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Polyphenols: Function and Scope Beyond Bioactivity: A Review

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Abstract

Polyphenols are considered one of nature's greatest nutrients. Approximately forty-five percent of deaths that occur in children under the age of five are attributed to malnutrition. These mainly occur in nations with low and modest incomes. Diabetes, some malignancies, and cardiovascular disease are examples of noncommunicable diseases (NCDs) associated with diet. Inadequate nutrition and poor eating habits are among the world's leading causes of chronic illness. A healthy diet should contain a range of foods high in polyphenolic substances, which are beneficial to people's overall health. Naturally occurring polyphenols are a kind of micronutrient that may be discovered in an array of foods, including fruits, vegetables, and beverages. While a low dietary intake of polyphenols may not cause a specific insufficient syndrome, consuming enough of them may have a good influence on health. Understanding the biological availability of dietary polyphenols may help find those that are beneficial to human health. It is quite accurate and covers a broad variety of diverse academic and scientific subjects. The latest study builds on previous studies on the health impacts of polyphenols.

Keywords: Antioxidants, Diet, Malnutrition, Non-Communicable Human Diseases, and Polyphenols

1. Introduction

The phenol has a hydroxyl group that is connected to an aromatic benzenoid ring. There is no difference between polyphenols and polyhydroxyphenols. Since 1894, the word "polyphenol" has been in use. Concentrated tannins, which are found in almost every class of plant life and are abundant in leaf tissues, the epidermis, bark layers, flowers, fruits, and other plant tissues, are the richest kind of polyphenols [1].

We are all well aware of the vital role that nutrition plays in our lives, beginning even before a child is born and lasting decades after. Given its significance for human health, nutrition deserves a great deal of attention. On December 20, 2023, the World Health Organization updated information or important data on its website. Malnutrition may be subdivided into several categories, including undernutrition (which includes wasting, stunting, and underweight), inadequate intake of vitamins or minerals, excessive weight, obesity, and the noncommunicable diseases that are the direct result of these conditions. Among adults, there are 1.9 billion who are either overweight or obese, whereas 462 million people are underweight. In the year 2022, it was projected that among children under the age of five, there would be 149 million stunted children (children who are too little for their age) and 45 million wasted children (children who are too thin for their height). More than half of the fatalities that occur in children under the age of five are attributed to undernutrition as a contributing factor. These mostly happen in nations with low and moderate incomes. The global burden of malnutrition has significant and long-lasting repercussions on individuals and their families, as well as on communities and countries in terms of development, economy, social concerns, and medicine. These effects are a result of severe and widespread malnutrition. People and their families, as well as communities and countries, are subject to severe and long-lasting repercussions as a result of the global burden of malnutrition [2]. These effects may be seen in the domains of development, economics, social services, and medicine. Many naturally occurring plant kingdoms have polyphenol groups, which are made up of multiple hydroxyl radicals on aromatic rings. As a result, many researchers have studied and written about a number of substances with phenolic structures. Polyphenols are often found in nature in conjugated structures, where one or more sugar residues are connected to a phenol hydroxyl group. However, direct associations between the sugar portion and an aromatic carbon atom are also possible [3–5]. Polyphenols have biological features that include antioxidant, anti-inflammatory, and anti-cancer effects. Because they kill microbes and stop the growth of cysts, polyphenols are a major source of anti-infective compounds that can help fight infections in humans that are resistant to antibiotics. Polyphenols are the most prevalent antioxidants in a man's regular diet. Enough studies have been conducted in the past few years to assess the physiological behavior of dietary components with functional characteristics and bioactive produced from food. The consumption of foods with bioactive components lowers the menace of developing a wide range of chronic diseases, which are the main causes of mortality and morbidity on a global scale [6, 7].

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1.1.The categorization of diverse polyphenols

It is essential to classify these polyphenols into the following four categories: phenolic acids, flavonoids, stilbenes, and lignans. Phenol is characterised by the presence of a hydroxyl group together with an aromatic benzenoid ring. [Figures 1–9] outline the phenol rings as well as the structural components that are responsible for connecting these rings.

1.1.1. Tannins

A distinct class of phenolic chemicals, tannins have molecular weights ranging from 500 Da to 30 000 Da. Condensed tannins and hydrolysable tannins are the two main categories of tannins [8]. Hydrolysable tannins are made up of phenolic acids (for instance gallic and ellagic acids) that are linked to a polyol core (such as D-glucose, quinin acid, etc.). Gallo tannins and ellagitannins are two main types of hydrolysable tannins. They are made up of gallic acids and ellagic acids, correspondingly [9–10]. Tannins have a remarkable antioxidant pote ntial that may even surpass that of conventional antioxidants such as VC or α-tocopherol.

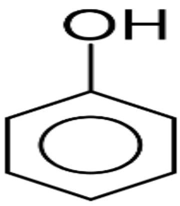

Figure 1- Structure of Phenol

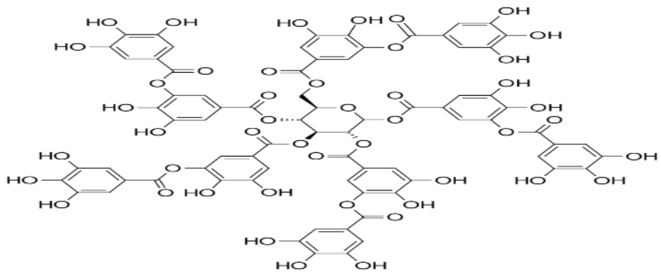

Figure.2. The structures of Tannins

1.1.1. Phenolic acids

These polyphenolic chemical compounds, which aren't flavonoids, fall into two main categories and are derived from benzoic and cinnamic acids. A kind of organic acid compound that makes up a significant number of phenolic compounds is phenolic acid. They may be produced throughout the development phase of plants, when they are found in bound, conjugated, and free forms [12]. The metabolites of anthocyanins, which were created by the in vivo fermentation of intestinal flora, also included phenolic acids [13]. Phenolic acids are classified as hydroxybenzoic and hydroxycinnamic acids based on their structural properties [14]. Vanillic acid, syringic acid, gallic acid, and p-hydroxybenzoic acid are examples of frequent forms of hydroxybenzoic acid [15][16]. On the basis of their arrangement structure can be seen in Figure 3.

