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Review Article

PHARMACOLOGICAL IMPORTANCE OF POLYPHENOLS: A REVIEW

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ABSTRACT

Importance of plants in human society is immense. Since the advent of human civilization, the plants have been a major source of food for the human beings. In addition to it, humans also utilised plants for as important source of medicines which is now known as traditional medicine. At present, plants are getting importance not only as a source of food but also as a very important source of medicine and health supplements. Scientists at present are using the knowledge of traditional medicines as backbone to explore the chemical and molecular aspects of mechanism of action. Thus, the present focus of medical science is to exploit plants and their natural products for harvest of various medicinally important principles. Among various natural products found in plants, polyphenols are one of the most abundant. Based on the chemical structure they can be classified into phenolic acids, flavonoids, coumarins, lignans, stilbenes etc. They are widely distributed in almost all plants and exhibit strong antioxidant potential due to its unique molecular design. They have their origin from phenyl alanine or tyrosine and take the phenyl propanoid pathway for their synthesis. Apart from conferring protection to the plants from herbivore and other microbial attacks, polyphenols also possess a wide array of beneficial pharmacological activity. Presently they are largely used for treatment of cancer, diabetes, cardiovascular disease, arthritis, neurodegenerative disorders and many others. This review focuses on the sources and chemical nature of polyphenols and its beneficial pharmacological activities.

Keywords: Polyphenols; flavonoids; phenolic acids; anti-oxidant; anti-cancer.

INTRODUCTION

The living system is equipped with elaborate and well-organized antioxidant defense machinery in the form of antioxidant enzymes which counteracts the harmful effect of free radicals and reactive oxygen species. Since this antioxidant defense system weakens with time and age of the individual, intake of external antioxidants becomes extremely relevant for combating the detrimental effects of these free radicals and reactive oxygen species. The polyphenols constitute an important representative of secondary metabolite of plants and have antioxidant properties. In nature over 8000 polyphenols has been identified.[1] They have a wide array of ecological roles for the plants including protection from biotic and abiotic stress. Polyphenols are abundantly available in every part of plants. They also form a major component of human diet and their consumption is related to various beneficial effects on health related issue.[2] Exploration of beneficial activity of poly phenol have been a matter of interest amongst the scientists for quite a long time and with popularization of herbal medicine with minimum side effect, research on polyphenols have been increasing day by day. Thus, considering the importance of polyphenols on humans, this review has been framed with efforts to highlight the various types of polyphenols and their selected pharmacological importance. Extensive literature survey has been made in the internet with pub med forming the search platform for pooling relevant updated information.

Types of Polyphenols

Polyphenols are most abundant secondary metabolites found in the plants. Most of them are synthesized from phenylalanine or tyrosine. They are de aminated to cinnamic acid and enter the phenyl propanoid pathway whereby one or more hydroxyl groups are attached to the phenyl ring.[3] All the polyphenols are derived from basic common carbon skeleton building moiety namely the C6-C3 phenyl propanoid unit. Accordingly, the biosynthesis of polyphenols diversifies to a number of pathways synthesizing a wide array of plant phenolic namely cinnamic acids (C_6-C_3), benzoic acids (C_6-C_1), flavonoids (C_6-C_3-C_6), proanthocyanidins [(C_6-C_3-C_6)n], coumarins (C_6-C_3), stilbenes (C_6-C_2-C_6), lignans (C_6-C_3-C_3-C_6) and lignins [(C_6-C_3)n],[4] The various types of polyphenols are schematically illustrated in Figure 1 while the molecular structures are illustrated in Figure 2

Grossly the plant phenolics can be classified into different groups on the basis of the number of phenol rings in their molecule and the structural elements that attach these rings to one another. The different groups are as follows:

a) Phenolic Acids: In this case the molecule consists of a single aromatic ring with a carboxylic acid side chain of one to three carbons. They can be distinguished into derivatives of benzoic acid (C6-C1) and derivatives of Cinnamic Acid (C6-C3).
b) Flavonoids: The basic structure is a flavan nucleus which contains 15 carbon atoms consisting of a pair of aromatic rings (A and B) that are bound together by an oxygenated heterocyclic C-ring (Figure 3). They can further be divided into 6 subgroups depending upon the type of heterocycle involved: flavonols, flavones, flavanones, isoflavones, flavanols and anthocyanins.
c) Lignans: The basic structure is composed of two phenylpropane units.

d) Stilbenes: The basic structure is composed of 1, 2-diphenyl ethylene.
e) Coumarins: The basic structure is composed of benzo-2-pyrone
f) Tannins: It comprises of two subgroups namely (i) hydrolysable tannins and (ii) condensed tannins. Hydrolysable tannins consist of a central core of glucose or other polyol esterified with gallic acid (Gallotannins) or hexadihydroxydiphenic acid (ellagitannins). Condensed tannins are polymers of flavan-3-ols linked to one another by interflavan carbon bonds.[5-7]

