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Nutritional Effects of Polyphenols, Dietary Fiber, Prebiotic effect, Compounds Associated with Dietary Fiber and Impact of Polyphenols on Human Intestinal Microbiota and Their Health Benefits

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Abstracts: As secondary metabolites found in plants, polyphenols have recently gained prominence as important bioactive chemicals that could have profound effects on human health. Polyphenols found in plants can modulate many different physiological pathways through their direct or indirect interactions with biomolecules. Polyphenols have attracted a lot of interest from researchers and doctors because of their structural variety and natural abundance. Afterwards, learning where polyphenols come from in the diet helps shed light on the natural plant-based sources that make them available all over the world. The intricate process from consumption to systemic effects is elucidated, and the conversation continues with the absorption and metabolism of polyphenols in the human body. The review primarily aims to dissect polyphenols' antioxidant activities, drawing attention to their function in preventing oxidative stress and related health problems. Their effects on a wide range of health issues, including hypertension, allergies, ageing, and chronic diseases (such as diabetes and heart attacks), are covered in detail in the analysis. New information about polyphenols' positive effects on a worldwide scale highlights their promise as medicinal and preventative agents. Depending on the phyto-antioxidant content, plant-based product consumption enhances human health and lowers the risk of developing and worsening numerous chronic diseases. Ultimately, our extensive analysis has shed light on the significant health benefits linked to the intake of phyto-antioxidant-rich plant-based foods. This eating style has shown a considerable decrease in the occurrence and worsening of various chronic diseases, supporting its promise as a foundation for improving human health. Despite the fact that most people believe polyphenols' antioxidant properties are responsible for their health benefits, we must not forget that the exact mechanisms of action of certain phenolic compounds are complex and yet not fully known. Addressing this information gap calls for a detailed investigation of polyphenol bioavailability in the hopes that this will lead to a better understanding of their health-promoting properties. Our inquiry has broadened to include the several functions of polyphenols in illness management. We have focused on their possible effects on metabolic syndrome, autoimmune diseases, respiratory health, pregnancy, and maternal health. This detailed analysis of polyphenols in different pathophysiological settings improves our understanding of their multipurpose uses and highlights their promise as therapeutic approaches in several health paradigms.

Keywords: Dietary Fiber, Polyphenols, Microbiota, Health Benefits.

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Introduction

Polyphenols (PP), also known as phenolic compounds, are among the most abundant and ubiquitous classes of chemicals found in plants. They play a crucial role in plant physiology and can be found in every organ of the plant. Thus, PP protect crops from plague and preharvest seed germination by aiding plant tolerance to parasites, diseases, and predators. However, flavonoids and other phenolic compounds have medicinal uses as antibiotics, antidiarrheics, anti-inflammatory agents, and in the treatment of diabetes, vascular fragility, radiation damage, allergies, and hypercholesterolaemia [1, 2]. In addition to its medicinal uses, PP have several industrial uses, including cosmetics, tanning agents, paints, and food additives. The fact that polyphenols are present in every section of a plant means that they will always play a significant role in the diets of animals and humans alike. In light of the foregoing, polyphenols emerge as an exceptionally significant class of plant compounds. Chemical, biochemical, pharmacological, nutritional, agronomic, and other methods have been employed to investigate PP in various plant products, despite their high chemical complexity [3]. We plan to take a nutritional approach to polyphenolic compounds within the context of this book, focussing on the role of PP in dietary fibre analysis. Polyphenolic substances and their presence in plant-based diets will also be briefly described chemically. Polyphenols are biogenetically derived from two primary synthesis processes in plants, the shikimate pathway and the acetate pathway, which are byproducts of the secondary metabolism of plants. Their fundamental molecular structures are benzene and flavone, and they vary from very simple molecules like phenolic acids to very polymerised substances like tannins. Most phenolic compounds in plants are found in conjugated form, mainly with hydroxyl groups attached to one or more sugar residues. Glucuronic and galacturonic acids, arabinose, rhamnose, xylose, mannose, apiose, and allose are some of the related sugars that can be present as mono-, di-, tri-, or tetrasaccharides. It is known that this chemical forms connections with other phenols as well as carboxylic and organic acids, amines, and lipids. As an example, quercetin, the most abundant flavonoid, can be found in 135 distinct configurations, including O-glycosides, O-sulfates, and sugars conjugated with acylated aromatic and aliphatic acids [4-6]. Consequently, there is a great deal of difficulty in studying this huge and complicated class of chemicals, since there are more than 8,000 phenolic structures identified to far.

Food Polyphenols

The nutritional and sensory value of plant-based foods is at least in part attributable to PP. Plants are able to withstand diseases because PP, at low quantities, protects them from oxidation. Unwanted colour and flavour in produce is caused by the browning process of phenolic chemicals, which can be enzymatic (catalysed by polyphenol oxidase) or nonenzymatic. The browning of chocolate and the oxidative polymerisation of tea polyphenols during the manufacturing of black tea are two examples of how PP undergoes oxidative modifications during processing, which in turn give some foods their unique and appealing organoleptic qualities. The amount of polyphenolic compounds in food and drink determines how astringent and bitter they are [7–11]. Fruits, vegetables, grains, beans, nuts, and a wide variety of plant-based beverages and meals contain dietary PP. Even within the same species, there is a wide range of concentrations in plants due to factors including heredity, environmental influences, and processes like germination, ripening, processing, and storage. Despite this, there is still no universally accepted system for classifying phenolic compounds or for analysing the many families of polyphenolic compounds [12–15]. This is likely due to the fact that these molecules are quite complicated. This means that there is a lack of consistent, up-to-date information about the amounts and types of PP found in plant diets in the scientific literature, which makes it hard to draw any firm conclusions. Referring readers to the recently released book by Shahidi and Naczk and Ku¨hnau's comprehensive review of food flavonoids, they provide substantial data. While the tannin amounts mentioned in the literature are typically quite low, the majority of polyphenols found in foods are phenolic acids and flavonoids, which include anthocyanins, flavanones, flavanols, and so on. However, the vast majority of studies use plant food extracts. The typical quantitative approaches are not applied to determine insoluble tannins, which are molecules that are strongly polymerised or tannins that are attached to components of the cell wall and proteins. As a result, the real tannin content is typically underestimated. There are likely to be significant quantities of insoluble tannins in foods

such as beans, grapes, chocolate, nuts, etc. No reliable data is available about the consumption of dietary polyphenols. During the winter and spring, Americans consume an average of 1 g of flavonoids per day, according to Ku¨hnau. This amount rises to as much as 1.1 g in the summer and fall, when fruit consumption also increases. However, these findings were limited to flavonoid consumption in 1971, when the scientific community knew of just approximately 800 distinct flavonoids. These numbers should be much higher, given that the number of flavonoid structures known rose to more than 5,000 by 1990. Despite this, new studies show that the Dutch consume significantly less flavonoids (flavonols and flavones, 23 mg/d) than what Ku¨hnau found (115 mg/d of these two flavonoids in the American diet) [18, 19]. But additional phenolic chemicals weren't even considered in any of these experiments. In addition, as previously stated, the real amount of polyphenols (PP) in plant-based foods is frequently underreported because the study of many PP—primarily insoluble compounds that can be quantitatively more significant than flavonoids—is often disregarded when estimating PP consumption [20-26]. Consequently, there are no reliable ways to estimate overall polyphenolic consumption. However, there is a lack of data on the bioavailability of phenolics found in food, which is a major consideration when assessing the nutritional value of these substances.

