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Chapter 4
Phytochemicals for Preventing and Treating Chronic Diseases

Gerardo N. Guerrero-Flores, Belén Carlino, Rocío V. Gili, Sara Leeson, and Martin L. Mayta

Abstract The rise of noncommunicable diseases (NCDs) as the leading threat to global health is clear, as these conditions cause nearly two-thirds of deaths worldwide, mostly in low and middle-income countries. NCDs are chronic conditions that last 1 year or more and that requiere medical care and lifestyle changes. Diet is one factor contributing to NCDs. While diets high in fruits, vegetables, nuts, and whole grains protect against developing several NCDs, increased mortality has been associated with a high intake of fried food, red meat, and processed meats. Phytochemicals, plant-derived bioactive compounds, have gained attention for their potential to benefit health and prevent or treat NCDs. Interestingly, phytochemicals interact with the gut microbiota that colonizes the human digestive system, which plays a crucial role in maintaining health and preventing diseases like metabolic syndrome and associated risk factors like insulin resistance and hypertension. This chapter aims to provide a comprehensive understanding of the role of phytochemicals in some chronic diseases and their prevention.

Keywords Noncommunicable diseases · Phytochemicals · Microbiota · Inflammation · Plant-based diet · Lifestyle

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4.1 Introduction

Noncommunicable diseases (NCDs) have been defined as conditions that last 1 year or beyond, requiring constant medical care and changes in lifestyle activities, or both [1, 2]. With NCDs accounting for nearly two-thirds of deaths worldwide, mainly from low/middle-income countries [3], the emergence of chronic diseases as the predominant challenge to global health is undeniable [4]. One of the factors contributing to the development of chronic conditions is diet [5]. Previous studies have identified the relationship between diet and mortality. A plant-based diet exerts a protective effect against the development of several chronic diseases, such as hypertension [6, 7], metabolic syndrome [8], diabetes mellitus [9, 10], and ischemic heart disease (IHD) [11, 12], which might be expected to result in lower mortality [13]. Those foods found to correlate with reduced mortality include nuts [14, 15], fruit, vegetables [16], cereal fiber [17], polyunsaturated fatty acids (PUFAs) [18], and green salad [19]; while association with increase mortality have been found for meat, red meat, processed meat [20], eggs [21], and fried potatoes [22].

Phytochemicals are plant-derived bioactive compounds classified as primary and secondary metabolites, according to their function in plant metabolism [23]. Primary metabolites, such as carbohydrates, lipids, and proteins, are directly involved in plant growth and metabolisms [24], while secondary metabolites are further grouped into three main classes: alkaloids, glucosinolates, and cyanogenic glycosides; phenolic compounds; and terpenes. These secondary metabolites in plants serve a variety of ecological and physiological functions. Phytochemicals have gained considerable attention for their potential to positively impact health and prevent or treat noncommunicable diseases like obesity, type 2 diabetes, cancer, and cardiovascular disease [25, 26]. A growing body of evidence shows a significant correlation between phytochemicals intake levels and their positive effects on NCDs [27, 28] (Table 4.1). Phytochemicals are important bioactive compounds that can prevent cardiovascular diseases (CVDs) through several mechanisms. For example, many studies have thoroughly examined how flavonoids can interfere with lipid metabolism, decrease platelet adhesion, and improve endothelial function [93–96]. Moreover, studies have shown that phytochemicals possess antidiabetic qualities, as they improve pancreatic function, glucose homeostasis, and insulin sensitivity [97]. Recent research has also uncovered phytochemicals' anticancer properties, with compounds like sulforaphane in cruciferous vegetables and curcumin in turmeric demonstrating potent antiinflammatory and antioxidant effects that can modulate signaling pathways involved in cancer development [25, 98–100].