Antioxidant capacity of Polyphenols

Polyphenols exert their antioxidant activity by a number of ways. They act as hydrogen donators, reductants and singlet oxygen quenchers. In addition some of them have the property to chelate metals.[8] Most of the phenolic compounds (POH) act as acceptors of free radicals and chain breaking agents. They interfere with oxidation of lipids and other bio molecules by donating their hydrogen atoms to radicals (R).

$$R + POH \rightarrow RH + PO^{\bullet} \quad \text{.....(Equation 1)}$$

The phenoxyl radical intermediates ($PO^{\bullet}$) are relatively stable due to resonance thereby preventing initiation of new chain reaction. Additionally, phenoxyl radicals also terminate further progression of chain reactions by reacting with other free radicals.

$$PO^{\bullet} + R^{\bullet} \rightarrow POR \quad \text{..... (Equation 2)}$$

The free radical scavenging activity of phenolic compound is largely due to the presence of hydroxyl group that can donate a hydrogen atom or an electron to a free radical. The phenolic compounds also possess a conjugated aromatic that delocalize an unpaired electron thereby bringing stability to phenoxyl radical intermediates.[9] Another way through which the polyphenols exert their antioxidant property is by conjugating with heavy metals thereby preventing heavy metal induced free radical formation. The redox transition metals such as Fe^{+2} and Cu^{+2} react with hydrogen peroxide to form hydroxyl radicals (●OH) through Fenton's reaction. The hydroxyl radical is highly reactive and cause damage to the bio molecules.[10]

$$Fe^{+2} \text{ or } Cu^{+} + H_2O_2 + H^{+} \rightarrow Fe^{+3} \text{ or } Cu^{+2} + \bullet OH + H_2O \quad \text{.... (Equation 3)}$$

Phenolic compounds with catecholate or gallate groups coordinate with Fe+2 and enhance its auto oxidation or form inactive complex with Cu^{+2}, Fe^{+2} or Cu^{+} (Figure 4).[11]

Pharmacological activities of Polyphenols

Polyphenols play an important role in inhibiting large number of diseases and physical ailments.

They have a unique molecular structure which enables them to accept electrons from other radicals generated in biological system and thus terminates oxidative chain reactions in the cell.[12] In the process they themselves get oxidized and reduce the harmful oxidative radicals to comparatively less harmful ones. This chemical property of polyphenol is responsible for its protective role in case wide number of diseases.

Anti-atherosclerotic activity

Atherosclerosis is a disease of vascular intima and in which the vascular system is intimal plaques.[13] It is a condition in which fatty substances gets deposited in the inner layers of arteries resulting in its thickening and alternation of normal function. It is one of the major cause of mortalities worldwide.[14] Epigallocatechin gallate has an attenuating effect on high fat diet induced atherosclerotic plaque formation in ApoE−/− mice along with decreased in levels of pro inflammatory (Interleukin-6) IL-6 and tumor necrosis factor-α (TNF-α) and increase in anti-inflammatory (Interleukin-10) IL-10 levels. This was accompanied by decreased cholesterol and Low density lipoprotein (LDL) level, increased high density lipoprotein (HDL) level, induction of hepatic liver X receptor α (LXRα) and liver X receptor β (LXRβ) expression and inhibited both precursor and mature sterol regulatory element binding transcription factor-1 (SREBP-1) expression.[15] Quercetin has also been reported to have a protective role against high fructose induced atherosclerosis in mice. Quercetin treatment resulted in decrease in number of atherosclerotic plaques, inhibition of reactive oxygen species production, reduction in Malondialdehyde (MDA) levels and increase in superoxide dismutase (SOD) activity. Inactivation of B-cell lymphoma (Bcl-2)/caspase-3 pathways, accompanied by decrease in levels of pro inflammatory cytokines, IL-1β, IL-8, TNF-α, IL-6 and down regulation of nuclear factor kappa B (NF-κB) pathways upon treatment with quercetin resulted in inhibition of atherosclerosis.[16]

Anti-inflammatory activity

Inflammation is a protective response of living system in response to harmful stimuli specially related to infection and injury.[17] Rutin exhibited an anti-inflammatory action on LPS stimulated RAW 264.7 macrophages through decrease in interleukin-6 secretion. It also resulted in decreased expression of NF-κB protein level in U937 monocyte lymphoma cells.[18] Treatment with Epigallocatechingallate (EGCG) also results in decreased population of neutrophil cells and suppression of levels of IL-1β secretion in monosodium urate (MSU) induced peritoneal inflammation in C57BL/6 mice model. This was also accompanied by inhibition of expressions of NLPR3 protein, pro inflammatory mediator neutrophil cytosolic factor-1 (NCF-1) protein, macrophage recruitment chemokine Monocyte chemoattractant protein-1 (MCP-1) and active inflammation marker Serum amyloid A (SAA). MSU induced activation of nucleotide-binding domain, leucine-rich-containing family, pyrin domain-containing-3(NLRP3) inflammasome in THP-1 cells was also inhibited by administration of EGCG all of which contributes to anti-inflammatory response.[19]