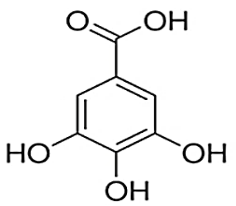

Figure-3A. A polyphenol - Structure of Gallic Acid

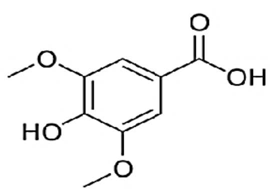

Figure-3B. A polyphenol - Structure of Syringic acid

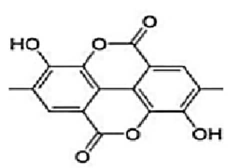

Figure-3C. A polyphenol - Structure of Ellagic Acid.

1.1.1. Flavanols

The primary subclass of flavonoids is called flavanols. They are identified by the presence of hydroxyl and carbonyl groups on the C3 and C4 positions of the C ring, respectively, and by the presence of three phenolic rings (A, B, and C). The number and location of hydroxyl groups on the B ring determines their type. Plants contain over 900 different types of flavanols, the three main types being isorhamnetin, kaempferol, and quercetin. Flavanols occur predominantly in the glycosylated form in nature, and the sugar moiety generally bonds with the 3, 7, 3', and 4’ sites of the aglycone. The most prevalent residue is glucose, which is followed by glucuronic acid, galactose, arabinose, xylose, and rhamnose. Due to their ability to provide free radicals with hydrogen atoms, flavanols' phenolic hydroxyl groups predominate in their antioxidant capability [17–19].

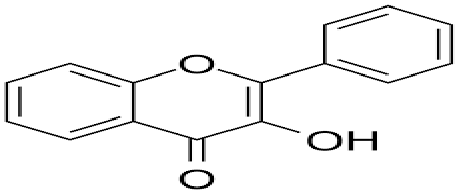

Figure.4. The structure of Flavanols

1.1.1. Flavonoids

They are made up of two benzenoid rings (A and B) that are connected by three carbon atoms to form an oxygenated heterocyclic (ring C). Ring C is additionally divided into flavanols, flavones, isoflavones, flavanones, anthocyanidins, and flavanols (catechins and proanthocyanidins). As depicted in **Figure 5.**

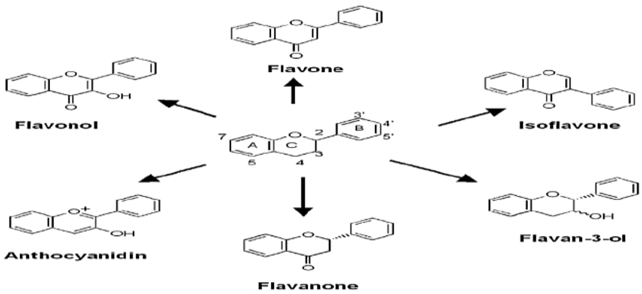

Figure. 5. The structure of Flavonoids.

1.1.1. Anthocyanins

Water-soluble pigments called anthocyanins are noticed in significant amounts in fruits, vegetables, and flowers [20]. Anthocyanins come in a variety of colours depending on the pH change; they may be red, orange, blue, pink, purple, and so on in nature [21]. An aromatic ring (A), an oxygen heterocycle (C), and a single carbon bond that connects them to another aromatic ring (B) make up the nucleus of anthocyanins [22]. The locations C3, C5, and C7 are where the glycoside ligands are typically found. The six primary anthocyanin categories are cyanindin, delphinidin, malvidin, peonidin, petunidin, and pelargonidin; the variations in their structures determine the variations in their antioxidant activity [23].

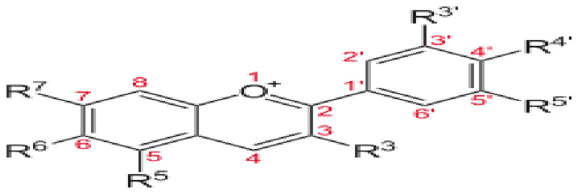

Figure.6. The structure of Anthocyanins

1.1.6. Catechins

The amount of catechins in a 250 mL brewed green tea beverage typically varies between 50 and 100 mg. [24]. Catechins' structure is based on the C6-C3-C6 structure [25]. This structure is based on the flavonoid skeleton, which is often used. Each catechin has its own specific structure as well as a set of distinguishing properties. This is because some of them contain hydroxyl or gallate groups in the C3 position, while others have ortho-dihydroxyl or vic-trihydroxyl groups in the B ring. Each of these groups adds to the overall structure of the molecule.

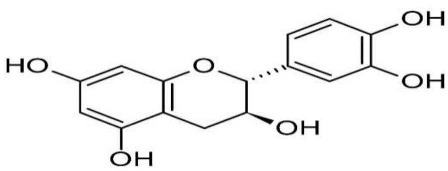

Figure.7. Structure of Catechin - Subgroup of polyphenol called flavonoids.

