### International Journal of Physiology, Nutrition and Physical Education



ISSN: 2456-0057 IJPNPE 2021; 6(1): 293-301 © 2021 IJPNPE www.journalofsports.com Received: 11-04-2021 Accepted: 15-05-2021

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# Classifications of polyphenols and their potential application in human health and diseases

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#### DOI: https://doi.org/10.22271/journalofsport.2021.v6.i1e.2236

#### Abstract

Polyphenols are naturally occurring organic compounds composed of several phenols' units. The polyphenols are the secondary metabolites produced by the plants which played an imperative role in industrial and therapeutic applications. The polyphenols are composed of the phenolic ring and structural element that bind these phenolic rings to one another. The polyphenols were categorized under different sub-categories according to their nature of action and their structural components. Different polyphenols were categorized under phenolics acids, flavonoids, stilbenes, lignans and other polyphenols together with xanthones, tannins and anthraquinones. Fruits, vegetables, cereals, legumes, herbs and spices are the prime source of polyphenols. The composition of these polyphenols is significantly altered by internal and external conditions like agro-climatic conditions, harvesting time, cultivation, origin and so on. Polyphenols represent pharmaconutrients that can be utilized in the manufacturing of drugs, functional foods, coloring and other human health supplements. With the advancement of scientific knowledge these polyphenols isolated from their natural source via different emerging techniques like ultra-highpressure extractions, supercritical fluid extraction, ultrasonic and heat reflux. Data from the clinical trials, In-Virto/Vivo, placebo-control, randomized and animals' trials suggest that the polyphenols have the potential in the pre-treatment or prevention of numerous chronic ailments including cardiovascular (CVD), degenerative diseases, neurodegenerative diseases, Parkinson's and Alzheimer's and other immune-related disorder.

Keywords: Polyphenols, flavonoids, therapeutic applications, phenolics acids

#### Introduction

Polyphenols are the naturally occurring secondary metabolites of higher plants, which played an imperative role in industrial and therapeutic application (Rasouli *et al.*, 2017; Singla *et al.*, 2019) <sup>[1, 2]</sup>. The polyphenols are the large molecules, molecular weight approximately 800 Daltons, which allow them to transverse the cell membrane, by which these polyphenols reach or attain space in intracellular sites as pigment or phytochemicals (Singla *et al.*, 2019) <sup>[2]</sup>. Approximately 8000 types of had been reported in the literature. The basic structure of these polyphenols comprises of the single or double aromatic rings bound with one or more hydroxyl group (-OH) (Rasouli *et al.*, 2017)<sup>[1]</sup>.

Fruits (apples, cherry, citrus fruits, pomegranate, strawberry, grapes) and vegetables (carrot, broccoli, chicory), legumes (beans, sprouts), dry fruits (almonds, flax seeds, chestnuts, walnuts), Cereals (rye, wheat, oats), herbs and spices (clove, cinnamon, cumin, basil, thyme) and beverages (wine, tea, coffee) and others are the adequate sources of polyphenols (ChauhaN *et al.*, 2018; Cheynier, 2012) <sup>[3,4]</sup>. The concentration and type of polyphenols in different food products are significantly dependent upon the origin, cultivation, environmental conditions, ripeness, pre-and post-harvesting, storage and transportation (S. Kumar *et al.*, 2020) <sup>[5]</sup>.

The major class of polyphenols was divided into flavonoids, polyphenolics amides, lignans, stibines and phenolic acid. The flavonoids include (flavonols, isoflavones, flavanones, anthocyanins, proanthocyanins), and lignans are those which are derived from the phenylalanine from the cereals or seed origins (Baniwal *et al.*, 2021; H. Kumar *et al.*, 2018; Mehra *et al.*, 2020; Rasouli *et al.*, 2017; Singla *et al.*, 2019) <sup>[1, 2, 6-8]</sup>.

The classification of these secondary metabolites is done based on their chemical structure, sugar rings, composition, and their synthesis pathways, for instance, the phenolics compounds are generally composed of simple sugars comprised of the benzene ring, oxygen and hydrogen.

