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**Review Article**

# Polyphenols: The Pharmaceutical Approach and International Health

**Karan Suyal*, Suraj Dhali, Dr. Abhijeet Ojha, Navin Chandra Pant**

**Six Sigma Institute of Technology and Science (College of Pharmacy) Rudrapur U.S. Nagar, Uttarakhand, Affiliated from Uttarakhand Technical University Dehradun, India**

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**Address for Correspondence:** Karan Suyal
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**Abstract:**
Polyphenols are the beneficial chemicals that are found naturally in plants. Their importance came into light because of their antioxidant and anti-inflammatory effects. The risk of many diseases such as diabetes, cancer, neurodegenerative diseases, obesity have been reduced by eating the rich sources of polyphenolic foods. Polyphenols are naturally occurring compounds which are obtained from plant products like in some fruits, vegetables, tea, dark chocolates and many others. It works as antioxidants, anti-cancer, gives nourishment to skin and increases collagen. Polyphenols are of various types like Flavonoids as kaempferol, Phenolic acid as lignans and polyphenolic amides. Onion, apple, tea, red wine, red grapes, grape juice, strawberry, raspberries, blueberries and certain nuts are the rich sources of polyphenols. They are secondary metabolites of plants. They give protection from ultraviolet radiations or from aggression by pathogens. They prevent our cells from damaging and also reduces the risk of various diseases like cancer, heart diseases (Cardial disorders) and diabetes. They also help in reducing inflammation (pain, redness, swelling, heat). Polyphenols also tend to reduce the risk of type 2 diabetes and obesity. It is important to understand the effect of polyphenols towards the international health and human diseases.

**Keywords:**
Polyphenols, antioxidants, anti-inflammatory, anti-cancer, coronary disfunction, gut microflora, hypertension, Cellular structure.

## Introduction

Polyphenols are compounds that occur naturally in many types of plants. They are obtained from wide variety of plant sources such as fruits, vegetables, beverages, cereals etc. Fruits contains up-to 300 mg of polyphenols per 100 grams of weight whereas beverages contain about 100 mg of polyphenols. Different varieties of polyphenols are found in plants. Polyphenols are of great importance because of their role as antioxidants that prevent our cells from damaging and also reduce the risk of various diseases like cancer, coronary disfunction and diabetes. They also help in reducing inflammation (pain, redness, swelling, heat). Polyphenols also tend to reduce the risk of type two diabetes and obesity. It is

important to understand the effect of polyphenols regarding the health and human diseases.

Polyphenols are classified into two types:

**1.** Flavonoids

**2.** Non- flavonoids

Their intake and bioavailability of these polyphenols alter the health effects and glycosylation of flavonoids and esterification of phenolic acid modifications will affect their absorption from gut and bioavailability.

By different mechanisms it can enter into the mucosa of the small intestine. Polyphenols are initially digested into the smaller phenolic structures by gut microflora in the colon.

As a general rule, the metabolites of polyphenols are rapidly eliminated from plasma which indicates that the consumption of plant products on a daily basis is necessary to maintain high concentrations of metabolites in the bloodstream.

**Some simple phenolic compound**

1 Gallic acid
2 Phenol
3 Resveratrol

It simply states that the polyphenols are the compounds of a rich source that are included in the plants in the form of the flavonoids and there is also a high source of polyphenols found in the beans as in black and white beans.

As by their name depicts, plant compounds relates to plant polyphenols can be understood into the subparts of flavonoids.

The flavonoids can be further understood by its six sub -types which are -

- Isoflavones
- Flavan-3-ols
- Anthocyanidins
- Flavones
- Flavanones

**1.** The ***flavones*** include many compounds which are named as – apigenin, luteolin, chrysin, orientin, baicalein, acacetin.