Protection against rheumatoid arthritis

Rheumatoid arthritis (RA) is an autoimmune disorder affecting all joints of the body and is one of the leading causes of chronic morbidity in developed countries. The disorder accounts of two thirds of fatalities worldwide and the figure is likely to increase in coming years.[20] during pathogenesis of RA, reactive oxygen species has a very complex interplay with inflammatory mediators. It has also been reported that free radicals are responsible for degradation of joint cartilage as it attacks the proteoglycan and inhibits its synthesis. Additionally oxidation of hyaluronic acid, oxidation of low-density lipoproteins, increase in carbonyl content as a result of protein oxidation and DNA damage are characteristic features of RA.[21] Avicularin is reported to significantly decrease the levels of inflammatory factors such as IL-1β, IL-6, IL-8, matrix metalloproteinases (MMP-1 and MMP-13), inducible nitric oxide synthase (iNOS) and (Cyclooxygenase-2) Cox-2 in TNF-α induced RA in human RA synovial MH7A cell line. The activation of the mitogen-activated protein kinase (MEK)/nuclear factor kappa light-chain-enhancer of activated B-cells (NF-κB) pathway were also inhibited by

avicularin. A concentration dependent decrease in viability of MH7a cell line and induction of apoptosis was also recorded upon treatment of avicularin. These findings suggest the protective role avicularin against RA through inhibition of MEK/NF-κB pathway.[22]

Protection against Alzheimer's disease

Alzheimer's disease (AD) is the most common type of demential in western countries and constitutes 60% of the cases. Projections indicate that the number of people affected by dementia will double between 2020 (42 million) and 2040 (81 million).[23] Presently, AD is the most common cause of disability in elderly persons and is characterized by abnormal deposition of amyloid β (Aβ) peptide and accumulation of neurofibrillary tangles of hyper phosphorylated τ protein within the cells accompanied by dementia. The entire phenomena leading to occurrence of the disease is largely initiated by oxidative stress.[24] It has also been reported that oxidative stress in AD results in augmentation of protein oxidation, protein nitration, glycol oxidation, lipid peroxidation and accumulation of Amyloid β (Aβ).[25] The ameliorating effect of EGCG on memory impairment and rescue of abnormal synaptic protein levels in the frontal cortex and hippocampus in a mouse model of AD has been explored. The results of the study indicate that long term consumption of epigallocatechin gallate resulted in improvement of memory function in SAMP8 mice. This was accompanied by decrease in levels of Aβ1-42 and Beta Secretase-1 (BACE-1) in frontal cortex, prevention of phosphorylation of tau and reversal of decreased synaptic protein marker synaptophysin and postsynaptic density protein.[26] Quercetin was reported to decrease extracellular β-amyloidosis, tauopathy, astrogliosis and microgliosis in the hippocampus and the amygdale in triple transgenic AD model (3 x Tg-AD) mice. This result was also supported by reduction in expression of paired helical filament (PHF), Aβ 1-40 and Aβ 1-42 levels and a decrease in BACE1-mediated cleavage of Amyloid precursor protein into β-secretase-derived fragment. Quercetin treatment also resulted in improved performance on learning and spatial memory tasks and greater risk assessment behavior.[27]

Neuroprotective action of polyphenols

Neurological disorders are one of the leading causes of disability adjusted life years (DALYs) and constitute 10.2% of DALYs and are the second leading cause of death. It accounts to 16.8% of global death.[28] The neuroprotective activity of naringenin nano emulsions was investigated by evaluating their ability to protect SH-SY5Y neuroblastoma cells against beta amyloid (Aβ) induced neurotoxic effect. Treatment of cells with naringenin resulted in significant reduction in reactive oxygen species production induced by Aβ. This was accompanied by reduction in ABB, BACE and Aβ protein levels along with reduction in phosphorylation of tau suggesting that naringenin alleviated the neurotoxic effects of Aβ on SH-SY5Y through regulation of amyloidogenesis and tau phosphorylation.[29] The neuroprotective effects of ferulic acid against cerebral ischemia/reperfusion-induced injury using rat as experimental system has been explored. The results from the findings indicated that ferulic acid treatment lead to attenuation of memory impairment, reduction in hippocampal neuronal apoptosis and oxidative stress in a dose-dependent manner. *In vitro* experiments suggested that ferulic acid conferred protection to PC-12 cells against I/R-induced ROS generation and apoptosis by inhibiting Ca^{2+} influx, superoxide anion (O2-), MDA and glutathione peroxidase (GSH-Px) production in a concentration-dependent manner. The expression level of Bax was decreased and Bcl-2 was increased upon treatment of PC-12 cells with ferulic acid suggesting anti apoptotic behavior of ferulic acid. Additionally, ferulic acid also reduced the expression of TLR4 and MyD88 in a concentration dependent manner.[30]