Emerging evidence from the clinical trials suggests that these polyphenols are effectively in the pre-treatment and prevention of numerous chronic diseases including degenerative diseases, type-2 diabetes, cancer, antiinflammatory, cardiovascular (CVD), immune-related, osteoporosis and other neurodegenerative diseases (Behl et al., 2020)<sup>[9]</sup>. These polyphenols exhibit a wide range of antimicrobial, anti-bacterial, anti-oxidant and virucidal actions (Rasouli et al., 2017)<sup>[1]</sup>. The polyphenols assist in the secretion of insulin, which further maintains the blood sugar level, increased glucose tolerance and insulin sensitivity. The consumption of a polyphenol-rich diet may reduce the lowdensity lipoprotein (LDL), and cholesterol level which ultimately control the blood pressure level (Tresserra-Rimbau et al., 2017)<sup>[10]</sup>. Moreover, polyphenols enhance the growth of healthy gut bacteria, prevents blood clots, suppress tumor growth, enhance immunity and pulmonary embolism. The plant-based secondary metabolites can be categorized into different classes including alkaloids, phenolic four compounds, terpenoids and sulphur-containing compounds which also exhibits a wide range of therapeutic or industrial applications (Rasouli et al., 2017; Shahidi & Yeo, 2018)<sup>[1, 11]</sup>. From the industrial perspective, polyphenols can be used as pharmaconutrients for the synthesis of drugs, coloring agent or dye, tanning leather, encapsulated medium, and other functional food ingredient (Ajila et al., 2011; Jovanović et al., 2017)<sup>[12, 13]</sup>. The polyphenols from the different origins can be extracted by employing the different extraction techniques including chromatography (thin or paper), Soxhlet, microwave, heat reflux, ultrasonic, Liquid-liquid extraction, supercritical fluid extraction and ultra-high pressure extractions techniques. Further, the identification (qualitative or quantitate) of polyphenols can be analyzed through the high-performance liquid chromatography (HPLC), reverse-phase liquid chromatography (RPLC), nuclear magnetic resonance (NMR) and other spectroscopic techniques (Ajila *et al.*, 2011; Jovanović *et al.*, 2017; Kamal Gandhi *et al.*, 2018; Rashmi & Negi, 2020) <sup>[12-15]</sup>. This review article aims is to present the classification of polyphenols with their potentials attributes towards human health and diseases from the published scientific evidence.

#### **Classification of polyphenols**

To present, approximately 8000 types of polyphenols had been identified and reported in scientific literature. The polyphenols are the sub-categorized into phenolics acids (hydroxybenzoic and hydroxycinnamic acids), Flavonoids (flavones, flavonols, isoflavones, flavanones, anthocyanins), Stilbenes (resveratrol, piceatannol), Lignans (sesamol, pinoresinol, sinol, enterodiol), and others including tannins (hydrolysable, non-hydrolysable, and condensed tannins), lignins, xanthones, chromones, anthraquinones (Cheynier, 2012; Rasouli *et al.*, 2017; Singla *et al.*, 2019) <sup>[1, 2, 4]</sup>. An overview of the classification of polyphenols is presented in Figure 1. The dietary polyphenols represent a wide range of secondary metabolites, primally derived from phenolic acid, catechins, flavones and isoflavones (Rasouli *et al.*, 2017)<sup>[1]</sup>.



Fig 1: An overview of classifications of polyphenols

#### Phenolics acid

Phenolic acids are composed of aromatic rings with one carboxylic acid group (-COOH). These phenolics represent the major class of plant-based phenolic compounds. The different type of phenolics acid is presented in Figure 2. As phenolic acid has antioxidant properties, it protects against cardiovascular diseases (Behl et al., 2020; Rasouli et al., 2017; Shahidi & Yeo, 2018)<sup>[1, 9, 11]</sup>. The aromatic ring can lose its electron, forming hydrogen free radical which acts as reducing agents and quenches free radical, this mechanism protects from cardiovascular diseases (CVDs). Plant-based food including seed, fruits skin and leafy vegetables are the prime source of phenolics acid. These phenolic acids represent a wide range of cosmetic, food and therapeutic applications (Rashmi & Negi, 2020)<sup>[15]</sup>. Phenolic acid is subcategorized into hydroxybenzoic and hydroxycinnamic acids. The Hydroxybenzoic acid composed of C<sub>6</sub>-C<sub>1</sub>, derived from the benzoic acid ( $C_7H_6O_2$ ). The salicylic acid, vanillic acid, protocatechuic acid, gallic acid, benzoic acid and ellagic acid categorized under the sub-category of hydroxybenzoic (Ozcan et al., 2014)<sup>[16]</sup>. It is the monomer of more structurally complex compounds such as hydrolyzed tannins and is commonly available in bound form. Some hydroxybenzoic acids are also present in olive products which have antioxidant, anti-inflammatory, and cardioprotective effects (Gupta *et al.*, 2018; Shahidi & Yeo, 2018; Singla *et al.*, 2019) [2, 11, 17]