Additionally, an intriguing relationship exists between phytochemicals and the gut microbiota (the bacteria, archaea, and eukaryotes that colonize the human digestive system). The gut microbiota impacts human health from innate immunity to appetite and energy metabolism [101, 102]. For example, phytochemicals influence microbiota composition in a way that hinders colorectal cancer development [103], and phytochemicals interaction with the microbiota may help prevent metabolic syndromes and its associated risk factors, like insulin resistance and hypertension, which heighten cardiovascular disease and diabetes risk [104]. The complex

Table 4.1 Dietary phytochemicals for prevention and treatment of NCDs

Chronic disease	Natural compound	Activity	Refs.
Diabetes	Anthocyanin	Improved glucose metabolism and insulin sensitivity	[29]
	Stigmasterol	Improved hyperglycemia	[30]
	Genistein diglucuronide	Lower T2DM risk	[31, 32]
	Dihydrocaffeic acid	Lower T2DM risk; lower concentrations of plasma glucose	
	P-Coumaric, ferulic, caffeic acids and quercetin	α-Amylase and α-glucosidase inhibitory activities	[33]
	Resveratrol	Substantial decrease in homeostatic model assessment of insulin resistance (HOMA-IR) and insulin levels	[34]
		It improves glucose and insulin metabolism	[35]
	Catechin, gallic, protocatechuic acids, and quercetin	α-Amylase and α-glucosidase inhibitory activities	[36]
	Gallic, p-coumaric acid, and Tyrosol		[37]
	Isoflavones and lignans	Improved glucose uptake in animal studies, but inconsistent results in humans	[38]
	Quercetin	Exerted effects on insulin release via changes in Ca^{2+} metabolism	[39]
		Reduced intestinal absorption of glucose, improves glucose absorption in tissues and organs; and improves insulin resistance	[40]
		Improved the function of pancreatic β cells through adenosine monophosphate-activated protein kinase (AMPK), among other mechanisms	[41]
	Vitexin, isovitexin and isorhamnetin rutinoside	α-Glucosidase inhibitory effects	[42]
	γ-Sitosterol	Increased insulin secretion in response to glucose	[43]
	Naringenin	Reduced glucose adsorption by the intestinal brush border, reduced renal glucose reabsorption, and increased glucose uptake and utilization	[43, 44]
	Rutin	Improves glycemic status	[45]
	Curcumin	Improved β-cell functions, prevents β-cell death, and decreases insulin resistance	[46]

(continued)

Table 4.1 (continued)

Chronic disease	Natural compound	Activity	Refs.
Cardio-vascular disease	Ellagitannin	Inhibited proliferation of myocardial fibrosis	[47]
	Curcumin	Decreased oxidative stress and fibrosis	[48]
		Promoted mitochondria function; Prevents apoptosis	[49]
	Icariin	Inhibits of myocardial apoptosis and prevention of inflammation on endothelial cell injury	[50]
	Ferulic acid	Vasorelaxation	[51]
	Resveratrol	Activated SIRT-1 (a class III histone deacetylase), eNOS, Nrf2, and antioxidant response element (ARE), and decreases TNFα production	[52]
	(+)-Catechin	Reduced NF-κB activation; reduction of ICAM-1 and E-selectin adhesion molecules	[53]
	(−)-Epicat-echin		
	Procyanidin dimer B2		
	Quercitin	Antihypertensive, hypolipidemic, hypoglycemic, anti-atherosclerotic, and cardioprotective	[54]
	Procyanidin trimer C1	Promoted Ca^{2+}-mediated signals such as the hyperpolarization via multiple K^{+} channel activations and the Nitric Oxide release in rat aortic endothelial cells	[55]
	Cinnamtannin A2	Protected low-density lipoprotein from oxidation	[56]
Cancer	Glucosinolate	Promotes apoptosis and inhibits proliferation of human liver cancer cells	[57]
		Induced senescence and apoptosis of human breast cancer cells; stimulated tumor suppressors; Inhibited tumor growth	[58]
		Stimulated tumor suppressors	[59]
		Reduced melanoma cell viability	[60]
		Enhanced gap junction activity and chemotherapy sensitivity; improved dendritic cell activity; activated tumor suppressor gene	[61]
		Inhibits tumor progression	[62]
	Baicalin	Inhibits proliferation of cancer cells	[63]
		Inhibited tumor growth and progression	[64]
	Daidzein	Inhibited tumor growth	[65]
		Promoted tumor growth	
	Epigallocate-chin-3-gallate	Eliminated toxic compounds and inhibits growth of cancer cells	[66]
	Emodina	Suppresseed the growth of various tumor cell lines	[67]
	Ellagic Acid	Anti-proliferative and apoptotic effects	[68]
	6-Shogaol	Akt and STAT signaling	[37]
	Allicin	Suppressed cell proliferation and invasion via STAT3 signaling and may be a potential therapeutic agent	[69]
	Alpinumiso-flavone	Suppressed tumor growth and metastasis of clear-cell renal cell carcinoma	[70, 71]
	Androgra-pholide	Suppressed cell proliferation and inducing cell apoptosis via inactivation of ER-α receptor and PI3K/AKT/mTOR signaling	[72]
	Apigenin	Cell growth arrest and apoptosis	[73]
	Curcumin	Modulated cell signaling and gene expression regulatory pathways	[74]