Protection against diabetes

Diabetes is another disease of widespread occurrence and also has an intricate relationship with reactive oxygen species. It is estimated that in the year 2017, 451 million people are suffering from diabetes worldwide and by the year 2045, the number of people suffering from diabetes could increase to 693 million.[31] Gallic acid and p-coumaric acid was found to modulate hyperglycemia and dyslipidemia in streptozotocin induced diabetic rats. Diabetic rats treated with gallic acid and Protocatecheuic acid exhibited amelioration in serum insulin levels. This was accompanied by reversal in elevated levels of serum cholesterol, triglycerides, LDL- and vLDL-cholesterol along with an increase in level of HDL. Oral supplementation of gallic acid and para coumaric acid also resulted in decrease in pro inflammatory TNFα, up-regulation of peroxisome proliferator-activated receptors-γ (PPARγ) mRNA levels and increase in adiponectin concentration. The results suggests the anti-hyperglycemic and anti hyperlipidemic efficacy of gallic acid and para coumaric acid which is brought about by elevation of adiponectin level in conjunction with attenuation of TNF-a level and PPARγ up-regulation in adipose tissue.[32] A recent study also reported that epigallocatechin gallate suppressed hydrolysis of starch, improved glucose homoeostasis, inhibited gluconeogenesis and lipogenesis in liver of diabetic mice. Additionally, treatment of epigallocatechin gallate activated pregnane X receptor (PXR)/constitutive active/androstane receptor (CAR)along with up gradation of PXR/CAR mediated phase II drug metabolizing enzyme expression involving Sulfotransferase1A1 (SULT1A1), UDP glucuronosyltransferase1A1 (UGT1A1) and Sulfotransferase 2B1b (SULT2B1b) in small intestine and liver in mice model.[33]

Protection against cataract

Cataract is a condition in which partial or complete opacification of human lens occur impairing vision.[34] An estimate by WHO reveals that 95 million people are affected by cataract in the year 2014.[35] It has been reported that reactive oxygen induced damage of eye lens consisting of oxidation of proteins, DNA damage, and/or lipid peroxidation mediate the formation of cataract.[36] It is reported from a recent study that treatment with epigallocatechin gallate and elagic acid resulted in significant lowering of mean cataract stages in sodium selenite induced cataract in mice. This was accompanied by lowering by total antioxidant status and mean MDA levels indicating a protective action via modulation of oxidative stress.[37] Administration of Luteolin in streptozotocin induced diabetic rat model resulted in increased antioxidant capacities including glutathione (GSH), glutathione peroxidase (GPx) activities and decrease in levels of MDA. This was accompanied by diabetes induced inhibition in elevation of IL-1β, vascular endothelial growth factor and NF-κB mRNA and protein expression in lens. These results suggested a protective action of luteolin against diabetes induced neuro degeneration through inhibition of inflammatory mediators and oxidative stress.[38]

Anti-cancer activity

Polyphenols have the ability to scavenge singlet oxygen and other free radicals all of which leads to DNA damage and tumor propagation. Polyphenols also impact the bio activation of

carcinogen by inhibiting cytochrome P450 enzymes of the CYP1A family, thus acting as chemo preventive agents.[39] A recent study explored the anticancer activity of apigenin using A549 human lung cancer cell. The results obtained from the study indicate that there is a concentration and time dependent decrease in viability of A549 cells upon treatment with apigenin. A dose dependent inhibition of cell migration, invasion and decrease in Akt protein expression was observed upon treatment with apigenin. Additionally, A549 cells transfected with Akt-active plasmids resulted in increased Akt expression, increased migration and invasion as compared to cells which were transfected with plasmids with inactive form of Akt where Akt expression, invasion and migration were low. Moreover, apigenin dose dependently decreased the gene expression of MMP-2, MMP-9, Glycogen synthase Kinase 3β, and human enhancer of filamentation 1 and silencing Akt resulted in inhibition of the these genes suggesting that Akt plays a vital role in proliferation, migration, and invasion of A549 lung cancer cell and was inhibited upon treatment with apigenin.[40] Another study investigates the effect of luteolin on gastric cancer. It was observed that administration of luteolin to gastric cancer cell resulted in inhibition of cell cycle progression, invasion, colony formation, proliferation and promoted apoptosis both *in vivo* and *in vitro*. On a molecular mechanistic level, luteolin treatment resulted in regulation of Notch1, phosphoinositide3-kinase (PI3K), AKT, mammalian target of rapamycin (mTOR), extracellular signal-regulated kinase (ERK), signal transducer and activator of transcription 3 (STAT3) and P38 signaling pathways and modulated a series of miRNAs expression deciphering the function of luteolin in molecular level for treatment of cancer.[41]

DISCUSSION

Most of the disease occurs due to imbalance in the oxidative homeostasis in the living system which in turn may trigger a cascade of biochemical pathway primarily related to inflammations and immunological response. In this review, the protective roles of polyphenols in counteracting a wide array of diseases have been discussed and it is quite evident that the polyphenols exert their protective action in a variety of ways. However, its potent antioxidant capacity forms the base of most of its health protective pharmacological effects. It is now a widely established fact that consumption or administration of polyphenols results in decrease of ROS in the living system whose one of the consequence is decrease in lipid peroxidation and protein oxidation, a process which is frequently associated to a number of diseases such as cancer, diabetes, cataract and Alzheimer's disease. Another approach through which the polyphenols seem to exert their health protective activities is my suppressing inflammations. In this process they inhibit a number of factors and enzymes that are directly related to inflammation process. NF-κB, a transcription factor, responsible for activation of genes producing pro inflammatory cytokines is inhibited by polyphenols at various stages of biochemical pathways (Figure 5).[42]

