ABSTRACT
Polyhydroxy phenols are an antioxidant phytochemical (as chlorogenic acid) that tends to prevent or neutralize the damaging effects of free radicals. Photochemical are chemical compounds that occur naturally in plants (phyto means "plant" in Greek). Polyphenols are natural phytochemical compounds in plant-based foods, such as fruits, vegetables, whole grains, cereal, legumes, tea, coffee, wine and cocoa; more than 8000 polyphenolic compounds, including phenolic acids, flavonoids, stilbenes, lignans and polymeric lignans have been act as a defense against ultraviolet radiation, oxidants and pathogens. Some are responsible for identified in whole plant foods. These compounds are secondary metabolites of the plants that color and other organoleptic properties, such as the deep purple of blueberries and the smell of garlic. These Polyphenols are used to treat antidiabetes antiarthritus, antiviral, antifungal, antioxidant, cardiovascular diseases. But consumption of high doses of polyphenol supplements causes a double edge sword.

Key words: Polyphenols, phytochemical, cardiovascular diseases, double edge sword.

INTRODUCTION
Polyphenols are the most abundant antioxidants in the diet and are widespread constituents of fruits, vegetables, cereals, dry legumes, chocolate, and beverages, such as tea, coffee, or wine. Experimental studies on animals or cultured human cell lines support a role of Polyphenols in the prevention of cardiovascular diseases, cancers, neurodegenerative diseases, diabetes, or osteoporosis. The 1st International Conference on Polyphenols and Health, held in 2005, reviewed impressive evidence strongly supporting a role for polyphenols in preventing degenerative diseases, especially cardiovascular disorders and cancer. Polyphenols can also block the action of enzymes that cancers need for growth and
they can deactivate substances that promote the growth of cancers. Polyphenols protect cells and body chemicals against damage caused by free radicals, reactive atoms that contribute to tissue damage in the body. For example, when low-density lipoprotein (LDL) cholesterol is oxidized, it can become glued to arteries and cause coronary heart disease.” Polyphenols also have beneficial effects on the endothelial lining of blood vessels by increasing the availability of nitric oxide, and by preventing the lipid oxidation underlying atherosclerosis. Apple polyphenols not only lower blood cholesterol, but also inhibit triglyceride absorption, without any apparent ill-effects. Like the blueberry, the black chokeberry is high in anthocyanins and antioxidant activity. Green tea, and its active compound, epigallocatechin gallate, which has been shown to possess anti-obesity, antihypertensive, antidiabetic, antioxidant, anti-inflammatory, and antimutagenic effects. Tea polyphenols break down at high temperatures, so freshly brewed tea contains a higher amount of polyphenols per serving than do canned or bottled tea drinks.. These compounds are secondary metabolites of the plants that act as a defense against ultraviolet radiation, oxidants and pathogens.

Consumption of new dietary supplements and polyphenol-rich foods such products can increase dietary polyphenol intake and subsequently plasma concentrations beyond expected levels are being developed for public use and potentially confer additional health benefits. But high-doses may elicit toxicity thereby establishing a double-edge sword in supplement use.\cite{1}

**Types of Polyphenols**

Polyphenols are the plant metabolites characterized by the presence of several phenol groups (i.e., aromatic rings with hydroxyls), which derived from L-phenylalanine. The most important classes are phenolic acids, which include polymeric structures, such as hydrolyzable tannins, lignans, stilbenes, and flavonoids. Flavonoids include flavonols (e.g., quercetin and kaempferol), flavones, isoflavones, flavanones, anthocyanidins (pigments responsible for the colour of most fruits).flavonols are generally present at relatively low concentrations of \(\approx15–30\) mg/kg fresh wt. The richest sources are onions (up to 1.2 g/kg fresh wt), curly kale, leeks, broccoli, and blueberries. Red wine and tea also contain up to 45 mg flavonols/L. These flavonols accumulate in the outer and aerial tissues (skin and leaves) because their biosynthesis is stimulated by light.
Phenolic acids
These are approximately a third of the polyphenolic compounds in the diet and include two main classes hydroxybenzoic acid derivatives (protocatechuic acid, gallic acid, p-hydroxybenzoic acid) and hydroxycinnamic acid derivatives (caffeic acid, chlorogenic acid, coumaric acid, Ferulic acid, sinapic acid); berry fruits, kiwi, cherry, apple, pear, chicory and coffee are the foods with high content of these phenolic acids.