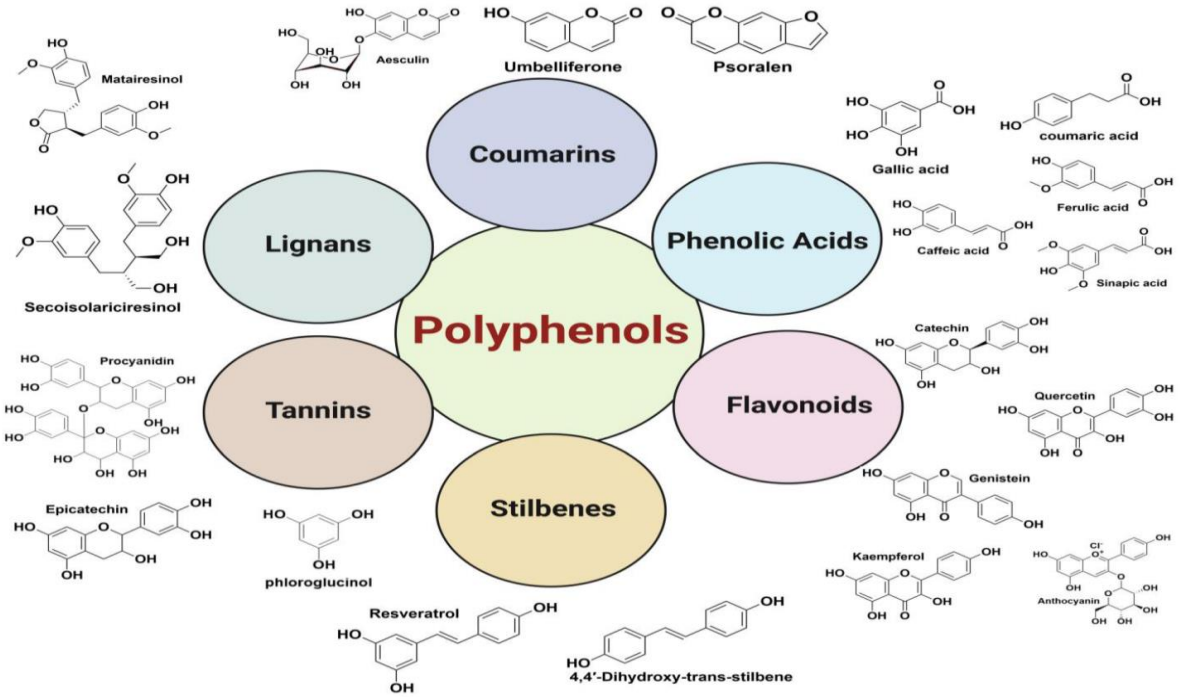

Figure 1. Chemistry of polyphenols.

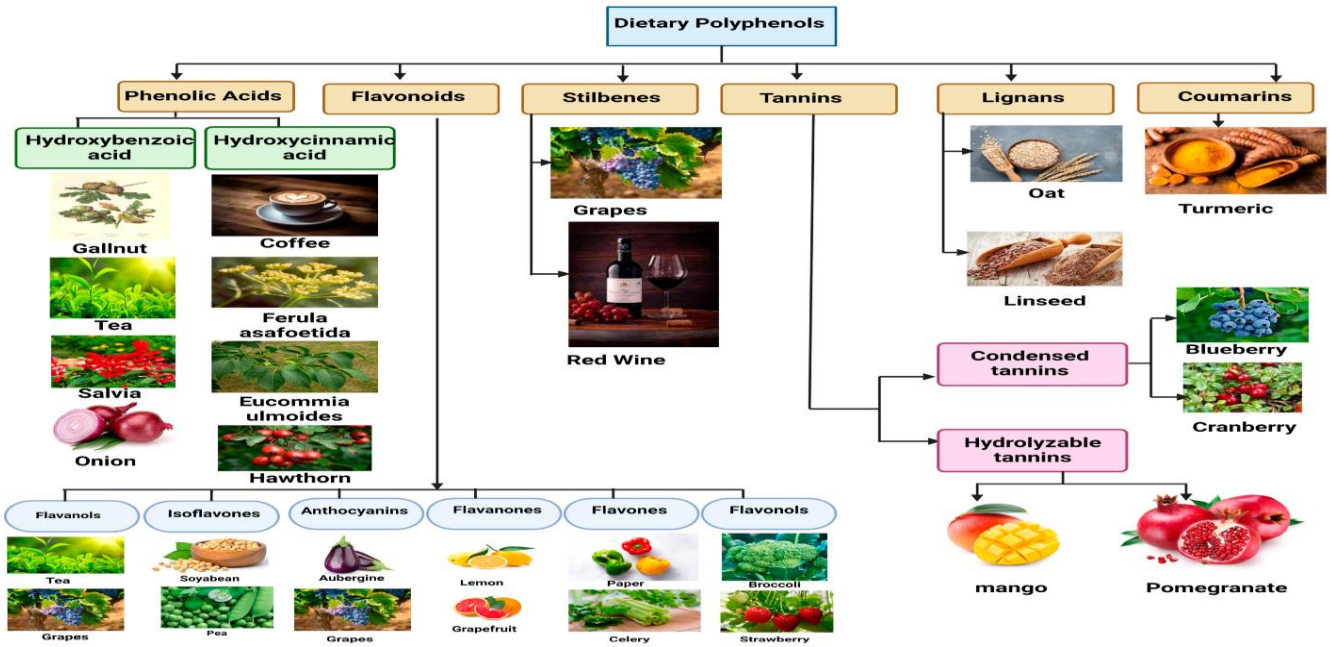

Figure 2. Various sources of dietary polyphenols.

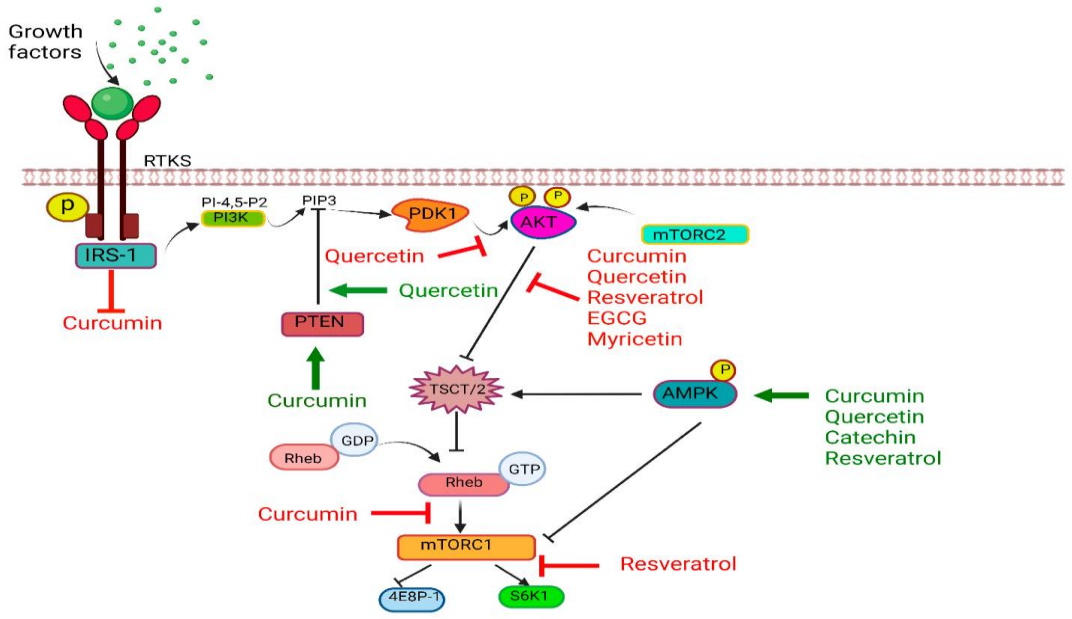

Figure 3. Polyphenol anti-inflammatory effects mitigate oxidative damage in type 2 diabetes.