Additionally, two more enzymes namely COX and lipoxygenase (LOX), involved in inflammation response in various diseases are also inhibited and down regulated by polyphenols (Figure 6).[43] This suppression of inflammation offers protection against a large number of diseases including atherosclerosis, RA and cancer. MMP, an enzyme responsible for the degradation of extracellular matrix is also inhibitive by polyphenols. This not only results in control of metastasis of cancerous cells but also provides protection from a number of other diseases including atherosclerosis and arthritis etc. The arthritic process and bone degeneration is also prevented by polyphenols by inhibition of local inflammation in synovial region and osteoclast formation (Figure 7).[44] Down regulation of serine/threonine kinases namely PI3K/Akt and mTOR by polyphenols, thereby forming a suitable environment of autophagy also forms a major line of defence against onset of cancer. In addition to it, polyphenols also exert its anticancer activity by modulating BCL-2 family of proteins which play an important role in apoptotic process. Polyphenols also target the cyclins and cyclin dependent kinases which are involved in progression of cell cycle. Cyclins and cyclin dependent kinases are effectively inhibited by polyphenols which results in stoppage of cell cycle before specific check points thereby preventing cancer cells from further division. Polyphenols also inhibit a large number of enzymes such as alpha glucosidase, amylase, glucose-6-phosphatase etc which are responsible for generating free glucose. This strategically helps in counteracting diabetes. Another approach by which polyphenols exert their anti diabetic action is by enhancing (Glucose transporter 4) GLUT4 expression and their transportation into the plasma membrane thereby enabling the transportation of free glucose from the blood to the tissue. The overview of the pharmacological activities of polyphenols has been depicted in Figure 8.

Polyphenols occupy a very distinct position among the wide array of plant based natural products and extensive research have been undertaken to find the beneficial activities of these compounds. It has been reported that the global market value of polyphenols in the year 2015 was 757 million USD and is expected to have more boost in future. The total polyphenols marketed in 2015 is 16380 tons with an 8.4% annual growth rate and is anticipated to reach 33800 tons by the end of 2024 with a value of 1.33 billion[45]. This gives a positive indication about the ever-increasing popularity of polyphenols. It is utmost important for the present-day population to focus on consumption of polyphenols and other plant based natural products for a healthy life.

In developing countries where industrial pollutants are causing havoc and are becoming a matter of concern for health, consumption of diets enriched in polyphenols will provide an efficient protection against onset of a number of diseases. As the polyphenols have strong antioxidant potential, their protective domain is quite broad in contrast to conventional medicines which are artificially synthesized. In addition to consumption of polyphenols, changes in lifestyle pattern are also of utmost importance in order to get the maximum benefit. Changes in dietary habits by shifting from junk foods to natural agriculture-based foods is the necessity under present scenario as the former group triggers oxidative stress leading to occurrence of various diseases whereas the plant based foods are laden with polyphenols and other natural products and possess immense health benefits.