Lignans
Lignans are formed from 2 phenyl propane units and richest dietary source is linseed, , leguminous plants (lentils), cereals (triticale and wheat), vegetables (garlic, asparagus, carrots), and fruit (pears, prunes) as minor sources. It contains secoisolariciresinol (up to 3.7 g/kg dry wt) and low quantities of matairesinol. Other cereals, grains, fruit, and certain vegetables also contain traces of these same lignans, but concentrations in linseed are ≈1000 times as high as concentrations in these other food sources. Lignans are metabolized to enterodiol and enterolactone by the intestinal microflora.

Tannins
Tannins fall into the phenolic acid category of Polyphenols found in plants. Their primary role in plants is to bind and separate proteins. Tannins also provide color, particularly in flowers and the changing leaves during the autumn season. In food, tannins are responsible for the astringent taste in foods like red wine and unripe fruits. The astringency of tannins acts as a defense mechanism that protects the fruit and plant from insect and other plant-eating predators.

Stilbenes
Stilbenes are found in only low quantities in the human diet. One of these, resveratrol, for which anticarcinogenic effect, is found in low quantities in wine (0.3–7 mg aglycones/L and 15 mg glycosides/L in red wine). However, because resveratrol is found in such small quantities in the diet, any protective effect of this molecule is unlikely at normal nutritional intakes.

Beneficial properties
Several biological activities and beneficial properties have been reported for dietary polyphenols, and some of them are antioxidant, anti-allergic, anti-inflammatory, anti-viral and anti-microbial, anti-proliferative, anti-mutagenic, anti-carcinogenic, free radical.
scavenging, regulation of cell cycle arrest, apoptosis, and induction of antioxidant enzymes; more interestingly, dietary polyphenols could modulate some important cell signaling pathways such as nuclear factor kappa-B (NF-κB), activator protein-1 DNA binding (AP-1), extracellular signal-regulated protein kinase (ERK), phosphoinositide 3 (PI3) kinase/protein kinase B (Akt), mitogen-activated protein kinases (MAPK), and nuclear factor erythroid 2 related factor 2 (Nrf2). \[^{4,5}\]

**Pharmacokinetics of polyphenol**

Dietary intake of polyphenols is approximately 1 g/day. Bioavailability of these bioactive components is dependent on food preparation processes, gastrointestinal digestion, absorption and metabolism. During the absorption pathway, dietary polyphenols must be hydrolyzed by the intestinal enzymes or colonic microflora, and then be conjugated in the intestinal cells and later in the liver by methylation, sulfation or glucuronidation. Polyphenols consequently reach and accumulate in the target tissue and induce biological properties; the polyphenol derivates mainly excrete through bile and urine. Several studies showed rapid absorption of the polyphenolic compounds, such as procyanidins, quercetin and flavanols into plasma, with plasma concentrations peaking at 2 or 3 hours after ingestion \[^{6,7}\]

**Table 1: Contents of phenolic compounds in fruits/beverages**

<table>
<thead>
<tr>
<th>Fruits/beverages</th>
<th>Polyphenols per 100g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rowanberry</td>
<td>103mg</td>
</tr>
<tr>
<td>Chokeberry</td>
<td>96mg</td>
</tr>
<tr>
<td>Blueberry</td>
<td>85mg</td>
</tr>
<tr>
<td>Sweet rowan berry</td>
<td>75mg</td>
</tr>
<tr>
<td>Dark plum</td>
<td>28mg</td>
</tr>
<tr>
<td>Green and black tea</td>
<td>36mg</td>
</tr>
</tbody>
</table>

**Table 2: Plants containing important phenolic acids**

<table>
<thead>
<tr>
<th>Plants</th>
<th>Polyphenols</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onions</td>
<td>Quercetin</td>
</tr>
<tr>
<td>Green tea</td>
<td>Epigallocatechin gallate</td>
</tr>
<tr>
<td>Grape seeds</td>
<td>Proanthocyanidins</td>
</tr>
<tr>
<td>Apple skin</td>
<td>Chlorogenic acids</td>
</tr>
<tr>
<td>Red wine</td>
<td>Resveratrol</td>
</tr>
<tr>
<td>Linseed</td>
<td>Secoisolariciresinol</td>
</tr>
<tr>
<td>Pomegranate</td>
<td>Ellagitannins</td>
</tr>
</tbody>
</table>
Common structures of polyphenols \[8,9\]