Prebiotic effect of dietary polyphenols

Prebiotics are substances that are specifically metabolised by microorganisms in the hindgut and have positive health effects. Recent research points to polyphenols as a potential prebiotic. Consuming polyphenols, particularly catechins, anthocyanins, and proanthocyanidins, has been shown in animal experiments to enhance the number of Lactobacillus, Bifidobacterium, Akkermansia, Roseburia, and Faecalibacterium spp. [27, 28]. Additionally, supplementing with polyphenols enhanced the synthesis of butyrate and other short-chain fatty acids (SCFA). Following the consumption of anthocyanins and ellagic acid, the included clinical trials demonstrated a decrease in plasma lipopolysaccharide-binding protein and an increase in Lactobacillus acidophilus, Bifidobacterium, and Faecalibacterium spp. The term "prebiotics" refers to substrates that the host's microbes specifically use to promote bone, mental, gastrointestinal, and metabolic health. A number of dietary fibres are widely known in the literature as prebiotics, particularly resistant oligosaccharides (galacto oligosaccharides, fructo-oligosaccharides, and inulin). In addition to dietary fibres, new research has demonstrated the relationship between polyphenols and the gut microbiota, indicating that they could be potential prebiotic chemicals [29–32]. The chemical structure of polyphenols, which are secondary metabolites of plants, ranges from that of a simple phenolic molecule to that of a complex high-molecular mass polymer. These rings are aromatic and include one or more hydroxyl groups. These substances prefer to interact with intestinal microbes due to their high metabolism in the large intestine and low bioavailability. In reality, there is a two-way relationship whereby microbes can influence the activity of phenolic compounds and polyphenols can influence the gut microbiota. Through this interaction, polyphenols' metabolism and bioavailability can be controlled, transforming them into metabolites that may have various health impacts on the host. Regular consumption of dietary polyphenols is linked to a lower risk of cardiometabolic disorders. Research indicates that polyphenols possess anti-inflammatory, anti-obesogenic, anti-diabetic, anti-lipidemic, and antioxidant properties [33, 34]. However, the metabolism, absorption, and bioavailability processes of dietary polyphenols have a major role in their health, and these processes are linked to the makeup and functionality of the gut microbiota. There is currently no solid proof that polyphenols have a prebiotic impact, despite the fact that they are known to modify the composition of the gut microbiota. Each polyphenol's prebiotic action can be affected by the dietary source [35,36], the compound's chemical structure, and individual variations in the composition of the gut bacteria. As a result, it can be difficult to link the ingestion of polyphenols, the development of microbes identified as prebiotic targets, the metabolites produced, and the impact on health.

Impact of Polyphenols on Human Intestinal Microbiota and Their Health Benefits

The scientific community is paying close attention to dietary polyphenols because of the chronic diseases they may help prevent and the health benefits they may provide. diseases affecting the cardiovascular system, diabetes, obesity, and the nervous system. Polyphenols alter the microbiome by inhibiting harmful bacteria and promoting good ones; they are antioxidants. Polyphenol bioaccessibility in the oesophagus and small intestine is influenced by interactions with dietary fibres. Microbiome diversity and population are influenced by dietary fibres, polyphenols, and metabolites of these compounds. Improve your gut health by eating pomegranate, cranberry, berry, and tea—all foods rich in polyphenols [37–39]. The role of gut microbiota in human health is intricately related to polyphenol-rich diets. Fruits, vegetables, cereals, coffee, tea, wine, and other drinks are good sources of polyphenols, which are secondary metabolites. Flavonoids, phenolic acids, stilbenes, and lignans are all part of this group of phenolic chemicals. There are a number of chronic diseases that polyphenolic compounds can help prevent, including cancer, diabetes, obesity, and neurodegenerative illnesses. These compounds also have antioxidant, antibacterial, anti-inflammatory, and anticancer effects [40]. Significant variations in polyphenol intake are observed among geographically diverse individuals worldwide due to distinct guidelines and dietary habits. The kinds of food matrices and the ways they are prepared also have a significant impact on the polyphenolic content. There are two kinds of polyphenols found in plants, fruits, and vegetables: bound and unbound. Research on dietary polyphenols has mostly focused on phenolic substances that have been extracted using aqueous organic solvents. This includes analytical, nutritional, and clinical investigations. Extractable polyphenols (EPPs) are the name given to these polyphenols. Notably, potentially bioactive polyphenols remain bound in residues comprising macromolecules such as cellulose, protein, and lignin. These polyphenols are referred to as non-extractable polyphenols (NEPPs) and are usually ignored during analysis. Several studies have indicated the presence of abundant NEPPs in specific foods and vegetables such as berries, brown rice, carrots, onions, spinach, apples, and oranges Peels, pomace, and seeds also have abundant NEPPs. NEPPs comprise substances with high-molecular-weight polymers and polyphenols associated to cell wall macromolecules (proteins and polysaccharides) or entrapped inside the food matrix. Major NEPPs constitute condensed tannins, proanthocyanidins, hydrolyzable polyphenols (including hydrolyzable tannins), or polyphenols. These bioactive chemicals have strong antioxidant, anti-inflammatory, antidiabetic, and other biological effects. Bioaccessibility is a significant component impacting the bioavailability, physiological impacts, and biochemical activities of polyphenols. Polyphenols are normally liberated from food matrices by interacting with digestive enzymes and bacterial microflora in the small and large intestines, respectively, and potentially become accessible for absorption. Significant variances are reported in the bioavailability of polyphenols, influenced by the kind of dietary matrix, molecular mass, conformations, and physicochemical activities, such as digestibility. Consequently, not all phenolic compounds are equally available to exercise their functions in the human body after the consumption of phenolic-rich meals. Bacterial flora ferment NEPPs in the lower GI tract because they are not released or absorbed into the GI tract. When polyphenols enter the small intestine, the microbes in the gut biotransform them into their metabolites, which then have a wide range of pharmacological and functional consequences. In addition to impacting the host's gut health, these polyphenols and their metabolites alter the colon's bacterial composition. Multiple studies have pointed to the possibility that the functional link between dietary fibres and polyphenols, as well as the variety and integrity of gut microbiota, can be influenced by their interactions. Nevertheless, the consequences of polyphenol-rich diets on human health are complex and poorly understood, particularly in regard to the role of gut flora. Similar to the amount of human cells, the human microbiota consists of 10-100 trillion microorganisms, the majority of which are bacteria but also viruses, fungi, and protozoa, mainly found in the gut. There are at least 400 different bacterial species and a microbiota abundance that rises steadily in the gastrointestinal tract, with the colon having the highest density (1010-1012/g) and the stomach having the lowest. The enormous surface area of the gastrointestinal system ranges from 250 to 400 m2. Over the course of a lifetime, the human digestive system processes almost 60 tonnes of food, carrying with it a plethora of microbes from the surrounding environment. In contrast to the around 22,000 genes included in the human genome, a human gut microbiome gene catalogue including 3.3 million genes has been published. Innocent bacteria make up the microbiota. Humans are home to 2,172 different species of bacteria, with 93.5% of those species falling into the Proteobacteria, Firmicutes, and Bacteroidetes phyla, according to research. Among humans, 386 species are known to inhabit the oral cavity and gastrointestinal tract entirely without oxygen.