(continued)

Table 4.1 (continued)

Chronic disease	Natural compound	Activity	Refs.
	Dicumarol	Inhibited PDK1 and targets multiple malignant behaviors of ovarian cancer cells	[75]
	Genistein	Inhibited AKT phosphorylation and suppression of GSK-3β dephosphorylation. Promotes β-catenin phosphorylation	[76]
	Gingerol	Induced apoptosis in the bladder cancer cell	[77]
	Glycyrrhizin	JAK/STAT signaling pathway	[78]
	Hispidulin	Intrinsic apoptosis pathway	[79]
	Licochalcone A	Induced cell cycle arrest in human lung squamous carcinoma cells *via* the PI3K/Akt signaling pathway	[80]
	Nimbolide	PI3K/AKT/mTOR and ERK signaling	[81]
	Physapubescin B	Ki-67, Cdc25C, and PARP	[82]
	Pterostilbene	Anti-tumor activity in ovarian cancer via anti-proliferative and pro-apoptotic mechanisms, possibly via downregulation of JAK/STAT3 pathway	[83]
	Resveratrol	Regulated cell cycle and apoptosis pathways	[84]
	Sulforaphane	Cell cycle arrest and apoptosis. Targets: caspase 8, p21, hsp90	[85]
	Thymol	Mitochondrial mediated apoptosis	[86]
	Thymoqui-none	Induced the apoptosis of A431 cells through generation of ROS and inhibition of STAT3 signaling	[87]
	Ursolic acid	Inhibited the growth of human pancreatic tumors and sensitized them to gemcitabine by suppressing inflammatory biomarkers linked to proliferation, invasion, angiogenesis, and metastasis	[88]
	Withaferin-A	Modulated the expression and activity of different oncogenic proteins	[89]
	Ellagitannin	Reinforced gut barrier function	[90]
Inflam-matory disease	Curcumin	Reduced inflammation and oxidative stress	[91]
	Baicalin	Inhibited pyroptosis and inflammation	[92]

interplay between phytochemicals and health highlights the promising potential of plant-based treatments to reduce the global burden of NCDs. This chapter aims to provide a comprehensive understanding of the role of phytochemicals in some chronic diseases and their prevention.

4.2 Phytochemicals, Microbiota-derived Metabolites, and Their Influence on NCDs

The human gut microbiome is a fascinating microbial universe living in the digestive system [105, 106]. In newborns, a complex community of bacteria, archaea, and eukaryotes develops based on the method of birth, whether the newborn is breastfed, and the exposure to environmental microbes. The microbiota plays a critical role in human health (Fig. 4.1) [107, 102], influencing everything from immune function to metabolism [108–110]. Most of the body's microbiota resides