**Hydroxybenzoic acids**

\[
\begin{align*}
R_1 &= R_2 = \text{OH}, \quad R_3 = \text{H} : \text{Protocatechuic acid} \\
R_1 &= R_2 = R_3 = \text{OH} : \text{Gallic acid}
\end{align*}
\]

**Hydroxycinnamic acids**

\[
\begin{align*}
R_1 &= \text{OH} : \text{Coumaric acid} \\
R_1 &= R_2 = \text{OH} : \text{Caffeic acid} \\
R_1 &= \text{OCH}_3, \quad R_2 = \text{OH} : \text{Ferulic acid}
\end{align*}
\]

**Flavonoids**

\[
\text{Chlorogenic acid}
\]

**Stilbenes**

\[
\text{Resveratrol}
\]

**Lignans**

\[
\text{Secoisolariciresinol}
\]

**Hesperetin**

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**FOODS HIGH IN POLYPHENOLS**

**Fruits**

The USDA lists blueberries, strawberries, raspberries, citrus fruits dark grapes, bilberries, cherries, apples, dark plums, blackberries and blueberries were all good sources as well. and other fruits as good sources of Polyphenols.

**Vegetables**

All vegetables provide polyphenols or other antioxidants, while onions and potatoes have been proven to be moderate to high in polyphenols. Vegetables should be chosen for their
bright color with all colors eaten each week, including red, orange, yellow, blue, purple, white and green.

**Grains, Beans and Nuts**

Rye and other whole grains found in breads, rolls and cereals contain various levels of Polyphenols. Soybeans, Peanuts are also listed as a good source of this antioxidant. Several servings of whole grain should be eaten each day, with beans and nuts.

**Other Foods and Beverages**

Several beverages are good sources of polyphenols, with coffee providing the most. Tea, especially green tea, should also be consumed regularly for its high content. Red wine, white wine and cocoa are more good options for polyphenol. Chocolate, seeds and margarine also contain this antioxidant.

**Food Storage and Preparation**

Food storage and preparation factors can greatly alter polyphenol content. Fresh fruits and vegetables usually contain higher levels of polyphenols than food that had been picked several weeks ago. Peeling food reduces the level of these important nutrients. While cooking food may reduce polyphenol levels, it often raises the bioavailability of the nutrient, allowing us to better receive the food's benefit[^10].

**PHARMACOLOGICAL ACTIONS**

**Antiplatelet activity**

Mattiello T, et al., studied that punica granatum polyphenols reduced cardiovascular accidents in high-risk patients; in particular, the inhibition of platelet function may be responsible for part of this benefit. The main constituent is hydrolyzed tannins such as ellagitannins. The polyphenol-rich extract from pomegranate fruit showed a stronger action in reducing platelet activation. These results demonstrated that the cardiovascular health benefits of pomegranate may in part be related to the ability of polyphenols to inhibit platelet function[^11,12].

**Antioxidant activity**

Katiyar SK et al., evaluated that Green tea is consumed as a popular beverage worldwide particularly in Asian countries. The polyphenol (epicatechins) showed antioxidant activity. Many Studies have shown that green tea extract also possesses anti-inflammatory activity.
These anti-inflammatory and anti-carcinogenic properties are due to the chemo preventive constituent (-)-epigallocatechin-3-gallate in green tea responsible for these biochemical or pharmacological effects. Results showed that topical treatment with (-)-epigallocatechin-3-gallate on mouse skin in prevention of UVB-induced immunosuppression, and oxidative stress [13,14].

**Anticarcinogenic activity**

Santosh K. Katiyar *et al.*, studied that overexposure of the skin to ultraviolet (UV) radiation has showed a variety of adverse effects on the development of skin cancers. The proanthocyanidins present in grape seeds (*Vitis vinifera*) showed to have some biological effects, including prevention of photo carcinogenesis. They conducted the study on SKH-1 hairless mice, dietary supplementation with proanthocyanidins is associated with a decrease of UVB-induced skin tumor. Results showed that the dietary proanthocyanidins could be useful in the adverse UV-induced health effects in human skin [15].

**Antiarthritis**

Nahrstedt A, *et al.*, showed the efficacy of willow bark extract in the treatment of painful mobility disorders, such as back pain and arthritis, due to the content of salicin and its derivatives as pro-drugs of salicylates. Based on clinical experience and the evidence of experimental pharmacological studies, the fraction of total salicin cannot satisfactorily explain the clinical efficacy of willow bark. In addition, salicins and their metabolites lack the acetylated potential of ASA and must therefore possess a different mechanism of action [16].

