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# A REVIEW ON THE APPLICATIONS OF NATURALLY OCCURRING ANTIOXIDANTS

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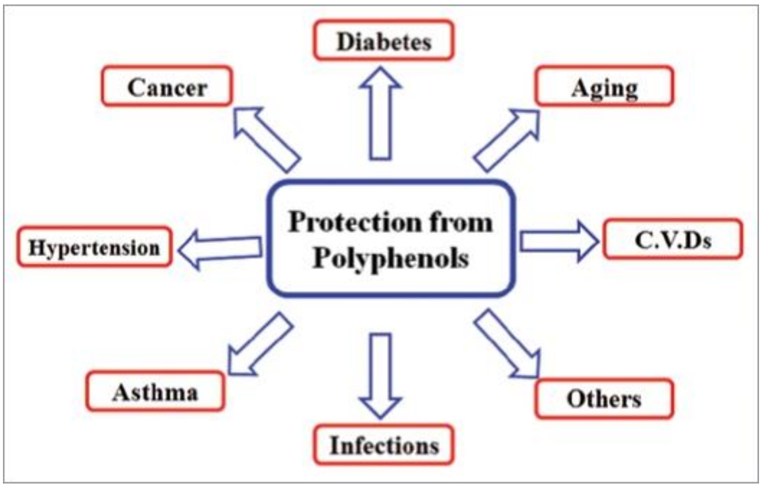
## ABSTRACT

In the last decade, there has been much interest in the potential health benefits of dietary plant polyphenols as antioxidant. Epidemiological studies and associated meta-analyses strongly suggest that long term consumption of diets rich in plant polyphenols offer protection against development of cancers, cardiovascular diseases, diabetes, osteoporosis and neurodegenerative diseases. Here we present knowledge about the biological effects of plant polyphenols in the context of relevance to human health.

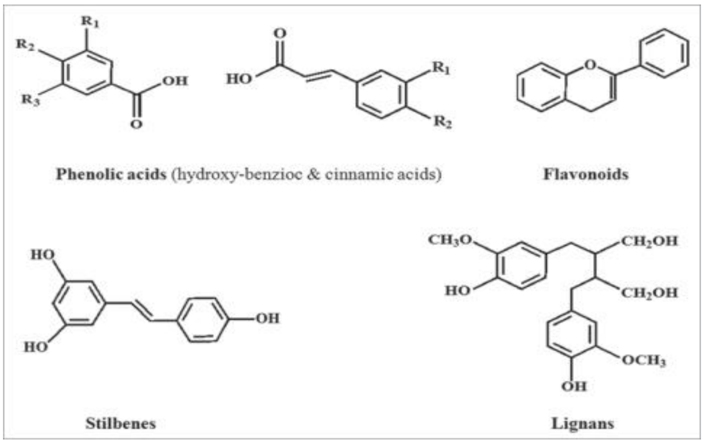
**KEYWORDS:** In the last decade, biological effects of plant polyphenols in the context of relevance to human health.

## INTRODUCTION

Polyphenols are secondary metabolites of plants and are generally involved in defense against ultraviolet radiation or aggression by pathogens.[1-5] In food, polyphenols may contribute to the bitterness, astringency, color, flavor, odor and oxidative stability. Towards the end of 20th century, epidemiological studies and associated meta-analyses strongly suggested that long term consumption of diets rich in plant polyphenols offered some protection against development of cancers, cardiovascular diseases, diabetes, osteoporosis and neurodegenerative diseases (figure 1). Polyphenols and other food phenolics are the subject of increasing scientific interest because of their possible beneficial effects on human health. This review focuses on the present understanding of the biological effects of dietary polyphenols and their importance in human health and disease.[6-8]




All plant phenolic compounds arise from a common intermediate, phenylalanine, or a close precursor, shikimic acid. Primarily they occur in conjugated forms, with one or more sugar residues linked to hydroxyl groups, although direct linkages of the sugar (polysaccharide or monosaccharide) to an aromatic carbon also exist. Association with other compounds, like carboxylic and organic acids, amines, lipids and linkage with other phenol is also common.[9-11] Polyphenols may be classified into different groups as a function of the number of phenol rings that they contain and on the basis of structural elements that bind these rings to one another. The main classes include phenolic acids, flavonoids, stilbenes and lignans. Figure 2 illustrates the different groups of polyphenols and their chemical structures.[12]




## Distribution

Distribution of phenolics in plants at the tissue, cellular and sub cellular levels is not uniform. Insoluble phenolics are found in cell walls, while soluble phenolics are present within the plant cell vacuoles.[13-17] Certain polyphenols like quercetin are found in all plant products; fruit, vegetables, cereals, fruit juices, tea, wine, infusions etc., whereas flavanones and isoflavones are specific to particular foods. In most cases, foods contain complex mixtures of polyphenols. The outer layers of plants contain higher levels of phenolics than those located in their inner parts.[18-22] Numerous factors affect the polyphenol content of plants, these include degree of ripeness at the time of harvest, environmental factors, processing and storage. Polyphenolic content of the foods are greatly affected by environmental factors as well as edaphic factors like soil type, sun exposure, rainfall etc. The degree of ripeness considerably affects the concentrations and proportions of various polyphenols.[23] In general, it has been observed that phenolic acid content decreases during ripening, whereas anthocyanin concentrations increase. Many polyphenols, especially phenolic acids, are directly involved in the response of plants to different types of stress: they contribute to healing by lignifications of damaged areas possess antimicrobial properties, and their concentrations may increase after infection.[24]