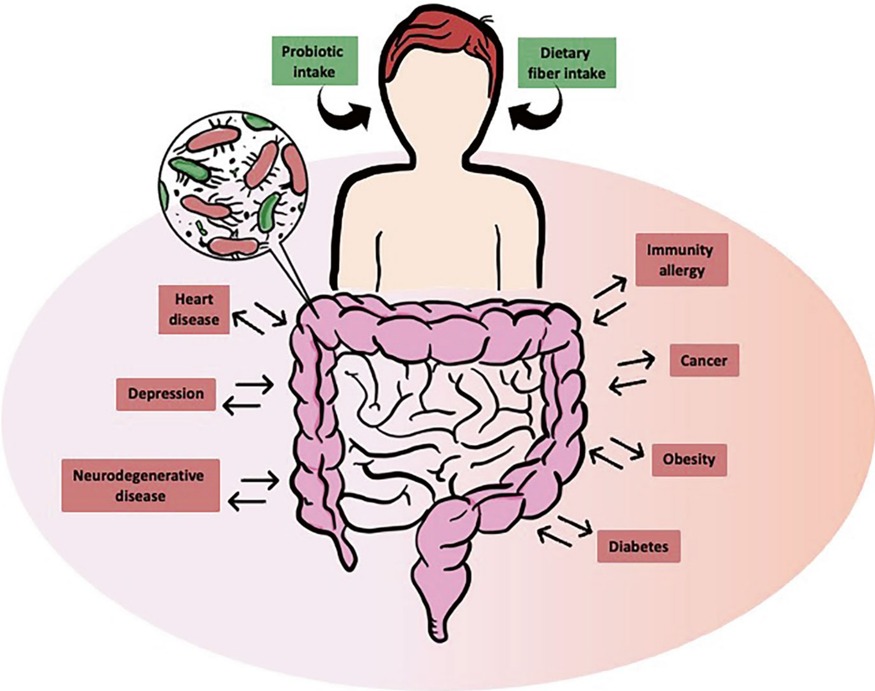

Fig. 4.1 Schematic representation of the crosstalk between the human microbiome and noncommunicable diseases. Microbiota plays a critical role in the development and progression of obesity, diabetes, immune function, heart disease, cancer, and neurological disorders

in the colon [111] and constantly influences the host's health by digestion and absorption of nutrients [112, 113]; production of energy [113], hormones [114], neurotransmitters [115], and vitamins [116]; modulation of the immune system [117]; and protection against pathogens and exogenous toxins [118]. Multiple factors play a crucial role in shaping the gut microbiota [119], and later in life, medications, diseases, genetics, and lifestyle preferences can alter the microbiota composition [120–123], being the diet the most influential factor in the gut microbiota and human health [124]. Phytochemicals can selectively enhance the growth of microbes [125], and the fermentation of non-digestible polyphenols by gut microbes generates beneficial polyphenolic compounds providing significant protection against many chronic diseases [111, 126–130]. Phytochemical beneficial effects likely involve microbiota, either by altering microbial metabolites or by interacting with host cells. For instance, ellagic acid, a polyphenol found naturally in many plants, is metabolized by colonic bacteria into urolithins, a class of anticancer agents (Fig. 4.2) [47, 111, 130–136].