Actinobacteria, Verrumicrobia, Acidobacteria, and Fusobacteria make up less than one percent of the bacteria in the human digestive tract. Bacteroidetes and Firmicutes predominate in the colon and small intestine. In humans, good bacteria in the intestines have multiple uses. Intestinal microbes help develop the immune system, keep pathogens out, and keep the mucus barrier in place. Nevertheless, metabolic disorders like obesity and type 2 diabetes can emerge when these systems are disturbed by an imbalance of microbes, a condition called dysbiosis. Folate, riboflavin, biotin, nicotinic acid, pantothenic acid, pyridoxine, thiamine, and vitamin K are all produced by the gut microbiota. Vitamin B12, produced by lactic acid bacteria, is critical for DNA synthesis and proper brain and nervous system function. Vitamin folate, produced mainly by bifidobacteria, is essential for many metabolic activities in humans, including DNA synthesis and repair. The human gut microbiota is formed during early development in the intestines and goes through significant transformations until it reaches a state of balance in adulthood. Microbiota mainly consists of Actinobacteria and Proteobacteria during the initial phases of development. The microbiome changes and becomes dominated by the Bacteroidetes and Clostridium species after 65 years of age. The microbiome changes over the course of a person's lifetime due to a number of factors. Some of these factors include the mother's microbiota, the method of delivery (vaginal or caesarean), the baby's food, and the effects of ageing on adults. Everyone has a unique microbiome that develops early in childhood and is stable throughout the lifespan. The intestinal microbiota reaches a steady state between the ages of 2 and 5 years. The gut microbiota is relatively stable in adulthood; however, it exhibits a higher individual variation in older people than in younger adults. This difference is also affected by heredity, personal cleanliness, illness, medicine, and food. Health in older adults is related to gut microbiota alterations. These are connected with changes in the GI tract and diets and a reduction in cognitive and immunological systems. The gut microbiota's responsiveness to dietary changes varies among individuals. Diet, lifestyle, antibiotics, other medicines, cleanliness, and the genetics and immune system of humans may cause changes in microbiota composition. Antibiotic treatment drastically alters the microbial equilibrium, lowering the abundance and diversity of the population. Dysbiosis occurs when the specific microbial group of the gut microbiota and the abundance and functions of the intestinal microorganisms are altered. Consequently, illnesses and diseases occur, ranging from cardiovascular, neurological, respiratory, and metabolic illnesses to cancer, inflammatory bowel and skin diseases, Alzheimer's disease, autism, multiple sclerosis, and allergies. Similarly, there is an increased incidence of metabolic disorders, including type 2 diabetes mellitus and obesity. Gut microbiota is influenced by geographical locations and vary across developed and developing countries, as well as rural and industrialized regions. Stability is a fundamental property of excellent microbial composition. Gut microorganisms resist alterations generated by ecological stress and recover to a balanced condition following a stress-related event. Diet contributes for roughly 50% of the variabilities determining the microbiome composition across time. Food availability in industrialised countries has led the desire for safer and longer-lasting foods, driving the industry to make pre-cooked and ready-to-eat food products containing large amounts of cost-effective, artificial additives such as preservatives, colorants, fats, sugar, and salt. The "Western diet" refers to a way of eating that emphasises sugar and saturated fat at the expense of fibre. The microbiome changes and disease is caused by an unhealthy diet. There is strong evidence that Western diets contribute to metabolic diseases and inflammation, and that these diets pose a threat to public health. The composition and variety of the gut microbiota are greatly affected by dietary factors. Human health and the diversity of gut bacteria are affected by the foods and diets that people consume. There is a distinct mix of gut bacteria in every person. Differences in the gut microbiota community translate into a distinct ability to process dietary components, resulting in different propensities to diseases. A change in food exerts various impacts on people owing to the distinct nature of their gut microbiota. The volume and makeup of the microbiota are significantly influenced by the food that people eat. The interactions between nutrients and microorganisms dictate the health benefits or drawbacks. Artificial sweeteners and emulsifiers are dietary additives that have the potential to alter the composition of the gut flora. Sugar substitutes made of artificial sweeteners are sweeter than sugars but lower in calories, and they may disrupt and damage the microbiota in the gut. Sugar substitutes such as sucrose, aspartame, and saccharin mess with the gut microbiota's diversity and balance, which can lead to metabolic disorders. Common emulsifiers found in processed foods have an effect on the gut microbiota as well, leading to a decrease in microbial diversity and perhaps leading to inflammatory disorders and metabolic syndromes. Additionally, the human microbiota varies from person to person due to dietary preferences. Obese individuals have more diverse microbial compositions than non-obese individuals do. Obese people have a decreased proportion of Bacteroidetes compared to normal weight people. Firmicutes