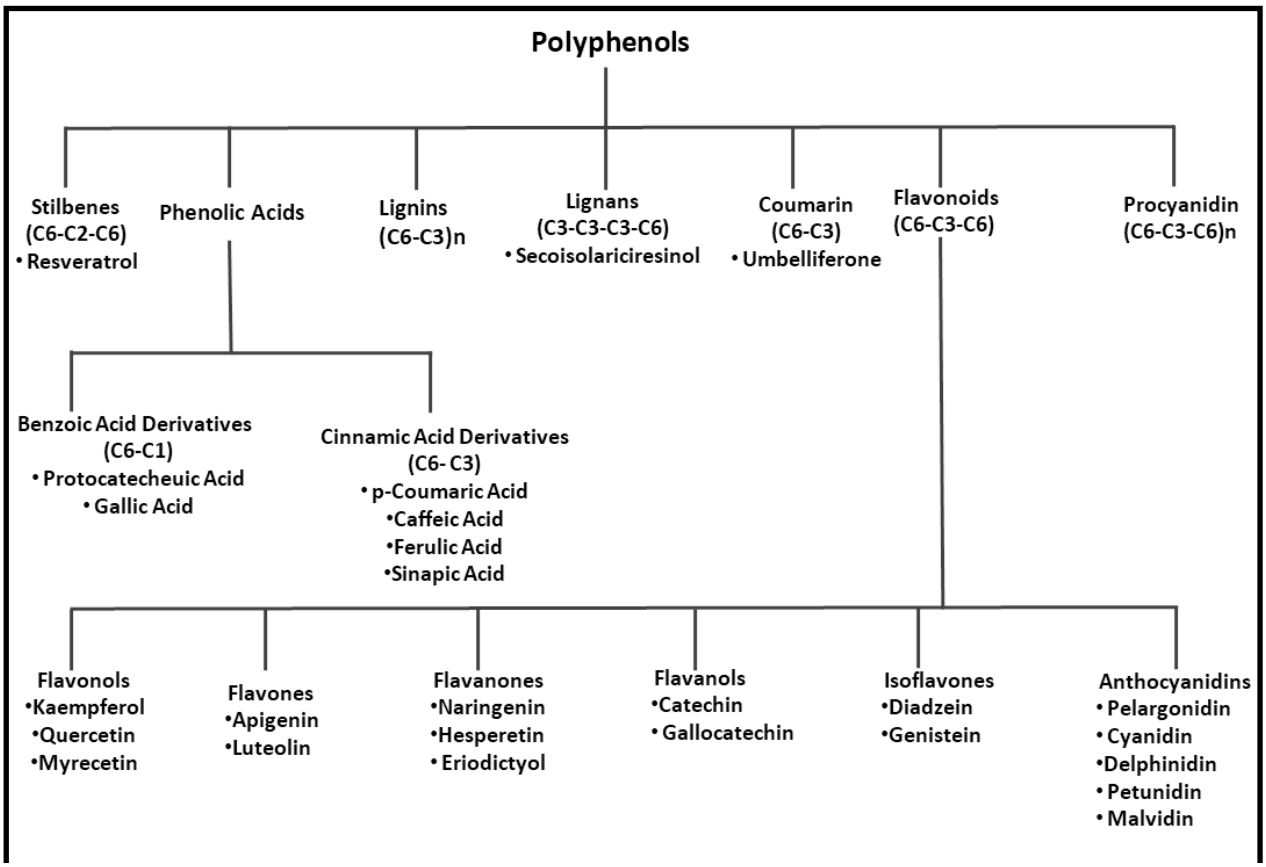

Fig 1: Schematic representation of different types of polyphenols

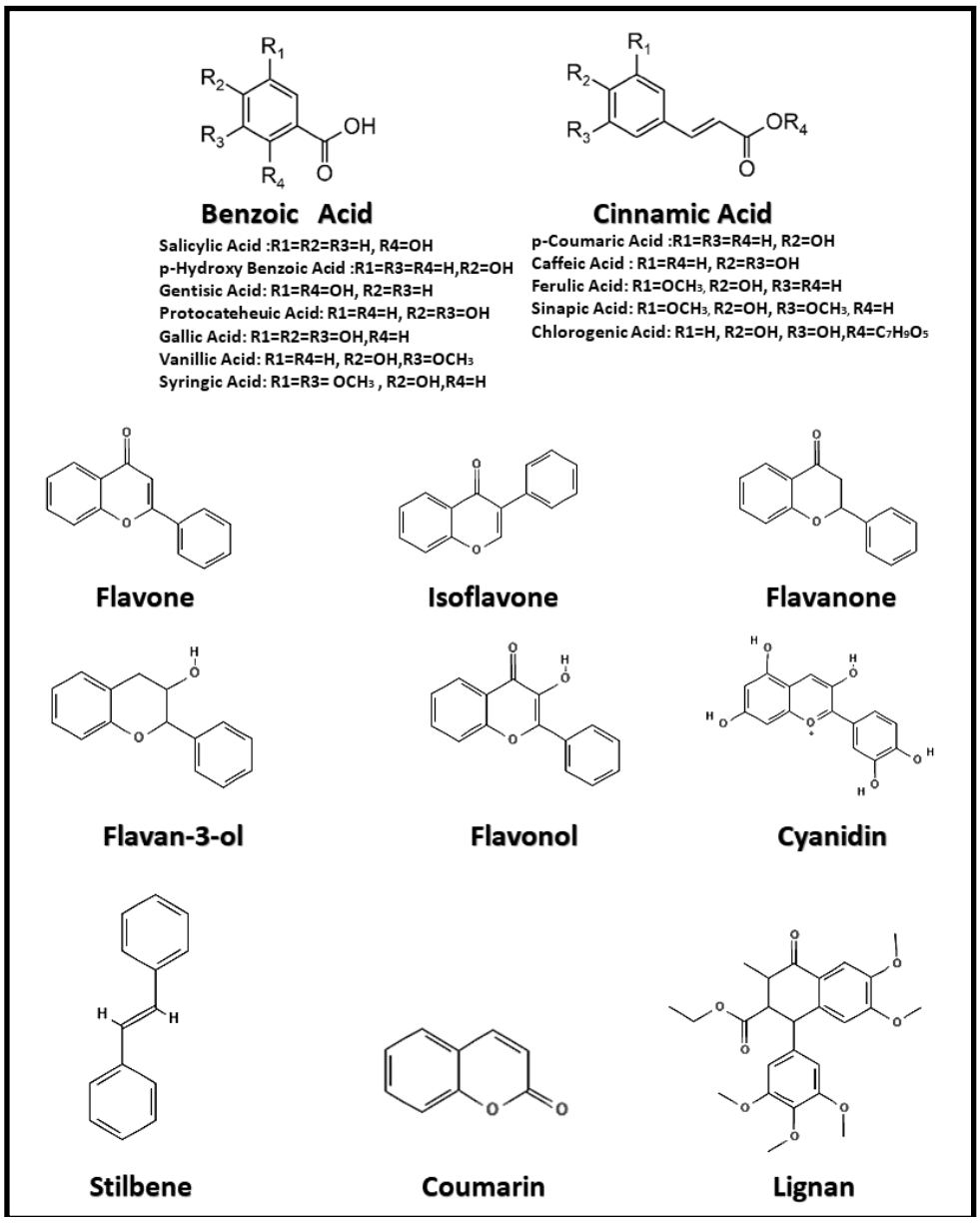

Fig 2: Basic chemical structures of various types of polyphenols