- Apigenin is a compound which shows anticancer effect in the cancer treatment, its formula is $C_{15}H_{10}O_5$. It is present in many fruits and also helpful in the treatment of many disorders and with variation of its dose it shows activity as relaxation of some muscles and also gives sedative effect to the body.
- Luteolin is a type of chemical compound which is derivative of flavones which is yellow in appearance; this plant polyphenol also helps in blocking the growth of cancer cells. Its chemical formula is $C_{15}H_{10}O_6$. There are some foods which have rich sources of luteolin which are as carrot, peppers and onion leaves.
- Chrysin is a polyphenolic chemical compound which helps to nourish the skin and show many skin benefits as it increase the collagen secretion. Chrysin is mainly found in honey, also in flowers and in mushrooms.
- Orientin compound show many pharmacological action as of antibacterial and also in inflammatory condition, It comes under the category of flavones.
- Baicalein is a type of compound mainly found from scutellaria baicalensis and scutellaria lateriflora . It is one of the most commonly founded polyphenols.
- Acacetin is flavones compound that shows effect by attacking the cancer cells.

~>There is a term called ROS which is also called Reactive Oxygen Species and this is explained as the providence of the normal plant growth, as in other words ROS is the molecule that consist of a oxygen and it can easily react to the cell with the other molecule and sometimes it is beneficial to the plant as building blocks and in some cases it can damage the cell wall of the genes of DNA and RNA.

ROS scavenging cell cycle arrest induce apoptosis while apoptosis refer to death of any

cell occur by any growth of organisms or its development.

**2.** The second category of classified compound under the flavonoids is ***anthocyanidins*** which includes cyanidin, capensiniden, malvidin, rosinidin, delphinidin, hirsutidin and these can be explained by short term as

- Cyanidin is comparatively a type of anthocyanidins whose chemical formula is C15H11O6 and it is noticed that it also helps to reduce the level of pressure of blood, cyanidin is mainly found in the berries which appeared to be red.
- Delphinidin is associated with the plant in the form of its pigment and provide colour of blue or bluish red to the grapes and found in various berries and wine.
- Malvidin is alsonexplained as one of the derivative of delphinidrin and it exhibit some properties of antioxidant and also it show the positive response against the ageing related properties and nourishes the collagen fibers in some ways.
- Hirsutidin is the compound mainly found in the catharanthus roseus whose chemical formula is $C_{18}H_{17}O_7$, hirsutidin is rich in polyphenols and it is very beneficial to decrease the level of cholesterol in the human body.
- Capensiniden is very unidentified and complicated type of polyphenolic compound found in plant under the anthocyanidins, it is also known by the name of Capensinidin chloride.
- Rosinidin is the type of flavonoid which is found in the catharanthus roseus, and it is tested in rat in which it is found that it shows inflammatory and some of the oxidative stress.

~> Suppress ROS Increase glutathione levels, Inhibit DNA adduct formation.

**3.** The third classified category of plant polyphenols under the flavonoids is Flavonols and its compounds are Rutin, Isorhamnetin, Quercetin, Fisetin, Myricetin, Kaempferol.

- Rutin is widely reffered as vitamin P highly found in fruits, it is the flavonols which increases the the blood vessels arteries and veins flexibility and provide nourishment with strength to them. The adipose tissue in the body is responsible for the shock absorbance in the infants and here rutin helps to reduce the adipose tissue as by working over weight loss.
- Isorhamnetin is mainly found in olive oils, onions, wines, and tomato sauce as the rich source of polyphenols and is a common derivative of quercetin. Isorhamnetin is also used in so many health-related factors such as it inhibits skin cancer through inhibition of $MEK_1$ and $P_{13}$-KI.
- Quercetin shows various effect on the cardiovascular activity by relaxation of smooth muscles and it shows various anti-inflammatory effect and responses towards them, also shows antiamoebic effect. It comes under the flavonols of flavonoids of the plant polyphenols.
- Fisetin is a compound which shows anti-oxidant properties with the cancer treatment as it is a chemotherapeutic agent. The highest source of fisetin are strawberries.
- Kaempferol is a type of plant polyphenols which is very effective for the chronic diseases and it is effective also against the cancer. It effects as a defensive mechanism to the body system. It is found in various plants such as of broccoli.
- Myricetin is a compound in which so many pharmacological studies stated that it have a variety of benefit to the body system and especially for the cancer, antioxidant and other like cardiovascular and inflammatory conditions.