1.1.7. Stilbene

Stilbene is a traditional class of phenolic chemical that is primarily produced by over 100 plant species and is the result of external stimuli such insect infestations, viral infections, and bacterial infections [26–27]. Stilbene molecules are therefore byproducts of plant stress. Stilbenes are made up of a C6-C2-C6 structural skeleton with two phenyl rings joined by a double-bonded ethylene bond, resulting in the trans (E) and cis (Z) forms [28]. Stilbenes are often classified into two classes: monomers and oligomers, and they are frequently found to have the aromatic rings modified with methoxyl, hydroxyl, prenyl, and geranyl groups [29]. The usual stilbene representatives include piceatannol, pterostilbene, and resveratrol [30]. Stilbenes are well acknowledged as constituents of antioxidants.

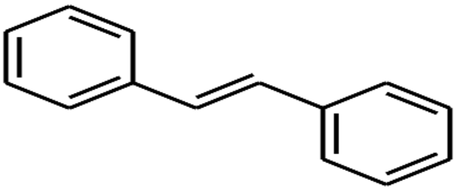

Figure.8. The structure of Stilbene.

1.1.8. Lignans

The secondary metabolites found in plants are called lignans, and they are often found in vegetables, legumes, and grains that are high in fibre. Plant life has a vast array of polyphenols known as lignans. Compared to most other foods, flaxseed and sesame are the finest suppliers of lignans. Essentially, the lignan chemical structures consist of a C-C link, also known as the β-β' bond, that joins the core atoms of the specific side chains (position 8 or β) with two phenyl propane groups. However, the properties of these compounds are different because of the way their structures are made [31–32]. Ab
ove all, plant lignans with antioxidant properties may be powerful pharmacological agents, as it has been illustrated in Figure-9.

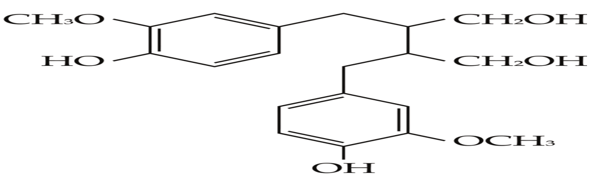

Figure. 9. The structures of Lignans**.**

1.2. Superfood items rich in polyphenols

There are already more than eight thousand different kinds of polyphenols recognized. Both free and bound forms of polyphenols have been found in food. In contrast to insolubly bound polyphenols, free polyphenols were readily extracted, and their antioxidant capacity could be precisely measured. High concentrations of polyphenols are mostly present in coffee, berries, dark chocolate, cocoa powder, olive oil, and several spices and seasonings, such as star anise and cloves. Table-A, lists a few of the best foods high in polyphenols that should be included in an everyday diet [33-35].

Table - A. Polyphenols in food that are consumed on a regular schedule over the day.

1	**Grains**	**Wheat, Rye, Oats, Whole,**
2	Nuts	Nuts and seeds, including walnuts, chestnuts, hazelnuts, almonds, and flax seeds
3	Fruits	Black chokeberries, black and red currants, black elderberries, black grapes, blackberries, blueberries, apples, apricots, and black olives are some examples of black fruits. Fruits of the Grapes, grapefruit, nectarines, peaches, pears, plums, raspberries, strawberries, and pomegranate in addition to peaches and pear.
4	Beans	Beans, sprouts, black beans, tempeh, tofu, white beans, soy milk, soy yoghurt, and soy meat are all examples of soy products.
5	Vegetables	Asparagus, Broccoli, Carrots, Red Chicory, Red Lettuce, Onions, Spinach, and Shallots are some of the vegetables that must be included in the list.
6	**Beverages**	In addition to olives, rapeseed oil, and olive oil To name a few, black tea, capers, coffee, dark chocolate, ginger, green tea, red wine, and red wine. Cider vinegar
7	Others items rich in polyphenols	Honey, dried herbs of basil, marjoram, and the following herbs are dried: parsley, peppermint, caraway, celery seed, cinnamon, cloves, and parsley. Pulverised cocoa, Cumin, and It is the curry powder. Chocolate in its darkest form, Spearmint, lemon, verbena, Mexican, oregano, rosemary, sage, and star anise seeds that have been dried.

1.2.1. Olive Oil

The well-known evergreen tree, Olea euroaea L, is endemic to the Mediterranean region and is used to make a extensive variety of goods, including food, trees, and cosmetics. However, olive oil is the most significant product that Olea euroaea L produces. The benefits of the Mediterranean diet (MD) are well recognized. Extra-virgin olive oil (EVOO), in particular, is widely seen as a sign of MD. A main characteristic of the MD and a significant distinction from other nutritious diets is the substantial amount of extra virgin olive oil (EVOO), which ranges from 15.3 to 23 kg per capita annually. Numerous studies highlight the advantages of EVOO due to its unique ingredients. The high amount of monosaturated fatty acids (C18:1, ranging from 55 to 83% of the total fatty acids) has been extensively related to the nutritional and health qualities of the diet. It's interesting to note that although olive oil makes up just 2% of its weight, its richer portion of bioactive compounds has received the majority of study attention. Extra-virgin olive oil is the least processed kind and has a rich blend of polyphenolic chemicals that are taken from the olive fruit [36-39]. Phenolic molecules have a wide range of biological actions, from stabilizing auto-oxidation to having positive impacts on human health [40]. OOPs' established procedures have shown that they have an impact on maintaining the stability and organic properties of OO [41]. These compounds may be found in free, bonded, or esterified forms and are part of the hydrophilic phenolic fraction that makes up EVOO [42]. With a total phenolic range ranging from 50 to 800 mg/kg, more than 30 distinct OOPs have been found in EVOOs [43]. Excessive intake of olive oil as part of a nutrition helps prevent metabolic syndrome, heart disease, cerebrovascular accidents, and some varieties of cancer [44].

helps prevent metabolic syndrome, heart disease, cerebrovascular accidents, and some varieties of cancer [44].