Hydroxycinnamic acid represents the class of aromatic acid (C6-C3), derived from cinnamic acid (Teixeira et al., 2013) <sup>[18]</sup>. Caffeic acid, ferulic acid, coumaric acid, sinapinic acid, cinnamic acid are a common example of hydroxycinnamic acid (Singla et al., 2019)<sup>[2]</sup>. This cinnamic acid is the structural and biological constituent that makes up the cell organelle. Tea, grape seeds are the plentiful source of hydroxybenzoic acids, and coffee, berries, apple, cereals, kiwi are the adequate source of hydroxycinnamic acids (Baniwal et al., 2021; Yadav et al., 2016)<sup>[6, 19]</sup>. Tea and grape seed (gallic acid), coffee (caffeine and chlorogenic acid), berries, apple (caffeic acid), cereals (ferulic acid) where the majority of citrus fruits contains (cinnamic acid). This phenolic acid is an easily digestible, excellent source of phytochemicals that offers numerous health potentials including anti-inflammatory properties, prevent the body from cellular damage, reactive oxygen species, oxidative stress, cardiovascular, anticancer, antidiabetic, neuroprotective, and food preservative (Teixeira et al., 2013)<sup>[18]</sup>.



Fig 2: Types of phenolics acids

#### Flavonoids

A flavonoid is a main group of plant-based metabolites of polyphenolic compounds. This structural composition of these flavonoids composed of 15- carbon atoms, comprises 2 aromatic rings linked by a 3-carbon-atom chain (Harborne, 2013) <sup>[20]</sup>. Flavonoids can be divided into several categories depending upon the C ring on which B ring is attached, its configuration, and oxidation of the C ring. The different categories of flavonoids including flavones (chrysin, apigenin, baicalein), flavonols (quercetin, kaempferol), isoflavones

(daidzein, glycitein), flavan-3-ols (gallocatechin, catechin, epicatechin), flavanones (hesperetin, naringenin) and anthocyanidins (delphinidin, peonidin, cyanidin, pelargonidin) are the major class of flavonoid (Rasouli *et al.*, 2017; Singla *et al.*, 2019)<sup>[1,2]</sup> as presented in Figure 3. They are mainly found in berries, onion, tea, grapes, apples, berries, coca and exhibits numerous health attributes including cell-signalling, anti-thrombogenic, neuroprotective properties (Ballard & Junior, 2019)<sup>[21]</sup>.



Fig 3: Types of flavonoids

#### Flavonols

Flavonols are a category of flavonoids family, comprised of double-bond between C<sub>2</sub>-C<sub>3</sub>, and carbonyl C<sub>4</sub>. Flavonols include quercetin, kaempferol, myricetin is ubiquitous plant flavonoids and occur in numerous fruits and vegetables e.g., Kale, onion, lettuce, and tomatoes (Sandu *et al.*, 2017) <sup>[22]</sup>. Emerging evidence from clinical trials showed that these flavonols have the potential in pre-treatment and prevention of cardiovascular disease, regenerate cell, prevent blood coating, human gingival, and other heart-related diseases (Behl *et al.*, 2020; Singla *et al.*, 2019) <sup>[2, 9]</sup>.