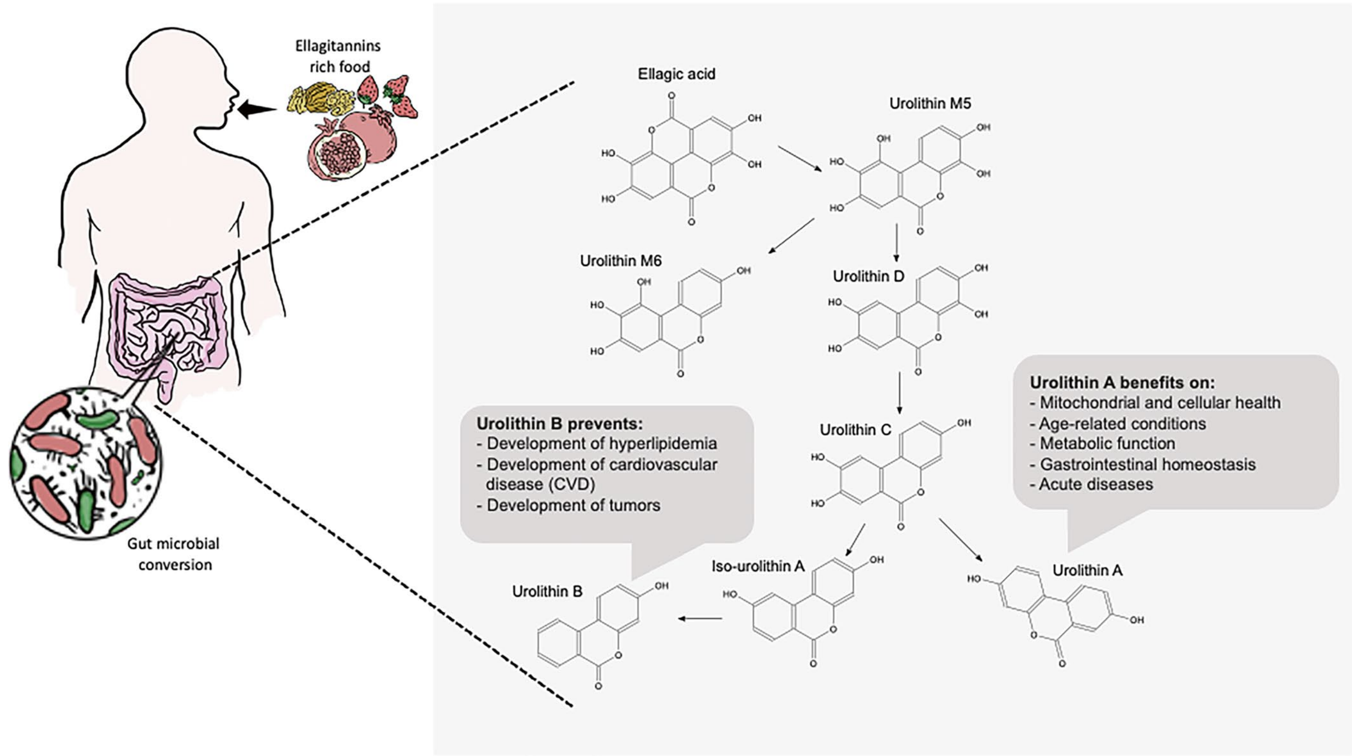

Fig. 4.2 Ellagic acid-containing foods are converted by gut microbes into various forms of urolithins. Urolithin A exhibits biological activities like reducing inflammation and enhancing mitophagy. Urolithin B demonstrates additional benefits, including cardiovascular and nephroprotection, neuroprotection, anti-carcinogenic, antidiabetic, antiobesity, anti-inflammatory, antioxidant, and antibacterial properties

4.2.1 Phytochemicals and Heart Diseases

Cardiovascular diseases (CVDs) remain the leading cause of death and disability in the USA and globally [137]. The principal risk factors for CVD involved are high blood cholesterol, higher body mass index (BMI), high blood pressure, glucometabolic disorders, and diabetes [138, 139]. Studies indicated that compared to omnivorous diets, vegetarian diets based on plant food groups such as fruits, whole grains, legumes, vegetables, nuts, and seeds are associated with considerable reductions in several modifiable risk factors; in contrast, incorporating animal products in the diet is positively associated with the risk to develop CVDs [11, 140–142].

Cohort studies, systematic reviews, and meta-analyses have shown that vegan and vegetarian diets improve various cardiometabolic risk markers, including blood lipids and body weight [11, 21, 138, 141, 143, 144], and compared with non-vegetarians, vegetarians have a lower risk of CVD and IHD mortality, respectively [144]. Moreover, blood pressure levels in those with a plant-based diet were also lower than meat eaters, and a reduced prevalence of metabolic syndrome and type 2 diabetes mellitus (T2DM)—prime risk conditions for CVD and stroke—was observed in vegan and vegetarian participants of the Adventist Health Study-2 (AHS-2) [8, 9]. These differences in the AHS-2 occurred although the non-vegetarians in this cohort eat less meat than the general population [11, 12]. Interestingly, clinical intervention studies utilizing plant-based eating patterns have additionally demonstrated the reversal of coronary artery disease in cardiovascular disease patients [11, 12, 145].