~> regulates gama-$H_2AX$ blocking agent caspase activity.

**4.** Flavan-3-ols is a polyphenolic flavonoids which include epicatechin, catechin, proanthocyanidins, thearubigins and EGCG.

- EGCG is known as epigallocatechin 3-gallate which is used now a days as like in the form of nutraceuticals, components mainly found in tea as catechins and beneficial for so many diseases like of Parkinson's disease, and shows antioxidant activity, also helpful in the treatment of diabetes.
- Thearubigins are widely found in tea in the form of coloured pigment of brown. TR also include the effect on anticancer activity with so many other beneficial uses as like it activates the mitochondria and improves the skeletal health.
- Proanthocyanidins are a polyphenolic compound which are mainly found in many fruits and flowers and this polyphenolic compound mainly prevent from cancer and help to fight against it.

~> ROS scavenging cell cycle arrest, induce DNA-PK expression, here DNA-PK is referred as DNA dependent protein kinase and inhibit gamma-$H_2AX$ where $h_2$-ax is a variant of $H_2A$ histone which is phosphorylated process when DNA double strand breaks of damage and this phosphorylated of $H_2$-ax is defined as gamma $H_2$-AX.

**5.** The fifth category is Flavanones which includes Sakuranin, Naringenin, Poncirin, Hesperetin, Butin and Eriodictyol.

- Sakuranin is a compound which comes under the category of flavanones which is soluble in water, it is found in cherry almond prunus it is mainly found in these food product . In many research is found that it also reduces the risk of diabetes in rats.
- Naringenin is found in many fruits like tomatoes and many other like citrus it shows protective mechanism against cardial, bacterial and some inflammatory conditions. It is the type of compound which is insoluble in water.
- Poncirin is a chemical compound which is found from the poncrius trifoliata fruit mainly , whereas in the other hand hesperetin is a type of compound which works by lowering the blood pressure, it also regulates the normal blood pressure. Hesperetin is poorly water soluble.
- Butin is a compound which is useful in the reduction of hydrogen peroxide as by inducing mitochondrial membrane.
- Eriodictyol is manly found in the region of north America and its chemical formula is $C_{15}H_{12}O_6$. It is mainly found in the citrus fruit and many vegetables. It shows many inflammatory effects.

ROS scavenging induce apoptosis, inhibit DNA damage by reducing COX-02.

**6.** Isoflavones is the last category of flavonoids of plant polyphenols which include Barbigerone, daidzein, formononetin, genistein, biochanin A.

**1.** Barbigerone is a type of isoflavones which shows the antioxidant property to the body system, in studies it is also seen that it is effective against the cancer of lung.
**2.** Daidzein is a compound whose molecular formula is $C_{15}H_{10}O_4$ and it also shows the anti-oxidant property with the anti-cancer and anti-inflammatory.
**3.** Formononetin is found in many plants as like in clover and in beans. It promotes the formation of new blood vessels by the process of angiogenesis.
***4.*** Biochanin A is a type of isoflavones which is highly extracted from the red clover and it is absorb orally with poorly soluble and prevent from cancer and some inflammatory conditions.

~> inhibit ROS generation.
Inhibition of $P_{53}$ expression.

In other words, polyphenols can be understood by two ways like, first is synthetic which include open chain, cyclic and miscellaneous whereas the second is Natural which consist of a plant originated like phloroglucinol derivatives, galloyl and hexa hydro-oxydiphenyl ester derivatives, hydroxycinnamic derivatives, Proanthocyanidin derivatives.

Polyphenols can help in maintaining the vessels healthy and it also makes them flexible and enhance the circulation, they can reduce chronic inflammation too and also reduce the glucose levels in human body.