#### Isoflavones

Isoflavones are a type of phytoestrogens that are nonsteroidal compounds derived from plants (Nikolić et al., 2017)<sup>[23]</sup>. Isoflavones are obtained from the Fabaceae family. Isoflavones have 2 phenyl-4H-1benzopyr-4-one as structure in place of the phenyl group (Singla et al., 2019)<sup>[2]</sup>. Isoflavones are obtained via the phenylpropanoid pathway which helps to produce flavone groups in higher plants. Isoflavones are obtained from soybean and soybean products. Isoflavone content is high in soybean as it has 2 key components namely daidzein and genistein (Zaheer & Humayoun Akhtar, 2017)<sup>[24]</sup>. Research suggests the potential use of isoflavones to cure menopause-related symptoms as well as they are thought to have chemo-protective properties (Rasouli et al., 2017)<sup>[1]</sup>. Studies also suggest it aids in treating various hormonal disorders, heart-related disorder. osteoporosis, cancer (breast and prostate). Studies also suggest that excessive consumption of isoflavones can lead to improper development of the hypothalamic-pituitary-ovarian axis and also results in the incomplete development of the reproductive system (Nikolić et al., 2017)<sup>[23]</sup>. Besides, the health hazards and the numerous health benefits isoflavones possess it is stated to be consumed in moderation as well as under supervision and further research on isoflavones is still being done (Wong et al., 2008; Zaheer & Humayoun Akhtar, 2017) [24-25]

#### Flavanones

Citrus fruits, some aromatic plants, and tomatoes are some parts of flavanones that form a small part in flavonoids. They are considered a great component of human health apart from their flavouring properties. Eriodyctiol from lemons, hesperidin from oranges, and naringenin from grapefruit constitute the flavanones (Calderón-Oliver & Ponce-Alquicira, 2018) <sup>[26]</sup>. Alongside, flavanones also undergo various chemical processes like o-methylation, glycosylation, and hydroxylation (Singla et al., 2019)<sup>[2]</sup>. Bergamot juice i.e., Citrus bergamia has found to be having large amounts of flavonoids in them (Mandalari et al., 2006)<sup>[27]</sup>. This has shown a decreased presence of serum lipids in Bergamot leading to various advantages of its extract over cardiovascular metabolisms such as atherosclerosis, lipid profile, and lipoproteins. It was also found that the consumption of this extract for over six months lead to decreased levels of lipids and cardiovascular events can be identified by detecting LDL levels (Behl et al., 2020)<sup>[9]</sup>.

#### Anthocyanidins

Anthocyanidins are the pigments, primarily responsible for the colour (red, pink, purple) in fruit and vegetable (Wrolstad, 2004) <sup>[28]</sup>. The various colours in the fruits, vegetables, and flowers are due to the presence of anthocyanidin in their epidermis. Different fruits and vegetable including radish, beetroot, berries, strawberries and cherries are an adequate source of anthocyanidins (Welch et al., 2008)<sup>[29]</sup>. Out of these, Aronia berries are quite famous due to their increased antioxidant properties (Krga & Milenkovic, 2019)<sup>[30]</sup>. They are obtained from chock berries and they exhibit various components such as flavanols, kaempferol, cyanidin glycosides, and some other bioactive compounds (Singla et al., 2019)<sup>[2]</sup>. Honey, olive oil, and berries have shown their immense advantages over human health over time. The consumption of anthocyanin results in total cholesterol, high triglycerides, low high-density lipoprotein cholesterol and high non-high-density lipoprotein cholesterol (Wrolstad,

2004) <sup>[28]</sup>. In another experiment revealed that the strawberry consumption for a month proved very beneficial for the lipid levels in the body, simultaneously reduce the levels of serum malondialdehyde (MDA), isoprostanes, and urinary-8-OHdD (Welch *et al.*, 2008) <sup>[29]</sup>. It was concluded that the consumption of strawberries will help in the attenuation of thrombotic and HCF-induced inflammatory responses. Anthocyanin capsules were produced using bilberry and blueberry (Gaspar *et al.*, 2021) <sup>[31]</sup>. These investigations proved those anthocyanin treatments create alternations in the mass of plasma Cholesteryl Plasma Transfer Protein (CETP). Reduced systolic BP can be achieved by the consumption of blueberries (Gaspar *et al.*, 2021) <sup>[31]</sup>.