Plants contain many protective nutrients and phytochemicals such as flavonoids, polyphenols, sterols, sulfur compounds, and terpenoids [146–148]. Studies indicate that these compounds provide cardiovascular benefits: flavonoids prevent low-density lipoprotein oxidation and improve vasodilation; plant sterols reduce cholesterol absorption; sulfur compounds activate antioxidant pathways; quinones boost mitochondrial ATP production; and terpenoids decrease atherosclerotic lesions on the aortic valve [149–153]. By providing these cardioprotective effects, the phytochemicals abundant in plants may explain the more favorable cardiometabolic risk profile observed in vegetarians compared to non-vegetarians.

Gut Microbiota, Phytochemicals, and Cardiovascular Diseases In recent years, studies evaluated how gut microbiota can directly modulate coronary artery diseases [154]. Research has shown that certain polyphenol-rich compounds can beneficially modulate the gut microbiota and reduce risk factors for cardiovascular disease. For example, correlation analysis has revealed a significant association between gut microorganisms such as *Roseburia*, bioactive phenolic metabolites -from *Aronia melanocarpa*- in plasma, and improved vascular function [155, 156]. Resveratrol increases *Prevotella*, *Akkermansia*, *Lactobacillus*, and *Bifidobacterium* bacteria, which correlates with reduced microbial production of trimethylamine-N-oxide (TMAO), an atherosclerosis risk factor [157]. Hesperidin increases *Lactobacillus* bacteria in the body and improves cardiovascular health by improving endothelial function, which enhances blood flow [158]. Furthermore, peanut skin extract, rich in procyanidins, catechin, and epicatechin, increases *Roseburia*, *Akkermansia*, and *Bifidobacterium* abundance and reduces atherosclerotic plaques [159]. Moreover, the administration of curcumin promoted weight loss in mice with obesity and hepatic steatosis induced by a high-fat diet, an effect associated with the growth of short-chain fatty acid-producing bacterial species, including *Bacteroides*, *Akkermansia*, *Parabacteroides*, *Alistipes,* and *Alloprevotella* [160]. Additionally, the proanthocyanidin found in wild blueberries reduces obesity by promoting the growth of the gut bacteria *Akkermansia muciniphila* and goblet cells [161]. On the other hand, studies that autotransplant fecal microbiota combined with a Mediterranean diet rich in polyphenols have been shown to increase the proliferation of beneficial bacteria, such as *Bacteroides massiliensis* and *Paraprevotella clara*, which attenuate weight gain, and maintain glycemic control [162].

4.2.2 Cancer and Phytochemicals

Cancer is one of the leading causes of death worldwide [163–165]. Estimates suggest that around 40% of cancer cases could be preventable by modifying risk factors [166] such as reducing tobacco use, increasing physical activity, controlling weight, restraining alcohol, and improving diet [167, 168]. Diet-related factors alone are thought to account for about 30% of cancers in developed countries [169]. Evidence from two large cohort studies of vegetarian populations—AHS-2 and the European Prospective Investigation into Cancer and Nutrition-Oxford (EPIC-Oxford)—suggests that increased consumption of nuts, fruits, legumes, and vegetables is associated with decreased overall cancer risk and cancer mortality [13, 170, 171]. Consumption of red meat has been associated with higher mortality from cancer overall, non-Hodgkin lymphoma, and cancers of the bladder, breast, colon, endometrium, esophagus, stomach, lung, and nasopharynx. Additionally, eating processed meats may increase the risk of death from cancer in general, non-Hodgkin lymphoma, and cancers of the bladder, breast, colon, esophagus, stomach, nasopharynx, oral cavity, oropharynx, and prostate [171–173].

Phytochemicals from fruits, vegetables, and other plant sources have promising anticancer effects [174, 175]. Some phytochemicals act as chemopreventive agents that inhibit tumor formation [176], while others have potential cancer treatments [177, 178]. These phytochemicals target molecular pathways involved in cancer growth and progression through mechanisms like carcinogen deactivation, antioxidant effects, halting proliferation, inducing apoptosis, and immune system modulation [177]. Ellagic acid, for example, a polyphenol present in walnuts, berries, pomegranates, and grapes [179], demonstrates antiproliferative effects against certain cancers [68, 132]. Resveratrol, found in grapes, berries, and peanuts, exhibits activity against breast, cervical, uterine, blood, kidney, liver, eye, bladder, thyroid, esophageal, prostate, brain, lung, skin, gastric, colon, head and neck, bone, ovarian, and cervical cancers [180]. Allicin, a compound derived from garlic, also shows promising benefits [181].