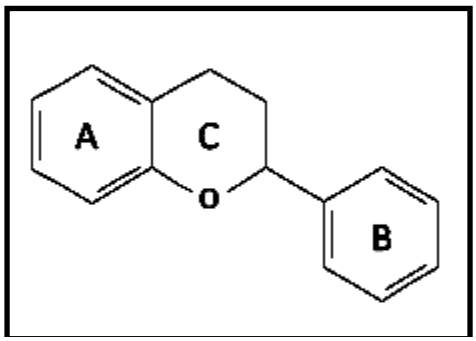

Fig 3: Structure of flavan skeleton showing A, B and C rings

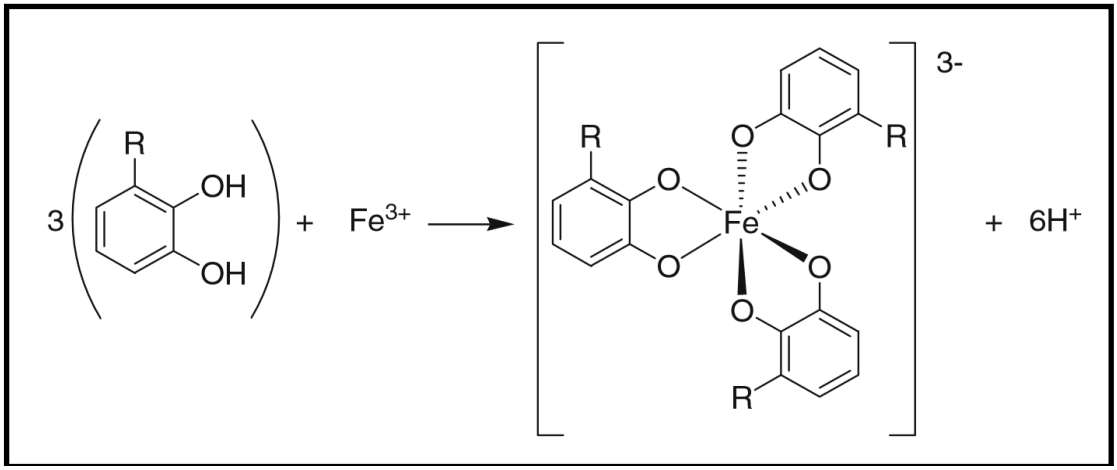

Figure 4: Coordination of polyphenols with Iron (III) forming Iron-polyphenol complex . [11]