#### Flavones

Flavones are commonly found in cereals, celery, parsley, and broccoli. They are also found in large quantities in the outer layering of citrus fruits. It was registered that the flavones have an inverse effect on CAD (Cutrim & Cortez, 2018)<sup>[32]</sup>.

Tangerine, a component of flavones, inactivates the formation of platelets which promotes the multiplication of the smooth muscles present in the body leading to atherogenesis and restenosis (Jiang *et al.*, 2016) <sup>[33]</sup>. Cancer and inflammation can be avoided by having citrus fruits having Nobiletin. Through various experiments, it is known that, nobiletin help in platelet activation. It also prohibits mitogen-activated protein kinase (MAPKs) and phosphorylation of protein kinase (Jiang *et al.*, 2016)<sup>[33]</sup>.

#### Other polyphenols

The other polyphenols including stilbenes (resveratrol, piceatannol), Lignans (sesamol, pinoresinol, sinol, enterodiol), and other including tannins (hydrolysable, non-hydrolysable, and condensed tannins), lignins, also possess a wide range of therapeutic and industrial application according to their nature of action (H. Kumar *et al.*, 2014; Rasouli *et al.*, 2017; Singla *et al.*, 2019) <sup>[1,2,34]</sup>. An overview of some other polyphenols that exists in nature is presented in Figure 4.



Fig 4: Other types of polyphenols

#### Lignin

In many plant tissues, there is a group of complex organic compounds, these compounds are called lignin. In plants and trees, lignin is specifically important as they help in the formation of the cell wall (Popa *et al.*, 2008) <sup>[35]</sup>. They are important as they help to provide strength and rigidity to trees. Lignin was first identified by a Swiss botanist named A P Candolle in 1813. Lignin is heterogeneous polymers that are obtained from few signal precursors that are cross-linked in different forms (Singla *et al.*, 2019) <sup>[2]</sup>. There are three types of cross-links, which are obtained from phenylpropane and those crosslinks are coniferyl alcohol, sinapyl alcohol, and paracoumaryl alcohol (Popa *et al.*, 2008) <sup>[35]</sup>. Some foods that are rich in lignin are flaxseeds, tomatoes, peaches, apples, and few berries.

#### Silymarin

Lignin silymarin is a type of flavonolignans that has antioxidant properties. This type of lignin is obtained from milk thistle seeds which are obtained from certain varieties of daisy and other herbaceous plants (Radko & Cybulski, 2007) <sup>[36]</sup>. For ages, this lignin is used to cure ailments related to the gall bladder and liver. Some researchers also suggest its usage like cirrhosis, jaundice, etc. Some also claim it is also used to treat diabetes specifically type 2 diabetes and also it is used to lower cholesterol levels (Křen & Walterova, 2005) <sup>[37]</sup>. Some research shows that consumption of lignin silymarin has side effects like nausea, itching, diarrhea, and bloating. Hence research suggests taking medical advice before consuming these flavonolignans (Radko & Cybulski, 2007) <sup>[36]</sup>.

#### Stilbenes

A category of metabolites derived from phenols is stilbenes (C<sub>14</sub>H<sub>12</sub>). Their biological activity and their health benefits for the overall health of humans is a research attraction and is a key interest for several studies (Shen *et al.*, 2009) <sup>[38]</sup>. Stilbenes are organic compounds that have a compact structure with a central ethylene fraction and one phenyl group. The phenyl group is located at the ends of the carbon double bonds (Chou *et al.*, 2018) <sup>[39]</sup>. The common name for stilbenes is Tran's stilbenes. Stilbenes were discovered by French chemist Auguste Laurent in 1843. The bioavailability,

metabolism rates, and absorption in the body are still in the research and their overall health benefits are still a question under study (Shen *et al.*, 2009)<sup>[38]</sup>.