1.2.2. Honey is an excellent source of polyphenols.

Researchers found that polyphenols in natural honey are beneficial to humans, and discovered many polyphenolic components in honey, including flavonoids and phenolic acid. Phenolic acid and flavonoids help to minimise free radicals and oxidation. While the proportional amounts of the beneficial flavonoid and phenolic acid components in honey vary across varieties, their identities remain similar. Each honey variety includes distinct bioactive flavonoid and phenolic acid components, as shown in **Table B**. Honey's medicinal efficacy is mostly derived from the flavonoids or phenolic acids that are known to possess antioxidant capabilities. These flavonoids and acids are present in naturally occurring trace amounts all throughout the honey. Honey is advantageous for medicinal reasons largely because of the well-established antioxidant properties of flavonoids and phenolic acids, both of which are found in trace amounts in nature [45-48]

Table-B: - Flavonoids and phenolic acids are two examples of the bioactive substances that may be found in honey.

S. No.	The origin of honey	Polyphenols	Honey varieties
1	West Amazonian Ecuador	Luteolin-7-glucoside, luteolin, quercetin, naringenin, isorhamnetin, Coumarins, fraxin, scopoletin, bergamottin,	honey derived from meliponinae and apis from Ecuador [49].
2	Brazil	Gallic acid, quercetin, isorhamnetin, vanillic acid, 3,4- dihydroxybenzoic acid, coumaric acid, Naringenin,	Stingless bee honey [50].
3	Malaysia	The following substances were found in the sample: p-coumaric acid, benzoic acid, naringenin, gallic acid, syringic acid, caffeic acid, vanillic acid, trans cinnamic acid, and luteolin.	Tualang, Gelam, Borneo tropical honey [46]
4	Bulgaria	4-hydroxybenzoic acid, vanillic acid, Gallic acid, ferulic acid, caffeic acid, p-coumaric acid, syringic acid, protocatechuic acid	Eucalyptus, lime, chestnut, heather, lavender, acacia, rosemary, orange, sunflower, and rapeseed honey [51]

1.3. The reason for plants producing polyphenols.

Knowing the vast number of compounds that have been extracted and identified from the Kingdom Plantae, as well as the potential that many more are still to come, it is possible that green plants are among the best chemists in the natural world. A variety of metabolic and biochemical processes occur in green plants to produce phytochemicals. Phytochemicals may have antinutrient or phytonutrient properties in addition to colour, taste, and fragrance. While phytonutrients provide green plants with their medicinal and health advantages, antinutrients are phytochemicals that hinder the body's capacity to absorb nutrients. Numerous poisonous phytochemicals found in plants shield them from UV-B radiation, which severely damages them, as well as diseases, insects, and herbivores. These substances, in essence, dictated the development of early terrestrial plants. Human health benefits have been shown for antinutrients such as tannins and phytate. The phytonutrient family contains "plant phenol," or polyphenols. Polyphenols, which differ in kind and structure across taxa, have an impact on plant development, regulation, and structure. Plant species alter the structure of their polyphenols to withstand stressors like heat, radiation, drought, salt, floods, etc.Polyphenols may be able to control auxin and other plant growth hormones. Plant pigments are increased, and UV-B protection is provided by polyphenols [52-54].

1.4. The characteristics of polyphenols that affect their antioxidant ability

1.4.1. Food matrix

Polyphenols are known to be present in foods where they may be found in both bound and free forms.The antioxidant capacity of insoluble-bound polyphenols, which are largely found in cereal grains and bond with food matrix such as protein and polysaccharide,could scarcely be evaluated entirely by conventional assays, which ultimately influenced the findings of the tests. On the other hand,free polyphenols could be extracted with relative ease, and their antioxidant capacity could be reliably evaluated [55].

1.4.1. Structure

Polyphenols' structure-activity link has been extensively researched and documented. Antioxidant effectiveness varies among polyphenols according to their nucleus structures, substituent kinds, and substituent locations [56]. The ability to scavenge free radicals is mostly depends on phenolic hydroxyl groups; other groups and their quantity and location also have a major impact. However, glycoside and methoxy groups might be detrimental [57]. Additionally, the degree of polymerization would have an impact, which would normally be beneficial for the antioxidant capacity [58-59].

1.4.1. Stability

Polyphenols have comparatively low stability, which makes it easy for them to lose. Their stability may be impacted by a few physical and chemical elements that are often encountered during processing, storage, and digestion, for example pH, temperature, light, oxygen, enzyme, ascorbic acid, sugar, and metallic ions [60]. Polyphenols' antioxidant structure would be destroyed by links breakage brought on by degradation [61–63]. Thus, a drawback was that polyphenols' poor stability would impede their ability to function as antioxidants in everyday situations.

1.4.2. Bioavailability

Bioavailability is the proportion of the total amount of active chemicals that can absorb and use. Their bioavailability is what determines this because the quantity of polyphenols that the body does not absorb but instead eliminates does not affect their antioxidant activity in vivo [64–65]. Four factors often restrict the bioavailability of polyphenols:

I. Solubility. Polyphenols' hydrophilicity promotes their bioavailability. For example, adding a promoter to enhance the solubility of quercetin might considerably improve its oral absorption and bioavailability [66].