abundance increases and Bacteroidetes abundance decreases in response to a high-calorie diet that maintains a constant ratio of carbohydrates, protein, and fat. As a result, the variety of microbes in the human gut is diminished. However, a restricted diet with reduced calorie intake enhances the diversity. In contrast to other carbohydrates, polysaccharides, such as resistant starch, oligosaccharides, and non-starch polysaccharides, are dietary fibers only accessible to the microbiota of the large intestine; they are not digested in the small intestine. Fermentable dietary fibres are those that can be broken down by certain species of bacteria. Gut microbiota, Bifidobacterium, Bacteroides, Faecalibacterium, Lactobacillus, and Roseburia ferment short-chain fructooligosaccharides to generate SCFAs, primarily butyrate, acetate, and propionate, in the large intestine. People don't need as many calories in their diets because of these SCFAs, which make up about 10% of our energy needs. Obesity and insulin resistance are both decreased in correlation with increased SCFA production. The gut microbiota is best when fibre is plentiful in the diet. A few research found that eating just plant or animal food for a short period of time changes the microbiome and reduces variation in gene expression among individuals. The plant-based diet is abundant in fruits, vegetables, grains, and legumes, whereas the animal-based diet includes dairy, meat, and cheeses. Eating more plant-based foods increases fibre intake. Animal diets tend to have more fat and less protein, while plant diets tend to have the opposite effect. No matter the diet, the variety of the sample species stays the same. The gut microbiota are more affected by a plant-based diet compared to an animal-based one. In contrast to the levels of Firmicutes (Roseburia, Eubacterium rectale, and Ruminococcusbromii), which break down plant polysaccharides, the numbers of bile-tolerant microbes Alistipes, Bilophila, and Bacteroides are increased in an animal-based diet. Both diets feature food-borne microorganisms, including bacteria, fungus, and viruses, that populate the gut. These imply that the gut microbiota quickly adapts to a changing diet. A diet over 24 h with high fat/low fiber or low fat/high fiber changes the microbiota moderately, with the microbial species being altered variably among individuals. This modest diet alteration has certain repercussions on human GI health. A “Western diet” promotes considerable changes in the microbiota compared with the effect of a low-fat diet and lowers the variety of the gut flora. People following this eating plan consume very little plant-based foods and a lot of animal protein, total and saturated fats, and simple carbohydrates. Similarly, resistant starch, non-starch polysaccharides, and dietary fibre are also severely lacking in this diet. This is associated with an increase in Proteobacteria and Firmicutes and a decrease in the quantity of Lactobacilli and Bifidobacteria, two groups of helpful bacteria. Neuronal function and structure might be impacted by this altered microbial ecology. Inflammatory bowel disease, obesity, and type 2 diabetes are all significantly increased by its low SCFA concentration. Neither people nor the microbiota benefit from this "Western diet." In contrast, plant-based proteins are abundant on the "Mediterranean diet," widely regarded as the healthier option. Fruits, vegetables, bread, olives, dairy, and polyunsaturated fats make up the bulk of the diet, whereas potatoes, red meat, and sugar are cut out. Metabolites of polyphenols in the colon by microbes in the intestines, such as Bifidobacteria and Lactobacilli, and by-products of these metabolites, such as reduced numbers of Firmicutes and Proteobacteria, significantly alter the gut microbial makeup. Better heart health and less inflammation have been linked to these plant-based diets. Better mental performance is another benefit of this eating plan. The small intestine and stomach are the typical sites of nutrition digestion and absorption in humans. Subsequently, the leftover food goes to the colon, where most gut microorganisms dwell. Most vitamins are taken from food and are absorbed in the intestine; just a few are generated by intestinal microbes. The microbiome consumes and creates energy and micronutrients, including important vitamins, such as vitamin K and several of the water-soluble B vitamins. There is no alternative way to manufacture them, which are essential for bodily functions and brain development. Inadequate vitamin intake or disruptions in intestinal absorption lead to vitamin deficiencies. Deterioration of neurodegenerative processes and impairment of cognitive function are consequences of vitamin deficiency. Iron and zinc are two important minerals that the microbiome microbes control. Transport of oxygen and energy generation, neurotransmitters, and DNA synthesis all rely on iron. Iron deficiency reduces butyrate levels in the gut microbiota by reducing the abundance of butyrate-synthesising bacteria. Nevertheless, elevated levels of propionate and lower levels of butyrate are the results of a rise in the abundance of Bacteriodaceae that produce propionate and a decrease in the number of Lachnospiraceae that do the same, as a result of excess iron. Zinc has an important role in neurogenesis regulation and differentiation and is essential for gene replication and expression. Antibiotics, metal-chelating agents, anticonvulsants, diarrhoea, malabsorptive bowel disease (IBD), and malnutrition are all potential causes of zinc deficiency. The composition of the gut microbiota and the number of species it supports may be altered by this deficiency.

The Phenolic-Fiber-Gut Microbiota Interaction

Plants and foods contain phenolics and dietary fibres in significant quantities. The bioaccessibility, bioavailability, and biochemical activity of polyphenols are greatly influenced by the interaction of dietary fibres with polyphenols in food matrices. The gut microbiota interacts with antioxidants and phytochemicals such phenolics that dietary fibres transport. Polyphenol adsorption and retention characteristics in the gastrointestinal tract vary according to the composition of polysaccharides and their interactions with polyphenols in dietary matrices. Covalent, non-covalent, electrostatic, van der Waals, hydrogen, and ionic bonding are all possible types of interactions. The degree of branching, surface porosity, glycosylation, steric hindrance, molecular size, stereochemistry of flavan-3-ol subunits in proanthocyanidins, polymerisation degree, surface porosity of polysaccharides, and gallolylation percentage are all factors that impact the interactions between polyphenols and polysaccharides. There are a number of plant cell wall arabinogalactans and arabinoxylanes that simple phenolic acids like ferulic acid, p-hydroxyphenyl, syringyl, and p-coumaroyl acids bind to in sugar beets, wheat, bamboo, maize, and spinach. The cell wall is bound to proanthocyanidins by means of hydrogen bonding and van der Waals forces, which are non-covalent interactions. Tropical and subtropical fruits, tomato peel, and flavonols including rutin, isoquercetin, and quercitrin were said to be components of NEPPs in these foods. Nevertheless, our understanding of how flavonoids interact with the cell wall is limited. According to Hu et al. (2023), pectin-polyphenols engage in unique non-covalent interactions through hydrogen bonding and hydrophobic interactions. According to Watrelot et al. (2013), pectin polysaccharides were hydrophobically interacted with by the aromatic groups in polymeric procyanidin. The potential interactions between polyphenols and polysaccharides are hindered by branched arabinan-pectic polysaccharides, according to Fernandes et al. (2020). In contrast, linear arabinans showed 2-8-fold greater retention for phenolic compounds like phloridzin and chlorogenic acid than the branched arabinans. The extent to which polyphenols can be extracted and their possible nutritional biochemical characteristics are affected by interactions with polysaccharides. The ideal polyphenol-polysaccharide ratio, pH, ionic strength of the extracting solvents, time, temperature, and ambient conditions determine the optimal extractability, however the majority of polyphenols are extracted using a typical water-organic solvent solution. The extraction rate of bound phenolics from the food matrix is affected by parameters such as acidity, alkalinity, and enzymatic hydrolysis, which are used to extract NEPPs. At several points in the digesting process, including the colon, lower gastrointestinal tract, and upper GI tract, the rate of polyphenol release is significantly affected by the polysaccharide interaction characteristics. The small intestine plays a role in the partial release of certain polyphenols because it disrupts interactions between phenolic polysaccharides and ester-phenolic carbohydrate linkages. Many NEPPs make it to the small intestine, where they are fermented by the colonic microbes to release various metabolites, including phenolic acids like ferulic and valeric acid, short-chain fatty acids (SCFA), and phenolic-SCFA conjugates. Microbiomes like Bifidobacterium spp., Clostridium spp., and Lactobacillus spp. secrete hydrolytic enzymes like protease and carbohydrolase in the colon. These hydrolyse the glycosidic linkages in polyphenol compounds and the covalent bonds between phenols and carbohydrates, weakening the phenolic-polysaccharide interaction. Metabolites may have greater biological activity than the original substances in certain instances. The sugarcane plant includes phenolic acids, flavones, flavanone, catechin, and flavonol attached to its fibres. It also contains phenolic acids, coumaric acid, hydroxybenzoic acid, vanillic acid, and syringic acid. These phenolic and polyphenolic chemicals are transported to the colon for fermentation by the sugarcane fibres via the small intestine. Because of the interactions between dietary fibre and polyphenols, apple fibre contains large quantities of non-extractable polyphenolic chemicals, which impact the variety of gut microbes. Apple matrices contain interactions between procyanidin and polysaccharides, which inhibit the breakdown of procyanidin by human gut bacteria. Not only do fibres and polyphenols help the colon by transporting phenolics there, but they also have synergistic benefits and may have biochemical qualities. Combining dietary fibres with NEPPs has a stronger physiological impact than either one alone, according to previous research. They work together to improve NEPP fermentation and metabolite bioavailability, which in turn improves their ability to perform different physiological tasks. Colonic bacteria may be provided with prebiotic fibres or polysaccharides that are present during the whole fermentation process. For instance, in vitro fermentation with dietary fiber-enriched NEPPs exhibited 53% fermentability, while fibre alone showed 23% (Saura-Calixto et al., 2010). Potential effects on the microbial community may result from the presence of a fiber-polyphenol matrix. Vitaglione et al. (2015) conducted a