Gut Microbiota, Phytochemicals, and Cancer A healthy gut microbiome can protect against cancers, though the mechanism remains unclear. For example, curcumin has demonstrated anticancer properties that are facilitated by the gut microbiome [182]. A 6-month observational study revealed that a combination of curcumin and quercetin reduced the number and size of polyps by over 50% in patients with an inherited form of colorectal cancer [183], however, bacteria were not a factor evaluated in this particular study. Additionally, green tea polyphenols substantially delayed the development of estrogen receptor-negative mammary tumors and increased populations of *Adlercreutzia* and *Lactobacillus* in a transgenic mice model [184]. Furthermore, administering a polyphenol from *Myrciaria dubia* (Camu camu) increased *Ruminococcaceae* growth and CD8+ T cells in the tumor microenvironment [185], consequently regulating the effectiveness of therapy against cancers [186].

4.2.3 Phytochemicals and Type 2 Diabetes Mellitus

The global prevalence of diabetes mellitus, especially T2DM, is rising sharply, as reported in the 2019 and 2021 editions of the Diabetes Atlas [187]. According to statistics, diabetes affected an estimated 537 million people between the ages of 20 and 79 years worldwide in 2021. Experts project this number will rise to 783 million cases globally by the year 2045 [188]. Type 2 diabetes mellitus can lead to numerous health complications like kidney disease, nerve damage, and vision loss, making it a leading cause of various chronic metabolic conditions [189]. The current treatment for T2DM relies on drugs that improve insulin sensitivity, supplement insulin levels, stimulate insulin secretion, or enhance glucose absorption [190]. For example, Metformin is one of the most used drugs for treating T2DM, but it can cause side effects ranging from mild to severe, which may lead patients to stop taking their medication as prescribed [191]. However, alongside pharmacological interventions, dietary plans focusing on balanced nutrition and portion control usually are also part of the treatment.

Combined therapies with medications that have different mechanisms of action can provide greater therapeutic control. These often include a glucagon-like peptide 1 receptor agonist and a sodium-glucose cotransporter 2 inhibitor [192]; nevertheless, therapies using multiple drugs may appear effective, but they can cause problems like toxicity, and side effects due to the complex pharmacological interactions [193]. Conversely, research indicates that people with T2DM benefit from phytochemicals due to their effectiveness, affordability, and probable low side effects [194, 195]. Studies have identified around 1200 plants rich in bioactive compounds with antidiabetic properties, with 400 specifically targeting T2DM [196–198]. Consequently, managing T2DM with phytochemicals appears to be a highly promising and appealing approach.

The Mediterranean and a plant-based diet consisting of whole grains, legumes, vegetables, and fruits contain compounds such as phenolics, carotenoids, and vitamins that may improve glycemic control and protect against T2DM and its complications [199–202]. Animal research shows that plant extracts containing high levels of phytochemicals exhibit antidiabetic effects equal to or better than some standard antidiabetic medications [203–206]. Several phytochemicals from plant food also have antihyperglycemic properties and disease-modifying effects [178, 195, 196, 203, 204]. Other phytochemicals including flavonoids, saponins, pectin, glucosides, and myrcelin have also demonstrated antidiabetic potential in studies [194].