Biotransformation. After being broken down by the gut bacteria, polyphenols could barely persist in their original molecular state; instead, they mostly exist as metabolites. Recent research indicates that the metabolites of polyphenols should be taken into account when determining their bioavailability [67]. The biotransformation that the gut bacteria cause would alter the polyphenols' natural structure, which would have an impact on their antioxidant capacity.

II. Assimilation.A significant factor in polyphenols' bioavailability is their ability to move from the stomach and intestine into the cells.

III. Polyphenols' bioavailable capacity is often suboptimal, which severely restricts their antioxidant action in vivo [68 - 69].

1.5. Health Effect of Polyphenols

Undoubtedly, food has the power to heal naturally; our diet has the power to shape our fate. The most prevalent phytochemicals in our diet are called polyphenols, and they include flavonoids, tannins, lignans, and stilbenes. Foods high in polyphenols, such as fruits, vegetables, nuts, and seeds, act as medication to prolong our lives and improve our health. More than before, the mechanisms of action of several polyphenolic chemicals are associated with a decreased risk of illness in humans; however, this association is not fully understood. Some exhibit characteristics associated with antioxidants, while others trigger defensive systems that enhance the body's ability to respond to oxidative stress and avert further harm. They have been linked to many beneficial effects on human health. Due to polyphenols' antioxidant properties, high dietary content, and potential to prevent a variety of oxidative stress-related illnesses, including cancer, heart disease, and neurological disorders, polyphenols are now the subject of many studies. Since diet is the primary source of polyphenols, ingesting a wide range of plant meals might help increase intake of these compounds. This dietary polyphenol comes from honey; polyphenols are also abundant in most fruits and legumes. On the other hand, fruits high in polyphenols include pomegranates, apples, strawberries, blackberries, Aronia berries, cranberries, blueberries, raspberries, cherries, melons, grapes, plums, and pears. Furthermore, a variety of foods and drinks, including olive oil, chocolate, white, black, and green tea, as well as veggies like parsley, broccoli, celery, cabbage, and onion, are high in polyphenols [70].

1.5.1. The Antioxidant Property of Polyphenols

Antioxidant compounds are those that suppress oxidation. Based on their action mode mechanisms, two measures - SET and HAT assays - generally classify the antioxidant assays. Instead of using conventional peroxyl radicals, the prevalent of SET approaches employ spectrophotometric analysis to measure the antioxidants' activity. The SET methodology depends on the solvent and pH. The HAT-based method evaluates the antioxidant potential to scavenge ROS by donating hydrogen atoms and breaking the radical chain. The SET reaction is comparatively slower than the HAT reaction because it requires more time to complete and stabilize the solvent. In general, the HAT evaluation process is significantly dependent on the bond dissociation enthalpy (energy) of the antioxidant's hydrogen-donating group. The HAT assay is faster than SET and is based on kinetic curves. Numerous mechanisms, such as direct scavenging of free radicals via hydrogen atom transfer (HAT) or single electron transfer (SET), as well as transition metal chelation, mediate the antioxidant action of polyphenols [71, 72]. Free radicals may be produced chemically during the oxidation process. Free radicals are defined as atoms or groups of atoms with one unpaired electron. Due to their propensity for unpaired electrons to form pairs with other electrons, they are often exceedingly reactive and unstable. An oxygen molecule (O_2) experiences a four-electron reduction during metabolism in a living being. The creation of reactive oxygen metabolites as a result of this process may be due to electron excitation, energy addition, or contact with transition elements. We refer to these highly reactive oxygen metabolites as active oxygen species because of their great reactivity toward oxygen. Active oxygen species include singlet oxygen ($^1O_2$), hydroxyl radicals (OH*), superoxide ($O_2{}^0$), and hydrogen peroxide (H_2O_2). The main reactions in living cells that create free radicals are red-ox reactions, photolysis, radiolysis, and homolytic chemical bond fission. Within living things, free radicals set off a series of reactions that may cause cell damage and thus give rise to a host of illnesses. Free radicals in a live organism start a chain reaction that antioxidants put an end to. Put another way, antioxidants prevent the damaging effects of reactive oxygen species (free radicals) on living things by neutralizing or deactivating their actions. Oxidative stress is the distinction between antioxidant defenses and the production of extremely reactive oxygen groups, or free radicals. Because produced free radical species have a strong attraction to interact with other molecules or ions, they assault the pro-oxidants that are already present. The human body uses a variety of endogenous resistance mechanisms to defend against free radical-caused cell damage. Aging and the onset or progression of illness are largely attributed to the damage that reactive oxygen species, or free radicals, cause to bodily cells. According to recommendations, inadequate dietary intake of a nutrient may jeopardize the effectiveness of these antioxidant resistance systems. Numerous everyday behaviors, like drinking, smoking, eating an irregular diet, and changing one's diet, are directly linked to oxidative stress. In addition to eliminating free radicals and promoting certain metal chelation events, polyphenol functions as an antioxidant. To preserve optimal metabolic performance, cells must continuously eliminate singlet oxygen, peroxy nitrite, and hydrogen peroxide, three distinct reactive oxygen species. Ion transport systems may have several advantages by removing and lowering reactive oxygen species (free radicals) in the environment. Because of the presence of an H-atom, which prevents chain reactions initiated by free radicals in living organisms, these substances are known as polyphenols (PhOH), which are antioxidants. Using Polyphenols as Antioxidants

$$R\bullet + PhOH \longrightarrow R\text{-}H + PhO\bullet$$

The phenoxyl radicals (PhO•) that are created have the potential to stabilize by resonance or through self-combination, resulting in the production of dimer products that will finally put an end to the chain reaction.

$$PhO\bullet + PhO\bullet \longrightarrow PhO\text{-}OPh$$

A total of over eight thousand different kinds of naturally occurring polyphenols have been discovered. Polyphenols, on the other hand, are composed of several phenol units and may be found naturally in a wide variety of dietary sources. Polyphenols are often linked with many health advantages owing to the antioxidant content that they contain [73–76].

