relation with alteration in the intestinal barrier, thus reducing the bacterial diversity, altering the immune response, and increasing the risk of inflammatory diseases (Figure 3). The intestine-associated lymphoid tissue is an integral part of the immune system, protecting the body against invasive microorganisms



Diabetes:

Diabetes mellitus (DM) is a public health problem. It affects the vital organs; nearly 40% of patients acquire diabetic nephropathy (DN), which leads to a renal system dysfunction that, if not reverted, leads to a terminal kidney disease. The factors that affect DN mainly include elevated ROS levels, persistently elevated glucose levels, the increase in proinflammatory cytokines, the advanced glycation end products (AGE), and alterations at the molecular level, such as altered protein kinase B (PKB), activated in turn by the adenosine-monophosphate-activated kinase (MAPK). Metabolic memory is a synonym of glycemic memory, an innate mechanism in which diabetic complications continue to worsen even after achieving good glycemic control. Hyperglycemia negatively affects all kidney cells, producing AGE and increasing the levels of growth factors such as angiotensin II and the transforming growth factor-beta 1 (TGF-(1)) in the kidney cells. The TGF plays an important role in DN because it possesses profibrotic actions ; some medicinal plant phytochemicals help

reduce the risk of DN, for example, silybin, deriving from *Silybin marianum*, *Curcuma longa*, *Berberis vulgaris*, and *Andrographis paniculata*, in which the antioxidants present in these provide protection to the nephrons on diminishing the oxidative stress ; the flavonoids not only act on the inflammation pathway but also contribute to low blood glucose levels, thus reducing the risk of diabetes-related diseases . *Abroma august* is widely utilized in the treatment of diabetes and its complications in reducing vascular inflammation, hyperglycemia, and oxidative stress, with its extract negatively regulating the expression of IL-1 β , NF- κ B, IL-6, and TNF- α , suggesting its capacity as a nephroprotective agent . Rutin significantly diminishes the levels of glucose, creatinine, ureic nitrogen, and proteins in the urine and can also improve oxidative stress, inhibit the accumulation of type-IV collagen, and reduce the levels of AGE and TGF- β 1. Rutin can be an effective drug for the prevention of early DN. Rutin is one of the flavonoid's greatest utilities against diabetes; it has been shown to reduce fasting blood glucose, improve glucose tolerance, and also reduce serum lipids more effectively. *Bebincad ceridera* prevents lipid peroxidation caused by oxidative stress; catechin prevents the development of diabetes and complications associated with it, and similarly, curcumin has multiple

nephroprotective effects due to its antioxidant property; soy delays the progression of DN; *Vitis vinifera* has resveratrol, which reduces kidney dysfunction; betanin obtained from beets, reduces glomerulosclerosis, the glomerular surface area, and tubulointerstitial fibrosis

In a meta-analysis that included six prospective studies, 284,806 participants were identified, including 18,146 cases. The relative risk (RR) of type-2 diabetes for those with a high ingestion of flavonoids compared with a low ingestion was 0.91 (95% CI 0.87–0.96); in addition, an increase in the consumption of 500 mg/day was associated with a significant risk reduction of 5% (RR = 0.95, 95% CI 0.91–0.98). Likewise, in 2015, the possible beneficial effect was evaluated of the consumption of β -carotenes in the development of type-2 diabetes; in this study, 37,846 participants were included, with an average ingestion of 10 ± 4 mg/day and an average follow-up of 10 ± 2 year, with 915 incident cases reported. After carrying out the adjustment for age, gender, risk factors for diabetes, dietary intake, waist circumference, and BMI, higher ingestion of β -carotenes was inversely associated with the risk of diabetes.

Quercetin reduces GLUT4 activity and diminishes gluconeogenesis and hepatic glycogenolysis; combining quercetin with sitagliptin improves β -cell function and glycemic control, as

well as the metabolic profile. Piperin promotes glucose uptake in the skeletal muscles; treatment of the rates of diabetes with piperin plus quercetin gives rise to a significant reduction in the concentration of blood glucose. Lipid peroxidation and oxidative stress are the causes of the development of DM; in a similar fashion, dysbiosis increases the risk of DM in that a diet rich in fats increases up to three times the production of LPS, thus favoring the inflammation process and insulin resistance. Intestinal dysbiosis also affects the production of SCFA, an important point in terms of the integrity of the intestinal barrier, the proliferation of the pancreatic cells, and the biosynthesis of insulin.