**Bioavailability**

Bioavailability is the proportion of the nutrient that is digested, absorbed and metabolized through normal pathways. Bioavailability of each and every polyphenol differs however there is no relation between the quantity of polyphenols in food and their bioavailability in human body. Generally, aglycones can be absorbed from the small intestine; however most polyphenols are present in food in the form of esters, glycosides or polymers that cannot be absorbed in native form[25-26] Before absorption, these compounds must be hydrolyzed by intestinal enzymes or by colonic microflora. During the course of the absorption, polyphenols undergo extensive modification; in fact they are conjugated in the intestinal cells and later in the liver by methylation, sulfation and/or glucuronidation.[27-28] As a consequence, the forms reaching the blood and tissues are different from those present in food and it is very difficult to identify all the metabolites and to evaluate their biological activity.[29-30] Importantly it is the chemical structure of polyphenols and not its concentration that determines the rate and extent of absorption and the nature of the metabolites circulating in the plasma. The most common polyphenols in our diet are not necessarily those showing highest concentration of active metabolites in target tissues; consequently the biological properties of polyphenols greatly differ from one polyphenol to another. Evidence, although indirect, of their absorption through the gut barrier is given by the increase in the antioxidant capacity of the plasma after the consumption of polyphenols-rich foods.[31-33]

**Biological Applications**

Epidemiological studies have repeatedly shown an inverse association between the risk of chronic human diseases and the consumption of polyphenolic rich diet.[34-35] The phenolic groups in polyphenols can accept an electron to form relatively stable phenoxyl radicals, thereby disrupting chain oxidation reactions in cellular components.[36] It is well established that polyphenol-rich foods and beverages may increase plasma antioxidant capacity. This increase in the antioxidative capacity of plasma following the consumption of polyphenol-rich food may be explained either by the presence of reducing polyphenols and their metabolites in plasma, by their effects upon concentrations of other reducing agents (sparing effects of polyphenols on other endogenous antioxidants), or by their effect on the absorption of pro-oxidative food components, such as iron. Consumption of antioxidants has been associated with reduced levels of oxidative damage to lymphocytic DNA. Similar observations have been made with plyphenol-rich food and beverages indicating the protective effects of polyphenols.[37] There are increasing evidences that as antioxidants, polyphenols may protect cell constituents against oxidative damage and therefore, limit the risk of various degenerative diseases associated with oxidative stress.[38]

**Drug Application**

Resveratrol, the wine polyphenol prevents the platelet aggregation via preferential inhibition of cyclooxygenase 1(COX 1) activity, which synthesizes thromboxane A2, an inducer of the platelet aggregation and vasoconstrictor.[39-41] In addition to this, resveratrol is capable of relaxing the isolated arteries and rat aortic rings. The ability to stimulate $Ca^{++}$-activated $K^{+}$ channels and to enhance nitric oxide signaling in the endothelium are other pathways by which resveratrol exerts vasorelaxant activity[42] Direct relation between cardiovascular diseases (CVDs) and oxidation of LDL is now well established. Oxidation of LDL particles is strongly associated with the risk of coronary heart diseases and myocardial infarctions. Studies have shown that resveratrol potentially inhibits the oxidation of the LDL particles via chelating copper or by direct scavenging of the free radicals. Resveratrol is the active compound in red wine which is attributed for "French Paradox", the low incidence of CVD despite the intake of high-fat diet and smoking among French.[43] Association between polyphenol intake or the consumption of polyphenol-rich foods and incident of cardiovascular diseases were also examined in several epidemiological studies and it was found that consumption of polyphenol rich diet have been associated to a lower risk of myocardial infarction in both case-control and cohort studies.

**Effects**

Effect of polyphenols on human cancer cell lines, is most often protective and induce a reduction of the number of tumors or of their growth.[44] These effects have been observed at various sites, including mouth, stomach, duodenum, colon, liver, lung, mammary gland or skin. Many polyphenols, such as quercetin, catechins, isoflavones, lignans, flavanones, ellagic acid, red wine polyphenols, resveratrol and curcumin have been tested; all of them showed protective effects in some models although their mechanisms of action were found to be different.[45]

Development of cancer or carcinogenesis is a multistage and microevolutionary process. Into the three major stages of carcinogenesis: initiation, promotion and progression. Initiation is a heritable aberration of a cell. Cells so initiated can undergo transformation to malignancy if promotion and progression follow. Promotion, on the other hand, is affected by factors that do not alter DNA sequences and involves the selection and clonal expansion of initiated cells. Several mechanisms of action have been identified for chemoprevention effect of polyphenols, these include estrogenic/antiestrogenic activity, antiproliferation, induction of cell cycle arrest or apoptosis, prevention of oxidation, induction of detoxification enzymes, regulation of the host immune system, anti-inflammatory activity and changes in cellular signaling. Polyphenols influence the metabolism of pro-carcinogens by modulating the expression of cytochrome P450 enzymes involved in their activation to carcinogens. They may also facilitate their excretion by increasing the expression of phase II conjugating enzymes. This induction of phase II enzymes may have its origin in the toxicity of polyphenols. Polyphenols can form potentially toxic quinones in the body that are, themselves, substrates of these enzymes. The intake of polyphenols could then activate these enzymes for their own detoxication and, thus, induce a general boosting of our defenses against toxic xenobiotics. It has been demonstrated that tea catechins in the form of capsules when given to men with high-grade prostate intraepithelial neoplasia (PIN) demonstrated cancer preventive activity by inhibiting the conversion of high grade PIN lesions to cancer.

**Daily life uses**

Polyphenols or polyphenol rich diets provide significant protection against the development and progression of many chronic pathological conditions including cancer, diabetes, cardio-vascular problems and aging. Although several biological effects based on epidemiological studies can be scientifically explained, the mechanism of action of some effects of polyphenols is not fully understood. A better knowledge of some variables of polyphenol bioavailability; such as the kinetics of absorption, accumulation and elimination, will facilitate the design of such studies.

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