1.5.2. Anticancer effects and Polyphenols

The whole scientific community faces significant hurdles in the treatment and prevention of cancer. WHO data indicate that cancer ranks second globally in terms of cause of death and is estimated to cause one million deaths annually. Put another way, around one in six cancer-related fatalities is documented globally. Between 30 and 50 percent of cancer occurrences may be avoidable. A balanced diet that provides the necessary nutrients is a better approach for cancer prevention than for cancer treatment. A key strategy for cancer control is dietary adaptation and modification. Eating fruits and vegetables has the potential to provide extraordinary defense against a variety of malignancies, among which are of the kidney, breast, oesophageal, colon, and endometrium. Eating a healthy diet lowers the risk of developing other non-communicable diseases [NCDs] and delays the onset of diet-related malignancies.[77]. Many investigations conducted by many researchers have confirmed the anti-carcinogenic properties of natural polyphenols. Natural polyphenols can help fight cancer because they are strong antioxidants and reduce inflammation. Additionally, they can alter molecular targets and signalling pathways that are involved in a variety of functions, including cell life, migration, separation, proliferation, immunological responses, detoxifying enzymes, angiogenesis, hormone activities, and other processes [78–83]. Delphinidin and anthocyanins work together to kill cancer cells very effectively. They do this by mimicking the processes of triggered apoptosis and cell cycle arrest in many types of cancer. Peonidin-3-glucoside and cyanidin-3-glucoside limit lung cancer cell growth by down-regulating matrix metalloproteinase (MMP) production, causing apoptosis, and specifically diminishing cell proliferation and aberrant development in HER2-positive breast cancer [84–87]. In addition to its preventative properties, cyanidin-3-O-sambubioside inhibits the growth of breast cancer cells [88]. Scientists found that non-acylated mono glycosylated anthocyanins were much better at stopping the unchecked growth of cancer cells than anthocyanins with pelargonic din aglycone and tri glycosylation [89]. Numerous polyphenolic compounds, including quercetin, catechins, isoflavones, lignans, flavanones, ellagic acid, anthocyanidins, xanthohumol, resveratrol, and curcumin, have been found to exhibit protective and suppressive effects via a variety of routes in a number of studies that have used carcinogenic models [90]. EGCG, which is also called epigallocatechin-3-gallate, is an ester of gallic acid, a type of catechin, and epigallocatechin. It is found in green tea and lowers the risk of several types of cancer, such as those in the stomach, esophagus, bladder, and prostate [91]. Diferuloylmethane, often known as curcumin, has anticancer potential that decreases angiogenesis and cellular proliferation. It also possesses anti-kinase action, stops the advancement of the malignant cell cycle, and produces programmed cell death both in vivo and in vitro. It also controls the phosphorylation of transcription-3 (STAT 3), the binding of AP-1 DNA, signal transduction, and the activation of NF-KB in vitro [92]. Astragalus mongholicus flavonoids have a wide range of biological activities, including anti-mutation and anti-injury capabilities. They also induce cell cycle retardation in the G0/G1 phase, particularly in the G1 phase, and they have a strong suppressive effect on the human hepatocellular carcinoma BEL-7402 cells. During the transition from the G0 phase to the G1 phase, cyclin-dependent kinases 4 (CDK4) and 6 (CDK6) establish a connection with cyclin-dependent kinase 1 (Cyclind1). This helps control the G1 phase and moves cells into the S phase (DNA replication). CDK4/CDK6 will cause an uncontrollably high expression of cyclind1 and dysregulation of the cell cycle. Due to flavonoids' capacity to restrict K562 proliferation and keep more cells in the G0/G1 phase, there is likely a reduction in cyclind1 expression [93].

1.5.3. Heart Diseases and Polyphenols

Globally, cardiovascular diseases (CVDs) are the leading reason of mortality, according to data from the World Health Organization (WHO). About 20 million fatalities annually, or 31% of all deaths, were attributed to CVDs. Heart attacks and strokes account for around 85% of the fatalities listed above. Approximately 75% of world-wide CVD-related mortality occurs in low- and middle-income nations [94]. In accordance with the most current heart disease and stroke statistics published by the American Heart Association, it is estimated that more than 100 million people in the United States, which is equivalent to more than fifty percent of all people over the age of 18, have hypertension, also known as high blood pressure. A class of illnesses known as cardiovascular diseases (CVDs) affects the heart or blood vessels.Numerous health advantages and cardiovascular disease have been linked to polyphenols found in numerous dietary sources, for instance apples, coffee, tea, and cocoa [95,100]. Epidemiological research strongly suggests consuming polyphenols because it is unmistakably associated with a lower incidence of CVD [101–102]. Researchers now think that polyphenolic substances work at the molecular level to improve endothelial function and lower platelet aggregation because they can stop blood clots, reduce inflammation, and stop platelets from sticking together. Thus, polyphenolic substances are significant in the prevention and treatment of cardiovascular disease. According to some research, those who consume more flavonoids in their diets than those who consume the least do not have a 47% increased risk of cardiovascular disease [103]. Research has shown that consuming flavan-3-ol from various food sources may have positive effects on cardiometabolic outcomes and reduce the risk of diabetes and cardiovascular-related outcomes (such as blood pressure, cholesterol, and myocardial infarction). Flavan-3-ols, a well-recognized polyphenol, are found in significant concentrations in a number of frequently eaten foods, including tea, almonds, cocoa (chocolate), grapes, and legumes [104–106]. Red and blue fruits and vegetables, including blueberries, raspberries, strawberries, bilberries, red grapes, cherries, etc., are rich sources of anthocyanins, a kind of flavonoid. Like other polyphenols, anthocyanins that are consumed through diet are metabolized by the microbiome and the host to create active metabolites that have anti-inflammatory properties, improve vascular outcomes, reduce the risk of myocardial infarction in both men and women, and have additional positive effects on cardiovascular risk factors [107–108]. A stilbene, resveratrol is mostly found in berries, red wine, and grapes. In addition to its antioxidant and anti-inflammatory properties, it also stimulates sirtuins, which slow down the aging process. Resveratrol supplements are said to significantly reduce fasting blood sugar, total cholesterol, C-reactive protein (CRP), and both systolic and diastolic blood pressure. Apple flavonol quercetin has been shown to lower systolic blood pressure, improve endothelial function, and lessen the risk of cardiovascular disease [109–111].