Adipokines, which are biologically active molecules secreted from adipose tissues or adipocytes, play major roles in the regulation of food intake, insulin sensitivity, energy metabolism, and the vascular microenvironment; they are involved in the obesity-induced chronic inflammatory response that plays a crucial role in the development of obesity-related pathologies such as type II diabetes and atherosclerosis. The dysregulation of adipokine release, which causes obesity-induced inflammation, is the common denominator that links obesity to the pathogenesis of insulin resistance and atherosclerosis. Capsaicin (an alkaloid) decreased the levels of IL-6 and MCP-1

and increased the level of adiponectin released from obese fat tissues and fat cells. This dual action of capsaicin may be favourable for improving the dysregulation of adipokine release through the normalization of the balance between the secretions of proinflammatory and anti-inflammatory adipokines in insulin resistance or atherosclerosis. Ginseng is one of the most valuable and commonly used Chinese medicines, not only in ancient China but also worldwide. Ginsenosides, also known as saponins or triterpenoids, are thought to be responsible for the beneficial effects of ginseng. The anti-diabetic effect of ginseng is positive for type-2 diabetic patients but has no significant impact on prediabetes or healthy adults. Ginsenoside Rb1 exerts various pharmacological effects on metabolic disorders, including the attenuation of glycemia, hypertension, and hyperlipidaemia, which depend on the modulation of oxidative stress, inflammatory response, autophagy, and anti-apoptosis effects by regulating the effects of glycolipid metabolism and improving insulin and leptin sensitivities.

Bone Diseases:

Osteopenia is a metabolic disorder that consists of a reduction in bone density. If undetected and mistreated, the gradual loss of calcification can eventually result in osteoporosis (OP) and fractures. It is a significant and impactful public health

issue, affecting more than 20 million elderly in the US, especially postmenopausal (PM) women, and it causes about 1.5 million fractures annually. In the developed world, 2–8% of males and 9–38% of females are afflicted with osteoporosis; however, this prevalence has increased according to the diagnostic criteria of the World Health Organization (W.H.O.); the prevalence of osteoporosis is greater in patients in developing countries (22.1%; 95% CI 20.1–24.1%) than in developed countries (14.5%; 95% CI 11.5–17.7%), and its prevalence varies substantially between countries and regions. Osteoporosis becomes more prevalent with age and is more prevalent in females than in males. In postmenopausal women, the hormonal changes linked to ovarian function after menopause cause many of the alterations in bone density. The estrogen receptor (ER) and androgen receptor (AR) that are expressed in osteoblast and osteoclast progenitors and their offspring influence the role of oestrogens and androgens on bone mass. Oestrogens increase the longevity of osteoblasts (OB) and osteocytes while decreasing that of osteoclasts, limiting skeletal turnover. Oxidative stress accelerates bone remodelling and bone mass loss, whereas antioxidants reduce oxidative stress and stop bone mass loss. The loss of oestrogens or androgens, similar to old age, increases reactive oxygen species (ROS) in bone cells. In

contrast, systemic administration of antioxidants attenuates bone loss due to sex steroid deficiency in male and female mice.

Soy isoflavones significantly increase bone mineral density by 54%; this was evidenced in a meta-analysis of 19 studies in which the association was investigated of soy isoflavones and the risk of osteoporosis (odds ratio [OR] = 0.54; 95% CI 0.13–0.94) in a similar way, they can prevent osteoporosis in postmenopausal women and the risk of fractures. It is known that nutrition and physical activity play an important role in skeletal health, achieving the highest bone mineral density (BMD) and maintaining bone health. In this review, the role of macronutrients (proteins, lipids, and carbohydrates), micronutrients (mineral–calcium, phosphorus, magnesium, as well as vitamins D, C, and K), and flavonoid polyphenols (quercetin, rutin, luteolin, kaempferol, and naringin), which appear to be essential for the prevention and treatment of osteoporosis; these last are also involved in bone formation. Dietary quercetin (2.5% for 4 weeks) can increase BMD and improve cortical and trabecular bone microstructure in mice. Following quercetin administration, enhanced BMD, trabecular bone microarchitecture, and improved bone strength have also been determined in OVX rats (50 mg/kg/day for 8 weeks). Ginsenoside compound K (GCK) could influence the occurrence and progress of