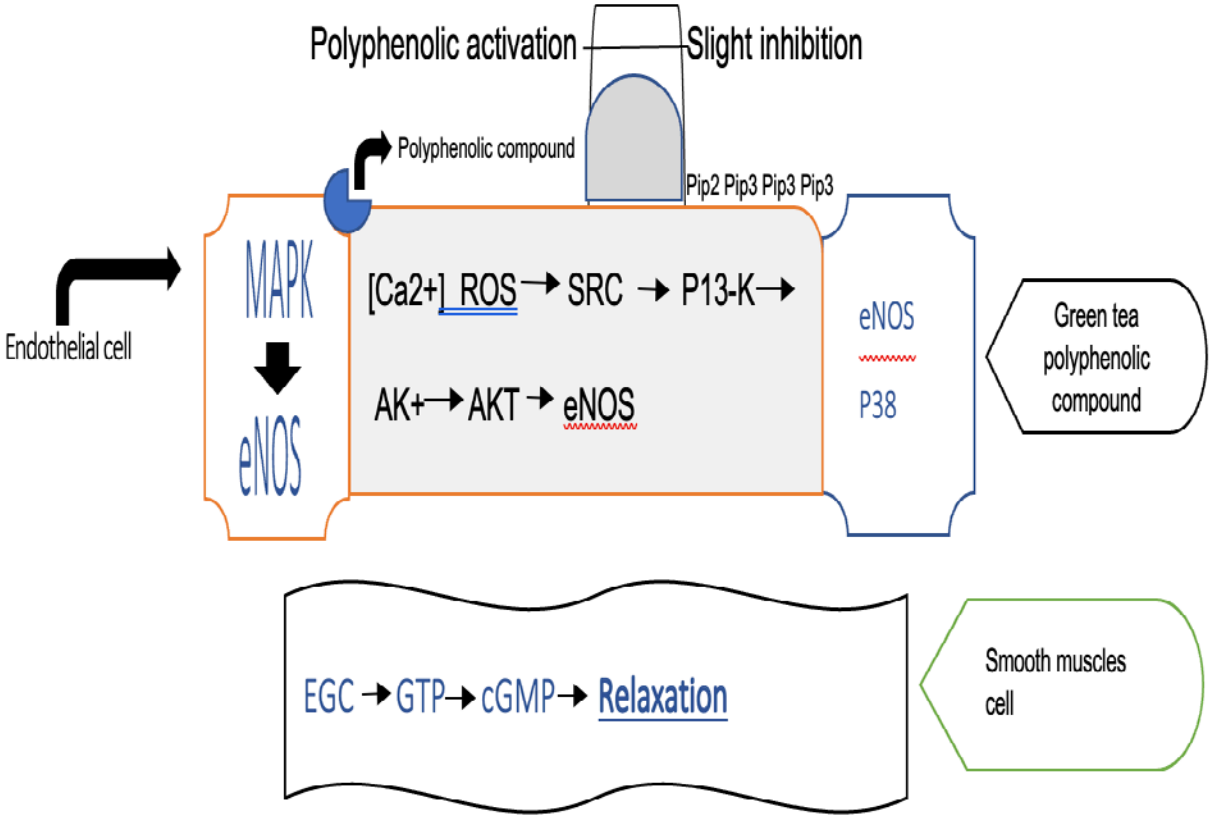
**Hypertension**

It is a major health problem which globally exists to most of the peoples around the world. It can be defined as systolic blood pressure (BP) greater than 140 mmHg or diastolic blood pressure greater than 90 mmHg.

On several observational studies on polyphenols intake and blood pressure as-

Intake of 5.5 ml/ kg body weight/day Concord grape juice daily 8 weeks by hypertensive Korean patients also reduced both systolic and diastolic blood pressure by an average of 6.2 and 7.2mm Hg respectively at the end of 8 weeks. The coronary flow- velocity reserve was increased in 10 healthy volunteers (age 24-37 years) after drinking polyphenol rich beverages the results was noticed that the endothelium - dependent vasodilation was also improved. Increase of extra virgin olive oil intake favourably affected blood pressure in hypertensive patients. All these studies support the view that polyphenol rich diets may reduce blood pressure or hypertension and improve endothelial function in hypertensive subjects.