1.5.4. The hyperlink between polyphenols and diabetes

Diabetes is one of the most significant problems facing the health of people all over the world, which ranks seventh among the world's main causes of death, according to WHO estimates [112]. Maintaining a nutritious diet may help delay the onset of diabetes and its consequences. Diets high in polyphenols may protect against type 2 diabetes, also recognised as adult-onset or non-insulin-dependent diabetes. To move sugar from the circulation into the cells and maintain healthy blood sugar levels, cells secrete the hormone insulin. Polyphenolic substances enhance the release of insulin. Additionally, it could stop starch from breaking down into simple sugars, which would stabilize blood sugar levels after meals. Diets high in polyphenols may aid in improving insulin sensitivity, glucose tolerance, and fasting blood sugar levels—all of which are protective against type 2 diabetes, according to several studies [113–114]. Additionally, compared to those eating the lowest levels, it is reported that those consuming the greatest amounts of diets rich in polyphenols had a 57% lower risk of acquiring type 2 diabetes during a 2- to 4-year period. The most powerful anti-diabetic effects of polyphenolic compounds are exhibited by anthocyanins and procyanidins, which are present in red, purple, and blue foods like berries, currants, and grapes, as well as in bark, leaves, and popular beverages like cocoa, coffee, and green tea, as well as in the seeds of numerous plants and foods derived from plants [115].

1.5.5. Polyphenols and Alzheimer's disease

Alzheimer's disease (AD) is a catastrophic situation neurodegenerative condition that affects elderly people worldwide. Damage to neuron structure and function is the primary cause, which ultimately results in the death of nerve cells in the human brain [116]. The World Health Organization (WHO) has disclosed that over 50 million people globally suffer from dementias, including Alzheimer's disease, and that figure is expected to rise to over 152 million by the year 2050. Approximately 60% of dementia patients globally originate from low- or middle-income nations [117]. Alzheimer's disease (AD) is thought to be at risk due to both genetic and environmental factors [118]. Free radicals are very reactive chemical groups that arise from both physiological and pathological processes. They have an odd number of electrons. At normal concentrations, reactive oxygen species (ROS) participate in many cellular and signalling pathways, including phagocytosis, enzyme activation, and cell cycle control. However, excessive ROS generation may lead to harmful consequences, such as damage to proteins, lipids, and DNA [119]. Cell damage may result from an imbalance in the status of oxidants and antioxidants. It has been proposed that oxidative damage, a consequence of reactive oxygen species, plays a role in the pathogenesis—the formation, process, and advancement of neurodegenerative diseases and disorders, cancer, diabetes, and aging [120]. Extensive scholarly research has shown that nitric oxide, hydrogen peroxide, hydroxyl radicals, and superoxide anion are essential components of oxidative stress, which ultimately results in Alzheimer's disease [121]. However, the defensive systems known as enzymatic and non-enzymatic antioxidants eliminate ROS. Polyphenolic chemicals have antioxidant properties and are primarily involved in neuroprotection. Pomegranate juice, dates, and figs are all high in polyphenols and should be added to the diet to help with behavioral problems and brain damage by keeping the balance between oxidants and antioxidants in transgenic APPs w / T g 2576 animals. Additionally, researchers found that extract from walnuts, whose polyphenols are the most effective among all nuts, has a great ability to shield PC12 cells from oxidative stress caused by amyloid-beta peptide [122].

1.5.6. Polyphenols' Anti-Cariogenic Properties

Tooth decay, or dental caries, affects 60–90% of children and most adults worldwide and is one of the most common and serious oral health issues [123]. Teeth, oral flora, and nutritional factors all have an impact on dental caries disease. Dental plaque absorbs dietary carbohydrates like sucrose or sugars, which bacteria (found in dental plaque on the outside of teeth) then convert into organic acids like lactic acid. Demineralization, or the net loss of mineral structure on the tooth's surface, is the result of the acid produced gradually removing calcium and phosphate from the tooth's surface. Polyphenols, which are present in tea, coffee, red grape seeds, and cocoa, have antibacterial properties that may help prevent cariogenic processes. They may slow down the growth of bacteria, protect the tooth surface, and inhibit the activity of enzymes like glucosyltransferase and amylase. It seems that flavonoids are effective anti-cariogenic compounds [124]. There are two groups that can be used to describe the anti-cariogenic effects of phenolic compounds: (I) plant extracts that have a lot of polyphenols but don't have any specific compounds identified; and (II) antibacterial polyphenolic substances. It has been shown that extracts derived from unfermented cocoa, green tea, and red grape seeds that include a high polyphenol concentration are effective against S. mutants and periodontal disorders. A flavonoid called quercetin-3-O-α-L-arabinose-pyranoside (guaijaverin) stops the growth of S. mutants, which is likely an anti-plaque effect [125-126].