#### Resveratrol

A class of naturally occurring phytochemical, stilbenes are found in grapes, berries, and few other plants. The most commonly known type of stilbene is resveratrol. Resveratrol is more extensively known because of its properties in disease prevention. Resveratrol is derived from stilbene (Baur & Sinclair, 2006)<sup>[40]</sup>. This compound has two isomers cis (Z) and trans (E). In plants, resveratrol is derived from an enzyme called resveratrol synthase. The primary source of resveratrol is red wine (King et al., 2006)<sup>[41]</sup>. Though the bioavailability of resveratrol in the body is very less, it showed protective action against cardiovascular diseases (CVDs) as well as it is also found to have a sun-protective effect and known to prevent skin cancer (Ferrazzano et al., 2011)<sup>[42]</sup>. It is also known to lower blood pressure and also research conducted so far shows the use of resveratrol in supplement form rather than obtaining it through natural good sources. Further research also claims the use of resveratrol being potentially beneficial for humans but the study on its exact action is yet under study (King et al., 2006)<sup>[41]</sup>.

#### Health Benefits of Polyphenols

Phenolic compounds are believed to have excellent antibacterial as well as anti-microbial properties for decades (Tresserra-Rimbau *et al.*, 2017) <sup>[10]</sup>. They also have been known to encourage protection against infectious diseases and inflammation through protein and enzyme modulation and neutralization mechanisms (Khan *et al.*, 2019; Mehra *et al.*, 2021) <sup>[43,44]</sup>. These phenolic compounds can be found in a variety of food components that have been derived from plants in four different criteria's i.e., flavonoids, tannins, phenolic acids, and stilbenes (H. Kumar *et al.*, 2014; Rasouli *et al.*, 2017) <sup>[1,34]</sup>. They show chelating properties in metal ions and terminating properties in free radicals via catalysation of the oxidation of lipids. The numerous health attributes of polyphenols toward human health are presented in Figure 5.

The main achievements of dietary phenolics have been accomplished due to their absorption and various chemical metabolisms in the body. This in turn depends on the chemical structure of the phenolic compounds along with molecular size, degree of acylation or glycosylation, conjugation with other phenolics and solubility (Cheynier, 2012)<sup>[4]</sup>. These processes take place during the passage of

food through the digestive system and after being absorbed into the circulatory system into the liver. Here, polyphenols are taken in the form of glucosides which undergo deglycosylation to form aglycone which facilitates absorption in the intestinal epithelium. To keep the blood metabolite levels high in the blood, it is important to keep up with an increased intake of plants since their metabolites are expeditiously consumed (H. Kumar *et al.*, 2014)<sup>[34]</sup>.

Bioavailability is an important factor since only the best bioavailable phenolic compounds in our diet will have their best effects on the human body (D'Archivio et al., 2010)<sup>[45]</sup>. These will differ from person to person depending upon their binding with the food matrix, structure of cell walls, and the location of glycosides. Epidemiological studies prove that phenolic compounds have plenty of health advantages like anti-deposition, triglycerides inhibit decaying microorganisms, reducing cardiovascular diseases, antiallergic effects, diabetes, stroke, cancer, and anti-inflammation (Behl et al., 2020; Ferrazzano et al., 2011; Tresserra-Rimbau et al., 2017) <sup>[9,10,42]</sup>. Earlier it was assumed that the health benefits achieved from phenolics were due to the secondary metabolites present in them. However, later it was found that it has been because of the coordinated effect of the metabolites in the circulatory system over the various components taking part in the intracellular process of signalling for important functions of the cell-like apoptosis, proliferation, and growth (Tresserra-Rimbau et al., 2017)<sup>[10]</sup>. The potential of the polyphenolic antioxidant properties depends upon the hydroxylation of their aromatic rings such as modulation of the endogenic antioxidant enzymes, the activity of the free radical scavengers, and chelating and stabilizing the divalent cations (Olszowy, 2019)<sup>[46]</sup>.

The World Health Organization (WHO) illustrated an annual death of 17.9 million people due to cardiovascular diseases along with cerebrovascular and coronary heart disease (*Cardiovascular Diseases (CVDs*), n.d.) <sup>[47]</sup>. Hypertension, atherosclerosis, peripheral arterial disease, rheumatic cardiac disease, stroke, CHD are some of the heart and blood vessel disorders coming under the CVDs (Tresserra-Rimbau *et al.*, 2017) <sup>[10]</sup>. These diseases can be avoided by diminishing alcohol consumption, hypertension, tobacco, obesity, unhealthy diet, and diabetes. However, there is a lot of hard work and dedication along with heavy expenditures required to be regarded to get rid of such diseases. Therefore, the WHO discovered further the health benefits acquired from the consumption of fruits and vegetables enriched with polyphenols.