The mechanisms by which phytochemicals produce their antidiabetic effect include (a) increasing insulin secretion, (b) improving insulin sensitivity, and (c) mimicking insulin action [207, 208]. For example, an 8-week study in humans found an extract of flavonoids, flavonol aglycones, phenolic acids, and steroid glycosides from the *Balanites aegyptiaca* fruit (desert date) significantly reduced postprandial plasma glucose, suggesting it improved insulin sensitivity by lowering fat levels [209]. Additionally, the consumption of 2 g of chocolate with 70% cocoa content was associated with improved fasting plasma glucose and insulin resistance parameters compared to milk chocolate, likely because it contains more flavonoids [210]. Resveratrol and quercetin, two phytochemicals extensively studied for their potential to prevent and treat diabetes, have demonstrated promising results. Resveratrol improves glucose metabolism and lipid profiles in patients with T2DM taking oral medication or insulin, according to multiple studies [34, 35, 211, 212]. Quercetin enhances glucose metabolism and pancreatic beta-cell function to lower plasma glucose levels [40, 213, 214].

The fight against diabetes is intensifying, indicating a need to break with some traditional medicine paradigms and combine conventional treatments with plant-based products. In coming years, prevention and treatment of this disease may shift toward a more holistic approach, as no plant compound nutraceutical or food derivative currently substitutes directly for antidiabetic drugs. A strategy prioritizing a diet high in plant-based foods will yield better outcomes than conventional medications alone.

Gut Microbiota, Phytochemicals, and T2DM Altered glucose homeostasis correlate with changes in gut microbiota composition and the progression of T2DM and its complications [215]. Both animal models and human studies show certain microbiota impact glucose metabolism in T2DM [216]. For example, higher ratios of *Bacteroidetes* to *Firmicutes* and *Bacteroides-Prevotella* to *Clostridium coccoides-Eubacterium rectale* positively correlate with plasma glucose, linking intestinal microbiota to T2DM [217]. Additionally, T2DM patients tend to have lower levels of beneficial *Bacteroides*, *Prevotella*, and *Bifidobacterium* genera. *Bifidobacterium* provides health benefits including improved gut permeability, reduced endotoxin, and inflammation, along with enhanced glucose tolerance, insulin secretion, and attenuated inflammation. Genera like *Bifidobacterium*, *Bacteroides*, *Faecalibacterium*, *Akkermansia*, and *Roseburia* associate negatively with T2DM, while *Ruminococcus*, *Fusobacterium*, and *Blautia* correlate positively.

Furthermore, obesity and T2DM are linked to depleted butyrate-producing bacteria in the *Clostridiales* order [218, 219]. Butyrate is a key compound that supports proper pancreatic beta cell function, especially post-meal. Overall, adequate butyrate is associated with improved insulin response, while abnormal propionate is associated with T2DM risk, both inducing inflammation [215, 220]. The characterization of gut microbiota dysbiosis in various diseases and the establishment of a causal relationship between gut microbiota and disease can be valuable in developing therapeutic interventions for T2DM and its associated complications [221].

4.2.4 Gut Microbiota and Neurological Diseases

A healthy gut with diverse microbes is vital for normal brain functions and emotional behaviors [222]. There is a well-established relationship between gut microbiota and various neurological diseases, including anxiety, Alzheimer's disease, and depression [223–228]. The diversity of gut microbes is vital for normal brain functions and emotional behaviors. For example, curcumin reversed anxiety-related behaviors in an anxious mouse model by upregulating *Muribaculaceae*, which counteracted the harmful effects of dextran sulfate sodium salt [227]. In another murine Alzheimer's model, quercetin significantly reduced attention deficit symptoms and parameters; this improvement correlated with an increased abundance of *Barnesiella*, *Lactobacillus*, and *Parasutterella* genera [226]. Additionally, higher blood carotenoid levels in humans were associated with a lower risk of developing depressive symptoms [228].

Studies of the gut–brain axis in the future will need to address research questions regarding the gut microbiota and associated neurological disorders in order to provide valuable insights into the beneficial or pathological role of the gut microbiota on the brain.

4.3 Conclusion

Chronic noncommunicable diseases are a major global health threat, causing most deaths in low and middle-income countries. High intake of animal-derived food has been linked to increased mortality, while diets rich in fruits, vegetables, nuts, and whole grains protect against NCDs. Phytochemicals, bioactive compounds from plants, and their interaction with the microbiota have potential health benefits. Combining conventional treatments with plant-based products may be necessary to fight NCDs.

Conflicts of Interest The authors declare no conflict of interest.

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