randomised control study and discovered that eating whole wheat grain increased the proportion of Bacteroidetes and Firmicutes, decreased the abundance of Clostridium, and reduced inflammatory markers. On the other hand, eating refined wheat grain decreased the abundance of Bifidobacteriales and increased the abundance of Bacteroidetes. In the course of breaking down food matrices, a two-way street of interactions between polyphenols and the microbes in the gut may develop. The gut microbiota helps polyphenols make their way to the colon, where they are converted into several bioactive metabolites. These compounds impact microbiome diversity, notably the Firmicutes/Bacteroidetes F/B ratio. Metabolites with a low molecular weight are the end result of most phytochemical transformations. The vast majority of polyphenolic chemicals found in food are either organic acids, monosaccharides, or their conjugates. Through O-deglycosylations, ester hydrolysis, C-ring breakage, delactonization, demethylation, dehydroxylation, and reduction of double-bond molecules, these derivatives are broken down by microbial enzymatic catabolism during digestion. Enzymes produced by microbes convert polymeric NEPPs into metabolites with low molecular weight. Phenolic acids such cinnamic acid, benzoic acid, phenylvaleric acid, phenylacetic acid, and phenyl propionic acid are formed after they undergo additional depolymerisation and catabolization through microbial enzyme-induced delactonization and decarboxylation. After making it past colonocytes, the metabolites travel through the bloodstream to the liver, where they are either absorbed by various tissues or eliminated through urine. The hydrolysable tannins undergo microbial transformation that begins with gallic acid and glucose hydrolysis, followed by the conversion of gallotannins to pyrogallol and phloroglucinol, and finally to their end products like butyrate and acetate. Ellagitannins undergo biotransformation through decarboxylation, hydroxylation, and lactone ring cleavage.

Problems Caused by Polyphenolic-Associated Compounds on the AOAC Dietary Fibre Determination Method

When it comes to evaluating dietary fibre (DF) in food, the AOAC enzymatic-gravimetric method is considered the gold standard. It is officially used in most European and American countries. To summarise, the process begins with enzyme digestion of the food sample, which mostly extracts starch and protein. After the ash and protein content have been accounted for, the remaining residues are gravimetrically quantified. You have two options: either measure the total DF content after the soluble fibre components have precipitated, or get the values of the insoluble and soluble DF fractions independently. The official source defines dietary fibre as lignin and non-starch polysaccharides, which is how this technique measures it. The high polyphenolic chemical composition of several plant-based foods, however, can throw off DF quantification and, in many cases, lead to an exaggerated DF concentration. The amylolytic and proteolytic enzymes used to assess DF are particularly resistant to hydrolysis of insoluble polyphenols like PP and highly polymerised condensed tannins found in cell walls. Therefore, the remaining residues would contain these compounds as insoluble dietary fibre (IDF) according to gravimetric measurements. There is a wide range of PP solubilities as well. Soluble dietary fibre (SDF) and phenolics with low or intermediate molecular weights can co-precipitate in an 80% ethanol solution. This allows us to quantify these polyphenolic compounds as DF ingredients, together with the fact that the SDF matrix is connected to PP. Thus, the real DF concentration of foods with a low polyphenolic content can be exaggerated due to these associated compounds. The evidence backs up these claims. The results showed that after evaluating food samples with CT concentrations ranging from 1% to 30% of the dry matter, there were significant amounts of CT in the IDF residues. Up to 97% of the CT originally contained in the sample can be recovered after the enzymatic treatments. Although they were not as resistant as the highly polymerised molecules, oligomeric proanthocyanidins and other low-molecular-weight CTs investigated in lentil and cocoa extracts with an acetone:water (70:30 v/v) ratio demonstrated significant resistance to enzymatic hydrolysis. When polyphenols are noticeable in the meal sample, it could be difficult to accurately quantify them without adjusting for their content in fibre residues. In addition, there is a chance of making qualitative errors since specific physiological characteristics shown by polyphenolic compounds could be incorrectly associated with DF. The amount of CT in the IDF residues would also rely on their complexity, as compounds with a higher degree of polymerisation are more resistant to enzymatic hydrolysis. Additionally, CT's ability to bind to polysaccharides found in cell walls and proteins determines the concentration of tannins in the fibre residues. Extremely high protein binding by CT results in the formation of insoluble tannin-protein complexes that are resistant to hydrolysis by gastrointestinal hydrolyses. Furthermore, CT has the ability to block proteolytic enzymes. Both of these processes reduce the digestibility of dietary protein and raise the concentration of resistant protein in the residual IDF. From fifteen percent to ninety percent of the original protein can be found in the IDF fractions as resistant proteins.

Reducing the protein concentration in the fibre residue would remove this CT interference from the official AOAC estimation of DF. Nevertheless, a variation of the AOAC enzymatic gravimetric approach is commonly used, mostly in scientific studies. Here, following acid hydrolysis, the chemical makeup of the insoluble and soluble DF fractions is analysed in relation to the neutral sugars and uronic acids that make them up. The residue that remains after acid hydrolysis of IDF is used for the gravimetric measurement of Klason lignin (KL) without additional adjustments. This is accomplished by first scattering the material in 12 M sulphuric acid and heating it to 30°C for 1 hour. Then, after 90 minutes at 100°C, hydrolyse it with 1 M sulphuric acid. However, there is still a significant amount of protein resistance in these KL residues due to the strong tannin protein interactions that can resist acid hydrolysis. Furthermore, after acid hydrolysis, phlobaphene-like molecules containing CT remain in the KL residues. Both the soluble and insoluble dietary fibre fractions retain SPP, although at higher quantities than what was found in the residue after the second round of methanol:water and acetone:water extractions. If enzymatic treatments of samples partially depolymerise condensed polyphenols, liberate polyphenols bound to other food components, or include them in cellular structures like vacuoles, then certain phenolic compounds may be soluble. Even after the acid hydrolysis of the IDF residue, there are still measurable levels of SPP. The PP content of soluble dietary fibre (SDF) remains high even after dialysis, and a portion of it is co-polymerized with polysaccharides found in cell walls. Therefore, polyphenolic compounds lead to inaccurate gravimetric quantification of IDF and SDF fractions following precipitation, dialysis, lyophilization, and other processes. One approach to avoid these kinds of errors is to include PP content correction in analytical processes for DF determination. The gravimetric value of either IDF or KL should be subtracted from the content of CT in the IDF residue before conducting the analysis. Checking and correcting the protein's KL residues is equally crucial. It is important to consider the possibility of SPP in the SDF fraction when gravimetrically quantifying this fibre fraction. Although SPP only accounts for a minor percentage and does not significantly affect the gravimetric result (due to their insignificant protein-precipitating capacity compared to CT), it is still advisable to calculate and modify SPP in IDF. However, DF isn't the sole theory that could account for SPP's notable physiological traits. Therefore, SPP connected to DF residues would cause less quantitative inaccuracies, but these bioactive compounds associated to DF would create much more significant qualitative errors if they were ignored.