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Fig 5: Potential health attribute of polyphenols towards human health and disease

Some of the important health advantages of different types of phenolic compounds are given. anti-mutagenic and anticarcinogenic effects are shown by hydrolysable tannins, phenolic acids, and flavonoids they protect the DNA from the free radicals through inactivation of the carcinogens and activation of the enzymes responsible for the xenobiotic detoxification (Naczk & Shahidi, 2003) [48]. L-ascorbic acid and flavonoids specifically inhibit the oxidation of DNA in lymphocytes. Neurodegenerative diseases including Parkinson's and Alzheimer's are inhibited by catechins and flavonoids through their therapeutic properties (Matsui, 2015) <sup>[49]</sup>. Trans-3,5,4'-trihydroxystilbene and resveratrol commonly found in red wine and grapes are the best-known agents for any effects against breast, heart, immune system, prostate, and uterus (Singh et al., 2010)<sup>[50]</sup>. Food rich in tannins such as herbal teas and betel nuts are known to have less nutritional value since the tannic acid is responsible for low protein digestibility, decreased feed efficiency, feed intake, and growth rate (Chung et al., 1998)<sup>[51]</sup>. Although tannins do have good physiological effects such as reduce blood pressure, production of liver necrosis, modulation of immune responses, and acceleration of blood clotting (Chung et al., 1998)<sup>[51]</sup>. Oleuropein also has an anti-adipogenicity effect and also works against Chronic colitis (Hassen et al., 2015)<sup>[52]</sup>. Thus, the polyphenols in olive leaf, mainly the Oleuropein, display many interesting health benefits on the human body (Gorzynik-Debicka et al., 2018, 2018)<sup>[53]</sup>. Polyphenols also prove to be quite useful in the food processing industry for an increased shelf of food products by inhibiting the growth of viruses, yeast, bacteria, and fungi like Enterotoxigenic E. coli (ETEC), Salmonella, vibrio cholera, clostridium, chlamydia pneumonia (Daglia, 2012)<sup>[54]</sup>.

#### **Future prospective**

Polyphenols are plant-based micronutrients. They are said to be full of benefits for health and antioxidant-rich. Some examples of polyphenolic compounds are flavonoids, tannins. The current information and understanding of the working of polyphenols are very little and further research and studies are required to fully understand their action mechanism to gain knowledge about their biological role in a better way. Many studies on molecular and gene-level are required to be done to see the part that polyphenols play in various disease prevention. Many studies have also used different screening methods like spectroscopy, electrophoresis, and chromatography to have a keen look at polyphenols and their mode of action in treating diseases like cancer and other chronic ailments and diseases like diabetes and insulin sensitivity. Some studies also show the potential use of polyphenols in weight loss and reduce fat accumulation. And few other studies and research show the benefits of polyphenols in reducing stress and also aid in curing hypertension and different heart diseases. But the exact mechanism and the way that they prove to be so useful to the human body is yet under research and studies are being conducted. Some studies reveal that a boom in the market of polyphenols is yet to come and these studies will prove to be key changes in how polyphenols are perceived so that they can be branded as potential key drugs in curing ailments as well as be used as nutraceuticals to confer benefits for overall human health and well-being.

#### Conclusion

In the past decades, exceptional advancements have been made to understand polyphenols and their role in overall human health. Various studies are also done to understand the activity polyphenols have in different body metabolisms and mechanisms. Other studies show the role of polyphenols in treating diseases as well as helping in improving health by aiding in fat loss and prevention of CVD, diabetes and reducing stress, etc. Few other studies also show that regular intake of vegetables rich in polyphenols is shown to show a positive effect on the overall health of humans. Research and studies also say and show with shreds of evidence that polyphenols are promising future micro-nutrients that can be used in the treatment of various health pathologies. But more studies are needed to classify polyphenols as a key food supplement full of bio-active components and to commercialize them as a key nutrient to be consumed for good health and to lead a holistic lifestyle.

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