osteoporosis by interacting with 138 potential target proteins, of which 16 targets act in the osteoclast differentiation pathway. β -carotene may improve BMD and reduce the risk of osteoporosis and fracture (95% CI [−0.391, −0.034], $I^2 = 87.30\%$, $p = 0.019$); subgroup analysis showed that the intake of β -carotene was negatively associated with the risk of osteoporosis in both the male subgroup [OR = 0.7, 95% CI (0.549, 0.893), $I^2 = 40.40\%$, $p = 0.004$] and female subgroup [OR = 0.684, 95% CI (0.487, 0.960), $I^2 = 86.40\%$, $p = 0.028$]. Anti-osteoporosis alkaloids are classified into six categories: they promote mesenchymal stem cell differentiation, improve osteoblast proliferation, stimulate osteoblast autophagy, suppress osteoclast formation, regulate multiple signaling pathways, including interrupting the tumor necrosis factor receptor-associated factor 6- receptor activator of NF- κ B interaction, inhibiting the NF- κ B pathway in osteoclasts, activating the p38 mitogen-activated protein kinases pathway in osteoblasts, and triggering the wingless and int-1 pathway in mesenchymal stem cells. The natural alkaloids exert anti-osteoporotic effects mainly by inhibiting bone resorption. Osteoarthritis (OA) is the leading cause of disability for millions of people; there is no effective treatment for OA, only the therapy that slows or prevents OA progression. Studies show that rosehip berries, ginger root, green

tea leaves, turmeric root, and pomegranate peel, containing a significant number of polyphenols and Phyto flavonoids have chondroprotective activity, which positively affects OA prevention and treatment . Daily consumption of green tea extracts slowed the progression of arthritis in rats, suppressed serum IL-17 levels, and increased serum IL-10 levels

Kidney Disease:

It has been reported that phytochemicals (catechin, epicatechin, epigallocatechin-3-gallate, diosmin, rutin, quercetin, hyperoside, and curcumin) are useful as antioxidants and are efficient for the prevention of urolithiasis (the process of the formation of calcium stones in the urinary tract). Kidney stones exert an effect on the health system; they have a prevalence of >10% and a relapse rate of 50% in 5–10 years ; it has been reported that 10–12% of persons in industrialized countries (10% of males and 3% of women) present a kidney stone during their life; the etiology of this disease is multifactorial and is related with genetics, diet, and sedentarism; the kidney stones that contain calcium are the most frequent (75–90%), including hypercalciuria, hypocitraturia, hyperuricosuria, and hyperoxaluria, which are found frequently in the formers of calcium kidney stones, the latter observed as being influenced therapeutically, this formation appearing to be the result of excessive

consumption of protein. These four factors favor the process of crystallization in urine; however, the urine is habitually protected in the nucleation, growth, and aggregation of calcium minerals through crystallization inhibitors. In the urine, calcium oxalate crystallization can only be induced by extreme oversaturation and deficient activity of crystallization promoters . Dietary fiber, which is abundant in fruits and vegetables, can diminish the formation of kidney stones due to the non-digestible ingredients that unite with the fats and minerals of the GI digestive tract, resulting in the urinary excretion of oxalate and calcium. Calcium in the diet can act on the uniting of the dietary oxalate in the intestine, which reduces the absorption of oxalate and the urinary excretion of it.

Green tea (*Camellia sinensis*) contains many polyphenols, which are protector-effect antioxidants against the development of kidney stones; likewise, its supplementation inhibits the growth of crystals in rats, diminishing the growth of crystals in the rat kidney, diminishing the excretion of oxalate Raspberries possess polyphenols and inhibit the formation of stones due to the presence of citrate, magnesium, and glycosaminoglycans . *Rubia cordifolia* is effective in the treatment of different kidney diseases and exerts preventive effects on the formation of urinary stones, inhibits the excretion of calcium, prevents hyperoxaluria and

hypocitraturia on diminishing the formation of urinary oxalate, and regulates the reabsorption of tubular citrate, respectively. The nephroprotective effect of these plants could be attributed to their antioxidant properties. The persimmon (*Punica granatum*), employed in traditional medicine, is a rich source of polyphenols, alkaloids, and anthocyanins, which are highly capable of eliminating free radicals. Phytochemicals produce relaxation of the urinary tract; consequently, the stone can be easily eliminated from the kidney.