Examination of Dietary Fiber-Related Polyphenolic Compounds

Correcting DF gravimetric readings or estimating their real quantity in plant meals necessitates suitable study of these compounds, regardless of whether PP are deemed DF components or not. But, as said before, it is not a simple affair to accurately determine polyphenols. Complete extraction of phenolic chemicals from plant material is the primary challenge in plant phenolic analysis. Since they are polar molecules, polyphenols dissolve to a considerable degree in polar solvents such acetone, methanol, ethanol, diethyl ether, and dimethyl sulfoxide. The chemical is typically made more water soluble by attaching glycosides to one or more sugar molecules; as a result, mixtures of organic solvents and water are commonly used to dissolve PP. Furthermore, conventional solvents are ineffective in extracting polymeric polyphenols (PP) attached to proteins or cell wall polysaccharides. These chemicals are typically not quantified since they stay in the insoluble residues. Underestimating the polyphenolic content of specific plant foods and missing or incorrectly attributing some of their physiological benefits to other food components are examples of quantitative and qualitative errors that arise from this. Although chromatographic analysis utilising reversed-phase HPLC has become increasingly common in recent years, most approaches for the analysis of PP use spectrophotometric techniques. There are some great monographs out there on the topic of flavonoid identification and the examination of phenolics in plants. In addition to the huge number of polyphenolic compounds, the absence of suitable standards further complicates the analysis of these chemicals.

Approach to Extracting and Analysing Polyphenolic Compounds

The Process of Soluble Polyphenol Extraction

This fibre fraction can be analysed in the dialysates before lyophilization or after precipitation to determine the SPP content in SDF, with the goal of correcting the PP content in DF fractions. A sequential extraction with aqueous methanol and acetone can be performed in the case of precipitated SDF fractions, similar to what is done with food samples. For one hour at room temperature with constant agitation, samples (either 1 g of food sample or SDF

residues) are extracted with 40 mL of a 50:50 v/v mixture of methanol and water. The next step is to spin the samples at 3000 rpm for 15 minutes, and then pour the liquid above into volumetric flasks. After resuspending the pellets in 40 mL of a 70:30 v/v mixture of acetone and water, the extraction process is carried out once more. The volume of the combined supernatants is 100 mL. In the mixed supernatants, soluble polyphenols are tested. It is recommended to conduct concentration under vacuum when using chromatographic methods to identify specific phenolics.

Polyphenol Solubility Investigations

Both the extracts and the dialysates can be used to determine the total soluble polyphenols. The total soluble polyphenol content in DF residues or complete sample foods can be quickly and accurately measured using a colorimetric approach that use Folin-Ciocalteau's reagent. The Folin-Ciocalteau's reagent is added to aliquots (0.5 mL) pipetted into 25 mL volumetric flasks. Ten millilitres of sodium carbonate solution (75 g/L) and twenty-five millilitres of water are added after three minutes of standing at room temperature. Read absorbances at 750 nm against a blank made in parallel with water instead of the sample after 1 hour at room temperature with periodic shaking. One option for a standard is to employ tartaric acid or gallic acid. The overall content of polyphenolic chemicals can be determined using this nonselective approach. Nevertheless, this approach is hindered by proteins. The Prussian blue technique is another option; it is said to have less interference with proteins. Furthermore, by utilising catechin as a standard, assays with the vanillin-HCl reagent can quantify flavan-3-ol derivatives in the dialysates and extracts. Using a pipette, transfer 2 millilitres into a 10-milliliter volumetric flask. Add 2 millilitres of the newly made vanillin-HCl solution (1 g/100 mL 24.5% HCl). The final volume is created by adding 24.5% HCl, which is formed by diluting 700 mL of 35% HCl with 300 mL of water. The finished volume is 10 mL. The absorbances are measured at 500 nm compared to a blank for the reagent after 25 minutes of shaking occasionally at room temperature.

Examining Condensed Tannins

It is important to examine the proanthocyanidins in the IDF residues while dealing with insoluble PP. The value examined in the IDF can also be utilised to correct the KL residue when distinct values for the constituent neutral sugars, uronic acids, and Klason lignin are needed; this is due to the fact that these polymeric tannins are resistant to acid hydrolysis. Samples (50 mg of IDF residues or the plant fraction insoluble in aqueous acetone and methanol) are treated for 3 hours at 100°C with 10 mL of butanol-HCl (95:5 v/v) to get a quantitative estimate of the CT content of foodstuffs or IDF residues. The anthocyanidin solutions are measured at 550 nm by comparing their absorbances to a blank for the reagent. The standard could be commercial cyanidin, carob pod, or grape tannins, or purified quebracho. Because CT can react with many food components, it's possible that after being treated with butanol-HCl, they will lose some of their anthocyanidin-forming abilities and won't be able to make the red solutions that can be measured spectrophotometrically. This holds true when CT scans of faeces are examined. An other gravimetric approach can be employed to sidestep this issue. Gravimetric measurement of this residue, adjusted for the resistant protein content (N 6.25 according to the Kjeldahl technique), would yield the CT value because CT remains quantitatively in the KL residue during acid hydrolysis (12 M H_2SO_4, 30°C, 30 min plus 1 M H_2SO_4, 100°C, 90 min) (20).

Dietary Fiber-Associated Polyphenols and Their Nutritional Importance

The way polyphenols behave in the gut has a significant impact on the nutritional value of phenolics in diet. The ability of polyphenolic compounds to interact with macronutrients, digestive enzymes, and the colonic microflora determines how well food components are digested, how much of the food is absorbed through the intestinal mucosa, and how it is metabolised in specific organs. Polyphenols can have either beneficial or harmful systemic effects, depending on their interaction with these factors. Since not all phenolic compounds appear to be equally soluble in water and digestible in the intestines, the opposite is true for polyphenols; their digestive fate will be determined by their molecular size, solubility, and chemical structure. The sheer variety of chemical structures and conjugates present in nature, however, poses significant challenges to research into the physiological implications and bioavailability of polyphenols. Research on the nutritional effects or intestinal digestibility of PP is mostly based on plant extracts containing a complex mixture of soluble phenolic compounds; however, this mixture makes it difficult to interpret the unique effects and metabolism of individual PP. Additionally, both people and animals have had their flavonoid metabolism examined, using either pure standards or complex meals. We cannot rule out the possibility that