**Antiulcer activity**

Osakabe N *et al.*, examined the antiulcer activity of cacao liquor water-soluble crude polyphenols, Alpha-tocopherol, sucralfate, and cimetidine were orally administered to male SD rats before ethanol treatment. Polyphenols reduced the activities of enzymes are main sources of oxygen radical. They reported that the antiulcer mechanism of cacao was not only radical scavenging but also modulation of leukocyte function [17].

**Anti Alzheimer’s activity**

David Vauzour *et al.*, studied Flavonoids exert a multiplicity of neuroprotective actions within the brain, including a potential to protect neurons against injury induced by neurotoxins, an ability to suppress neuroinflammation, and the potential to promote memory, learning and cognitive function. The consumption of flavonoids-rich foods throughout life
holds the potential to limit neurodegeneration and to prevent or reverse age-dependent losses in cognitive performance. Development of drugs capable of enhancing brain function means that flavonoids may represent important precursor molecules in the quest to develop of a new generation of brain enhancing drugs.\cite{18}

**Antiviral activity**

Yang ZF *et al.*, studied that Influenza poses a particular risk of severe outcomes in the elderly, the very young and those with underlying diseases. Tea polyphenols consist of catechins, proanthocyanidins, flavonols, and theaflavins used for inhibiting influenza virus infection their results are expected to provide guides for rational design of antiviral drugs based on polyphenols.\cite{19}

**Antibacterial activity**

Nikitina VS *et al.*, evaluated that Polyphenolic compounds present in extracts of plants belonging to the families Geraniaceae and Rosaceae have been tested for their activity against gram-positive and gram-negative bacteria of the genera Azotobacter, Bacillus, and Pseudomona. The plants of the families Geraniaceae and Rosaceae offer promise as a source of raw material for isolation of polyphenolic compounds exhibiting bactericidal activity, including against opportunistic pathogens.\cite{20}

**Hypoglycemic effect**

Ruela HS *et al.*, investigated the hypoglycemic effect of *Bumelia sartorum* (Sapotaceae) extracts, rich in polyphenolic compounds, for treatment of several diseases, including diabetes. Different extracts of B. sartorum, were able to reduce blood glucose in normoglycemic mice and inhibit sarco/endoplasmic reticulum Ca (2+)-ATPase activity. One of the mechanisms involved in glucose decrease. They reported that this inhibition could prolong the increase in cytoplasmic Ca^2+ concentration, thus leading to an increase of insulin release\cite{21}

**Anti-inflammatory and anti-arthritic activity**

Sachin Vetal *et al.*, studied the Type-A procyanidine polyphenols extracted from Cinnamon (*Cinnamomum zeylanicum*) bark in animal models of inflammation and rheumatoid arthritis. Carrageen an-induced rat paw edema and adjuvant induced established arthritis. They concluded, Type-A procyanidine polyphenols showed disease-modifying potential in animal models of inflammation and arthritis in rats.\cite{22}
Atherosclerosis

Giuseppe Lippi et al., studied the healthful and nutritive properties of wine have been acknowledged for thousands of years, but they observed that moderate consumption of red wine on a regular basis may be preventative against coronary disease. Now mounting evidence that light to moderate wine intake is beneficial for the cardiovascular health, acting through a variety of mechanisms that target all the crucial steps of atherosclerosis, from early formation of the atherosclerotic plaque to its life-threatening complications. They observed the cardiovascular benefits of moderate red wine consumption on cardiovascular health and that would make red wine a promising therapeutic supplement to prevent and even perhaps treat coronary artery disease.\cite{23}

CONCLUSION

Polyphenols, due to their biological properties, may be unique nutraceuticals and supplementary treatments for various aspects of ailments. In this article we have reviewed the potential efficacies of polyphenols, including phenolic acids, flavonoids, stilbenes, lignans and polymeric lignans. Based on several review conducted on in vitro, animal models and some human studies, dietary plant polyphenols and polyphenol-rich products modulate carbohydrate and lipid metabolism, attenuate hyperglycemia, dyslipidemia and insulin resistance, improve adipose tissue metabolism, and alleviate oxidative stress and stress-sensitive signaling pathways and inflammatory processes. Polyphenolic compounds can also prevent the development of long-term diabetes complications including cardiovascular disease, neuropathy, nephropathy and retinopathy. Natural polyphenols used in the management of major depression.

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