Polycystic kidney disease (PKD) is inherited and is characterized by kidney cysts; it is one of the principal causes of terminal kidney disease. The polyunsaturated fatty acids can modify multiple steps in the pathogenesis of PKD. Phytoestrogens and phytochemicals affect the development of physiological events. Rats fed with soy proteins with a high content of isoflavones Favor a greater reduction in the inflammation process, conserve normal kidney function, and reduce changes in the cysts, compared with soy products with a low content of isoflavones. It has been informed that curcumin exhibits beneficial effects against inflammatory diseases; cells treated with curcumin reduce the epithelial proliferation of cysts and prevent the development of renal insufficiency. Parsley (*Petroselinum*

crispum), belonging to the family *Umbelliferon*, is commonly known as an herb, spice, and vegetable and is widely distributed in Western Asia, the Mediterranean, and several European countries. These beneficial activities could be due to its bioactive constituents, including flavonoids, carotenoids, coumarins, tocopherol, and ascorbic acid. Parsley and its extracts have been used potentially as a complementary/alternative treatment for various renal diseases. *P. crispum* has been used as a promising anti-urolithiasis remedy. Its ethanolic extract prevented the nucleation and precipitation of calcium oxalate, urine supersaturation, and urinary protein excretion in a rat model of calcium stone formation.

Cardiovascular Disease (CVD):

It is estimated that 90% of CVD can be prevented with a healthy diet, physical exercise, avoiding the consumption of tobacco, and limiting the consumption of alcohol. Using a systematic review, the association was evaluated of the daily ingestion of flavonoids and the risk of CVD, determining that the increase of every 10 mg/day of flavonoids is associated with a 5% diminution in the development of CVD ; Zhou et al. demonstrated the association between the consumption of flavonoids and the reduction in the risk of mortality (hazard ratio [HR]: 0.87; 95% CI 0.81–0.94) in women aged 50 years and over

[147]. An increase in the consumption of flavonoids of 20 mg/day was associated with a risk reduction of 14% for the development of a cerebrovascular accident [4]. Chrysin is a flavone; it reduces right-ventricle systolic pressure and the mean pressure of the pulmonary artery, diminishing in the same manner the expression of collagen type-I and -III and of NF- κ B, thus preventing pulmonary hypertension in the rat model. Morbidity and mortality from acute myocardial infarction (AMI) remain substantial, although interventional coronary reperfusion strategies are widely used and successful. MI remains the most common cause of heart failure (HF) worldwide. Panax notoginseng saponins (PNS), the extract of Panax notoginseng, exerts a cardioprotective effect in AMI, and the underlying mechanism refers to inducing cardiomyocyte autophagy, antiplatelet aggregation, enhancing endothelial migration and angiogenesis. Berberine is an alkaloid found in such plants as Berberis; in vitro, it exerts significant anti-inflammatory and antioxidant activities. In animal models, berberine has neuroprotective and cardiovascular protective effects. In humans, its lipid-lowering and insulin-resistance-improving actions have clearly been demonstrated in numerous randomized clinical trials. Moreover, preliminary clinical evidence suggests the ability of berberine to reduce endothelial inflammation, improving

vascular health, even in patients already affected by cardiovascular diseases. Epidemiological studies have demonstrated that polyphenol-rich foods reduce cardiovascular events in the general population and patients at risk of cardiovascular diseases. Kaempferol, quercetin, and resveratrol prevent oxidative stress by regulating proteins that induce oxidation in heart tissues. In addition, polyphenols modulate the tone of the endothelium of vessels by releasing NO and reducing LDL oxidation to prevent atherosclerosis. In cardiomyocytes, polyphenols suppress the expression of inflammatory markers and inhibit the production of inflammation markers.

Conclusions and Future Perspectives:

There are multiple pathways implicated in the pathogenesis of diseases, one of these being oxidative stress induced by a disequilibrium between the production of reactive oxygen species and reactive nitrogen species; phytochemicals have attracted increasingly more attention as potential agents of the regulation of oxidative stress, as well as of the release of free radicals, inflammation, the immune response, insulin resistance, lipid metabolism, and the intestinal microbiota, the scientific bases that have opened the possibility of these being utilized in the prevention and treatment of various diseases. The intestinal microbiota has important functions for

health since different metabolites with beneficial potential are produced by digesting dietary products. There is solid evidence that supports the role of the microbiome in the development and progression of diseases, and this microbiome is modified (dysbiosis) by the diet; therefore, the consumption of phytochemical products aids in the maintenance and restoration of health. Future investigations are necessary to evaluate the bioavailability, metabolism, and efficiency of phytochemicals in health; because of this, despite knowing their metabolism and the amount of some phytochemicals that remain in the organisms, little is known regarding the doses that humans can consume, as well as the potential adverse effects that these can condition at these doses.

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