these substances' absorption and metabolism will vary depending on whether they are supplied as a supplement or as part of a complex diet. Furthermore, it is not apparent how outcomes acquired in animal models apply to humans. Furthermore, there is a dearth of information regarding the intestinal fate of insoluble PP, which consists of highly polymerised or bound tannins, as well as their nutritional and physiological significance. This is in part because of the challenges associated with analysing and characterising this fraction. Typically, it is just ignored. One way to categorise PP is by whether they are soluble in extractable or nonextractable polyphenols. This will help us understand the nutritional effects of dietary phenols by considering their distinct behaviours. Some hydrolysable tannins and oligomeric proanthocyanidins are examples of extractable polyphenols (EPP), which are phenolics with low to intermediate molecular weights that can be extracted using various solvents such as water, aqueous methanol, or acetone. Nonextractable polyphenols (NEPP) are phenols coupled to other dietary components (such as cell wall polysaccharides or proteins) that are insoluble in typical solvents. These molecules have a high molecular weight. Dietary protein binding and precipitation is one of the most well-known characteristics of phenolics found in food. Protein digestibility is decreased because insoluble polyphenol-protein complexes remain unchanged as they travel through the GI tract and are eliminated in faeces. Other naturally occurring proteins, including those in saliva or digestive enzymes, are inhibited by this protein-binding capability. Notwithstanding the fact that this characteristic is shared by the majority of polyphenols as a result of their high hydroxylation level, NEPP could only bind to molecules that are physically accessible to soluble proteins if so desired. Their capacity to precipitate salivary proteins or block digestion enzymes is diminished when insoluble NEPP create insoluble tannin granules or become embedded in a complex matrix with cell wall polysaccharides. Thus, EPP amplifies these effects, particularly with hydrolysable tannins and oligomeric proanthocyanidins, two classes of soluble chemicals with greater molecular weights than the basic phenols, which are incapable of precipitating proteins. Also, PP can form complexes with polysaccharides other than starch, which can lower the postprandial glycaemic response. However, this property hasn't been thoroughly studied and may be attributable, in part, to the suppression of amylolytic enzymes. The impact of dietary phenolics on lipid metabolism is another feature that has received very little research. There have been reports of increased fat excretion levels with both NEPP and EPP. The precise mechanism by which polyphenolic compounds, particularly EPP (grape proanthocyanidins, tannic acid), exert their hypocholesterolemic effects remains unknown; nonetheless, this effect is likely to be mediated by a decrease in intestinal cholesterol absorption. Polyphenolic substances have an effect on mineral absorption, which is another key aspect of small intestine nutrient bioavailability. Animal and human studies have shown that EPP can decrease iron absorption by forming compounds with nonheme iron. One theory is that the galloyl and catechol groups are responsible for this impact. There is a lack of consensus on the effect of flavonoids on iron absorption, and studies have shown conflicting findings. Additionally, EPP can hinder or enhance copper and zinc absorption, depending on the animal model employed. It does not appear that these chemicals influence the absorption of magnesium, manganese, or calcium. Only EPP may be impacted by the acid pH of stomach fluids, leading to the partial hydrolysis of some hydrolysable tannins, when it comes to the metabolism of polyphenolic compounds in the upper intestine. Only a limited fraction of the polyphenols attached to cell wall polysaccharides or protein (NEPP) can be released when their alkali-labile connections are hydrolysed during their journey through the small intestine. Microbes that colonise the terminal ileum can hydrolyse flavonoid glycosides, releasing the free aglycones. The small intestine mucosa allows for the absorption of some EPP, including aglycones and free simple phenolic compounds. Much of the polyphenolic compounds, including NEPP and a sizeable quantity of unabsorbed EPP (flavonoid glycosides and oligomeric tannins), would be able to withstand the acidity and digestive enzymes' actions, thus they would make it undamaged into the large intestine. Dietary fibre fermentation releases PP tied to cell wall polysaccharides, but the colonic bacteria only metabolise a small fraction of NEPP once it reaches the large intestine. The majority of NEPP, which include tannin-protein complexes, highly polymerised tannins, and a sizeable portion of fiber-bound phenolics, are neither absorbed or broken down in the colon and are instead expelled in large quantities in the stool. The amount of NEPP that can be excreted varies from 70% to over 95%, depending on how complex they are and how much they are polymerised to other components of cells. Normal concentrations of short-chain fatty acids (SCFA)—acetic, propionic, and butyric acids—the primary byproducts of colonic fermentation would be generated if NEPP were to pass inertly through the colon without impacting the intestinal microbiota or its fermentative ability towards other substrates.

CONCLUSIONS

The analysis of foods containing dietary fibre is frequently obstructed by polyphenolic chemicals because of their tight association with fibre constituents. Dietary fiber-rich meals often contain DF and PP because their combination prevents the full removal of polyphenolic chemicals. There is a lot of room for error when trying to quantify the DF content of these items, and because the physiological effects of DF and PP are similar, it's also easy to make qualitative mistakes. It is true that there are some similarities between polyphenols and the components of dietary fibre when one takes into account the whole scope of dietary polyphenol effects and how they behave in the digestive tract. Similar to insoluble dietary fibre components, NEPP are insoluble and nondigestible substances that are not much impacted by the fermentation microbes. They have the potential to decrease the digestibility of other food components, leading to an increase in faecal bulk as well as the excretion of fat and protein. Conversely, EPP are soluble chemicals that are primarily broken down by the bacteria in the colon. They work similarly to soluble dietary fibre in that they influence mineral absorption, lower postprandial glycemia, and increase fat excretion. The proposed addition of polyphenolic compounds as DF components is based on these facts and the persistence of PP linked to DF. Antioxidant dietary fibre (ADF) is a relatively new kind of DF that has just been characterised as a fiber-rich substance with high levels of antioxidant polyphenols linked to the fibre matrix. The health benefits of polyphenols and dietary fibre would be amplified by this ADF. The composition of gut microbiota regulates microbiome diversity and quality via its role in the biotransformation of polyphenols to bioactive metabolites. The interaction between fibre and polyphenols plays a crucial role in the efficient release of polyphenols throughout the digestive process. Furthermore, it affects how bioavailable and active these polyphenols are in the colon, where bacteria ferment them to create many metabolites. In addition, the diversity and activity of the gut microbiota are impacted by the interaction level and the composition and structure of dietary fibres. The function of fibre and polyphenol matrices in diet in regulating the gut flora is complicated and interacting. Improving human gut health through microbiota modulation may be possible with the development of novel products containing the desired polyphenols and fibres. The development of new functional food products that are both affordable and easy for consumers to consume could benefit from future research into a) the effects of different types of dietary fibres and polyphenols on microbial diversity and metabolite production and b) the best combinations of these ingredients to increase bioaccessibility and bioactivities in the colon. In addition, we have investigated polyphenols in food processing and their impact on processed foods' bioactivity and nutritional profile. We now have a better grasp of the polyphenols' potential impact on cellular homeostasis and gene expression thanks to research into the rapidly growing area of polyphenols in epigenetics. We have talked about using polyphenols made from leftover food because we know how important it is to be environmentally conscious. This aspect does double duty: it reduces food waste and finds new ways to get polyphenols' health advantages from places you wouldn't expect. Despite progress, there are still many unanswered questions about polyphenols, such as how structural changes affect metabolic kinetics, modes of biological activity, and optimum bioavailability. Consequently, there is a continuous effort to improve the bioavailability and therapeutic effectiveness of polyphenols through structural changes. The goal of this strategic endeavour is to discover all the ways polyphenols can help with health, so we can better prevent and treat diseases. This will further solidify the importance of plant-based goods for people's overall wellness. The need for ongoing research is shown by the thorough examination of these various aspects, which also highlights the potential of polyphenols as beneficial factors to human health in various situations. The basic premise supporting the necessity of the comprehensive review states that in order to advance our knowledge of the significant effects of polyphenols in plant-based products enhanced with phyto-antioxidants on human health, it is crucial to conduct an exhaustive investigation and synthesis of the current literature on the subject. The underlying assumption of this hypothesis is that the complex relationship between food choices and health outcomes can be better understood by conducting a comprehensive review of the many functions and action mechanisms of polyphenols in relation to different chronic diseases and physiological processes. Clinical practice, dietary guidelines, and public health initiatives are all meant to promote optimal health and prevent chronic diseases; the comprehensive review will do more than just add to scientific knowledge; it will also critically analyse the present state of knowledge, identify gaps, and propose future research directions, according to the hypothesis. The hypothesis concludes that comprehensive reviews are crucial for advancing research and healthcare practices by synthesising evidence, encouraging scientific discourse, and driving innovations.

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