Endothelial cells and regulations of vascular homeostasis.



**Abbreviations**

[Ca 2+] – Systolic concentration of calcium
CGMP - cyclic guanosine monophosphate
EDHF - endothelium derived hyperpolarizing factor
eNOS - endothelial nitric oxide synthase
NO - nitric oxide
P38 MAPK - p38 nitrogen activated protein kinase
P13 kinase/AKT - phosphatidylinositol 3-kinase/ AKT
ROS - reactive oxygen species

PIP3 - effector of multiple downstream targets of the phosphoinositide 3 kinase (PI3K) pathway

Lumen surface of vessels have endothelial cells which provide vascular homeostasis by chemical mediation. It releases a factor called NO, endothelial derived hyperpolarizing factor, PGI2 which is a relaxing factor and it plays a very important role to maintain the vascular tone. The enzyme endothelial NO synthase synthesized gaseous NO from L-arginine and diffuse in smooth muscles which is underlying to dilate blood vessel. It also diffuse to prevent platelets adhesion to the lumen and it also prevent coagulant factor and oxidized low density lipid. The role of EDHF to control artery tone by hyperpolarizing the vessels and cox (cyclo-oxygeneses) generate PGI2 which activate the cAMP pathway during vasodilation.

**Important terms to remember**

Systolic Calcium concentration, Cyclic guanosine monophosphate, endothelium derived hyperpolarizing factor, endothelial nitric oxide synthase, nitric oxide, nitrogen activated protein kinase, phosphatidylinositol 3-kinase/ AKT, oxygen radical absorption value

There are many classes of antihypertensive which lower the blood pressure by different means. Among the most important and most widely used medications are thiazide diuretics, calcium channel blockers, acetylcholine inhibitor, angiotensin 2 receptor antagonists (ARBs), and beta blockers.

Polyphenols have so many aspects in various disorders of human body which helps in its prevention and these are as follows.

| **Disease type** | **Prevention and effects** |
|---|---|
| **1.** Inflammation | Phenolic compound present in body can prevent the inflammation in a positive manner as it can alter the response and hyper reactivity reaction towards it. |
| **2.** -Obesity | The phenolic compounds include catechin and resveratrol are very effective against the reduction of obesity and hence it decreases the weight and are preferred. |
| **3.** Cancer | Some of the flavonoids have capability of stabilizing and prohibiting the growth of cancer cells in the human body so the risk of development of new cancer cells can be lower by their polyphenolic compounds under the flavonoids as discussed above. |
| **4.** Neurodegenerative diseases | It is a type of disorder in which the nerve cells of human body start damaging or dead due some severe harmful factors and here the big role comes for Polyphenolic compounds like catechins as because they may protect against Alzheimer's disease, Parkinson's disease by modulating the immune properties and these compounds also inhibits the toxicity in the nerve cells. |
| **5.** Type 2 diabetes | When the level of glucose rised up in the blood then the disease called diabetes arises and here Polyphenolic compounds prevent the risk of type 2 diabetes by protection of beta cells by inhibition the toxicity of glucose in the blood. |

## Conclusion

The polyphenols have different case of absorbance that it is not completely absorb by the small intestine and it is noted that only 11 to 16% absorbance held there. It is said to be versatile reducing agent. The results mentioned in this review provide a better understanding on the importance and effects of polyphenols in accordance to the human health. The polyphenols are the rich dietary sources which protect our body from various diseases. The types, occurrence, bioavailability and absorption of polyphenols are also included in this result. For avoiding any type of risk factor a human being should have at least 654-701 mg of polyphenols in a day from any of given sources. Polyphenols greatly help in the prevention of many diseases which are increasing in today's date rapidly because of the imbalanced diet. Polyphenols are absorbed easily by the body but the heavy phenolic compound have different case as they can-not easily pass the gut barrier.

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