6. Possible Negative Impact Of Polyphenols

People use polyphenols, an essential component of plant-derived food with numerous health benefits, to prevent and cure multiple diseases. Tragically, like any chemical substance, polyphenols may be harmful depending on dosage, circumstances, and environmental interactions. One of the important negative consequences of polyphenols is their ability to block iron uptake in the human body. Despite being a trace element that is necessary for human survival, iron deficiency is a widespread ailment that affects people all over the globe. Polyphenols have the capacity to bind to transition metal ions such as iron and copper. This stops free radicals from being produced by the Fenton and Haber-Weiss reactions. In addition to the polyphenolic compound's structure, the pH or ion form (Fe^{2+} &. Fe^{3+}) influences both binding strength and total ion concentration. Anaemia occurs when an individual consumes a diet rich in polyphenols or takes supplements containing these compounds. Polyphenols bind to iron in the gastrointestinal tract, inhibiting its absorption. Additionally, they may influence the regulation of iron homeostasis [127, 128]. Flavonoids can form complexes of proteins by both nonspecific mechanisms such as hydrogen bonding and hydrophobic effects, as well as with covalent bond formation. Polyphenols form complexes with proteins, which may be either soluble or insoluble. These complexes alter the structure, isoelectric point, hydrophobicity, solubility, and susceptibility of the proteins to enzymes [129]. Polyphenols may have detrimental effects on the digestive system's function by impacting the composition of the intestinal flora and inhibiting digestive enzymes [130].

7. Discussion

It was announced on April 1, 2016, by the General Assembly of the United Nations that the United Nations Decade of Action on Nutrition would run from 2016 to 2025. The decade provides a never-before-seen opportunity to address all forms of malnutrition. As promised at the Second International Conference on Nutrition (ICN2), it sets a specific date for meeting some global nutrition targets and diet-related NCD targets by 2025. Sustainable Development Objectives 2 and 3 (guarantee healthy lifestyles and promote wellbeing for everyone at all ages) and SDG 2 (end hunger, achieve food security and better nutrition, and promote sustainable development) are other key objectives that are included in the 2030 Agenda for Sustainable Development. The agenda also includes these goals. The World Health Organisation (WHO) and the Food and Agriculture Organisation (FAO), responsible for coordinating the United Nations Decade of Action on Nutrition, recommend the implementation of policies in some major areas.

- It needs to promote better nutrition through the policies governing trade and investment.
- It needs to provide a secure and encouraging environment for people of all ages to learn about nutrition.
- It needs to coordinate health systems to meet nutrition requirements, provide universal access, and provide nutrition education to all individuals.

The Polyphenols Applications 2024 World Congress, which will be held at the Università degli Studi di Milano Statale, Milan, Italy, from September 19 to 20, 2024, will support two projects aimed at advancing polyphenol technologies. They talked for a long time about different ways to make new products, such as finding new sources of phenolic compounds, studying and using new nutrients made from plant phenolic compounds, and creating methods for extracting and mixing polyphenols to a significant degree. In addition, they highlighted cutting-edge ways for advancing polyphenol research. Furthermore, corporations and scientists collaborated in order to fulfil the shared objective of assisting everyone by doing research on the bright future of polyphenols. Considering the well-established nutritional advantages of polyphenols for human health, the present trends indicate that polyphenol studies and research will continue to be an essential component of worldwide academic and industrial studies for the foreseeable future. This is because polyphenols have been shown to have benefits for human health. Even though there has been a significant amount of progress made in terms of health advantages, there are still areas that need more investigation. It is necessary for us to be able to continue screening traditional edible plants that have the ability to produce a large number of polyphenols in order to properly govern the use of polyphenols for the fortification of food, beverages, and cosmetics. We must also address questions of dosing and safety, plant tissue extraction optimization, and polyphenol bioavailability in the human body. Finally, the most recent research and analysis indicate that we should pay particular attention to the relationship between bioavailability, metabolism, and bioactivity. We should work to prevent neurological and noncommunicable diseases (NCDs), such as type 2 diabetes, most malignancies, and heart and metabolic issues [131–132].

8. Conclusion

People's poor diets are one of the primary reasons for the rise in the prevalence of numerous chronic illnesses, as well as cancer, diabetes, hypertension, and cardiovascular issues, among others. The likely existence of phenolic chemicals in foods has been associated with several types of benefits for human health. These benefits have been seen in a variety of ways. If we understand the bioavailability of these components, we will be able to identify nutritional polyphenols that are good and protective for the general public's health much more easily. As a result, dietitians are responsible for educating people about the health benefits of phytochemicals. Furthermore, people must be educated about the foods high in these phytochemicals and how to prepare them so that the body can absorb them more easily. Fruits, vegetables, nuts, and seeds are some common examples of polyphenol-rich foods. These meals may serve as natural pharmaceuticals, prolonging our lives and improving our overall well-being. Without a doubt, our eating choices have the capacity to shape how our lives unfold. In these conditions, the saying "It is preferable to prevent than to cure" is often employed. It is not only very accurate, but it also covers a wide range of intellectual and scientific issues that span several fields. The study is based on previous research on the impact of polyphenols on human health.

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10. Conflict of Interest

The author declares that there isn't a conflict of interest.

11. Ethics Statements

This is a review article and not submitted somewhere else.

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