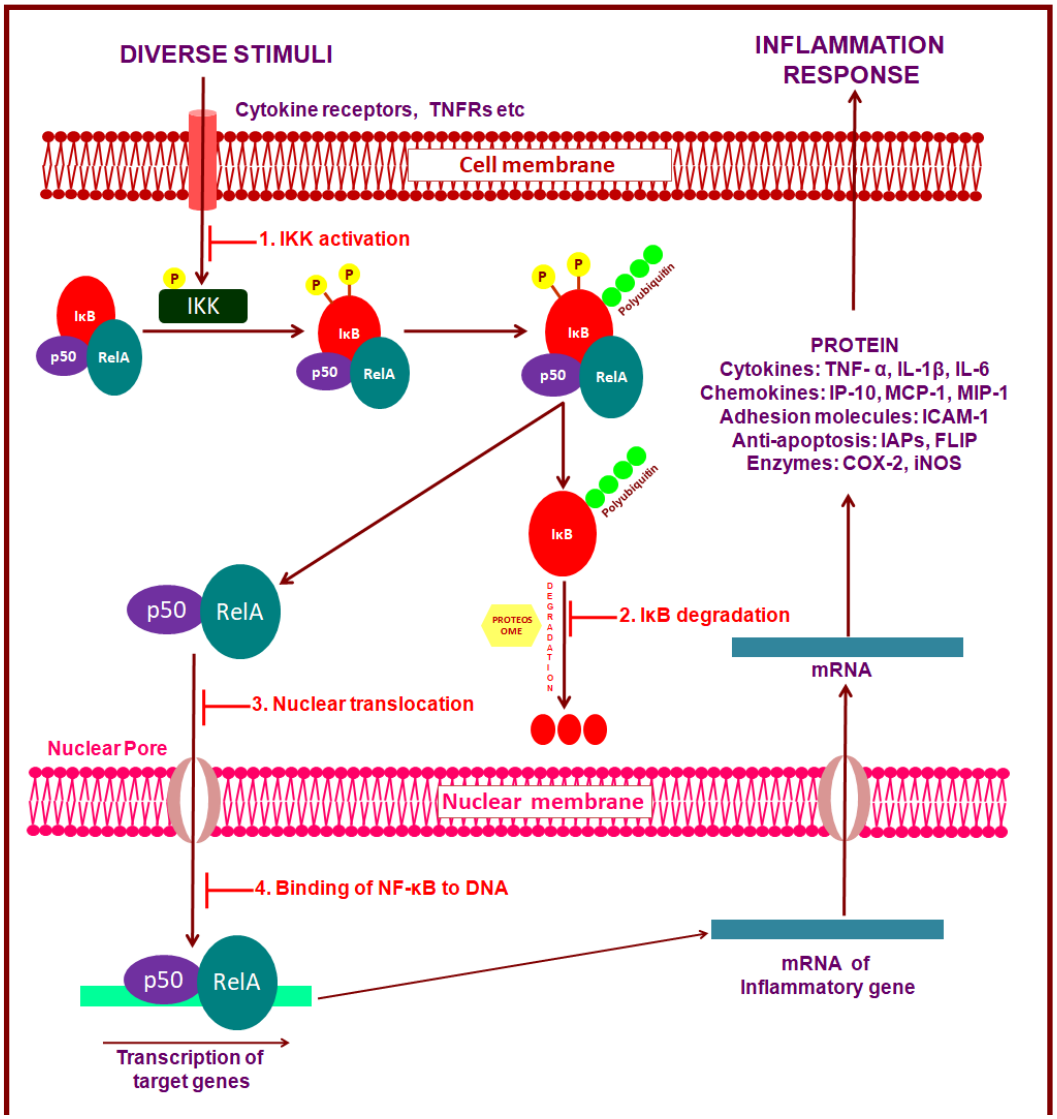

Figure 5: In NF-κB signaling pathway various types of stimuli activate Toll-like receptors (TLRs), tumor necrosis factor receptor (TNFR) and cytokine receptors respectively. This leads to activation of IκB Kinase (IKK) complex through a variety of adapter proteins and signaling kinases, which consequently phosphorylates inhibitor of κB (IκB) on Serine S32 and S36 residues respectively and leads to subsequent polyubiquitination, which in turn results in proteasomal degradation of IκBα. NFκB homo- or heterodimers then translocate to nucleus and activate target gene transcription. Points in NF-κB pathway in which polyphenols exert their inhibitory actions. (1) Inhibition of IKK activity thereby preventing phosphorylation of IκB. (2) Inhibition of protease activity thereby preventing IκB degradation. (3) Inhibition of nuclear translocation (4) Inhibition of DNA binding thereby prevention transcription of inflammatory genes. [4]

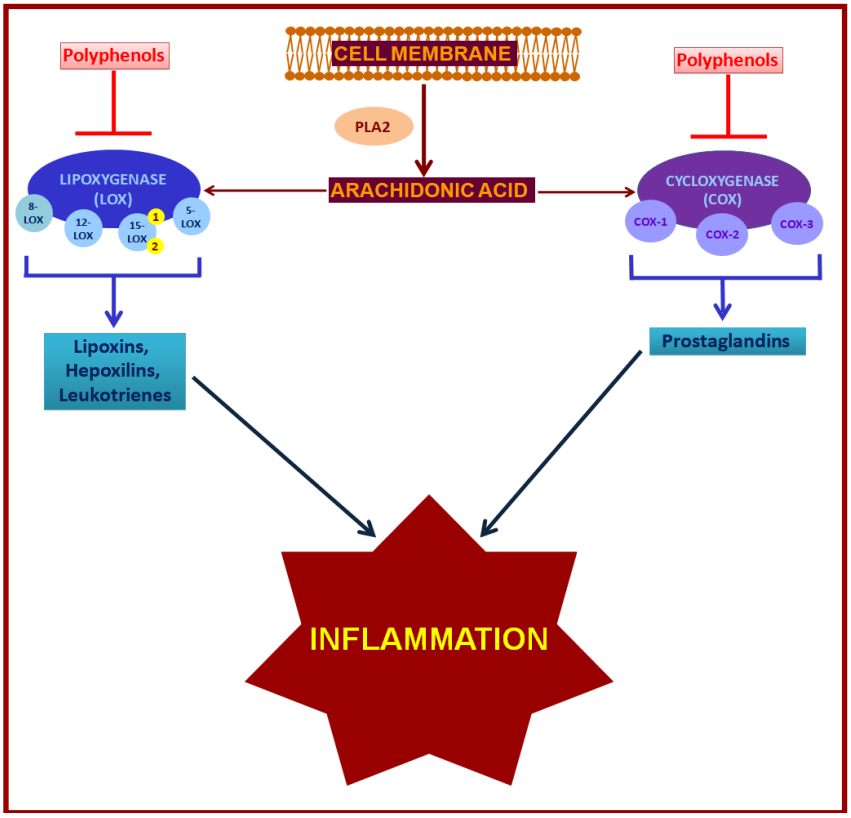

Figure 6: Representation of phospholipid arachidonic acid metabolites generated by lipoxygenase and cycloxygenase. Polyphenols inhibit both lipoxygenase and cycloxygenase thereby stopping the generation of lipoxins, leukotrienes and prostaglandins [43].

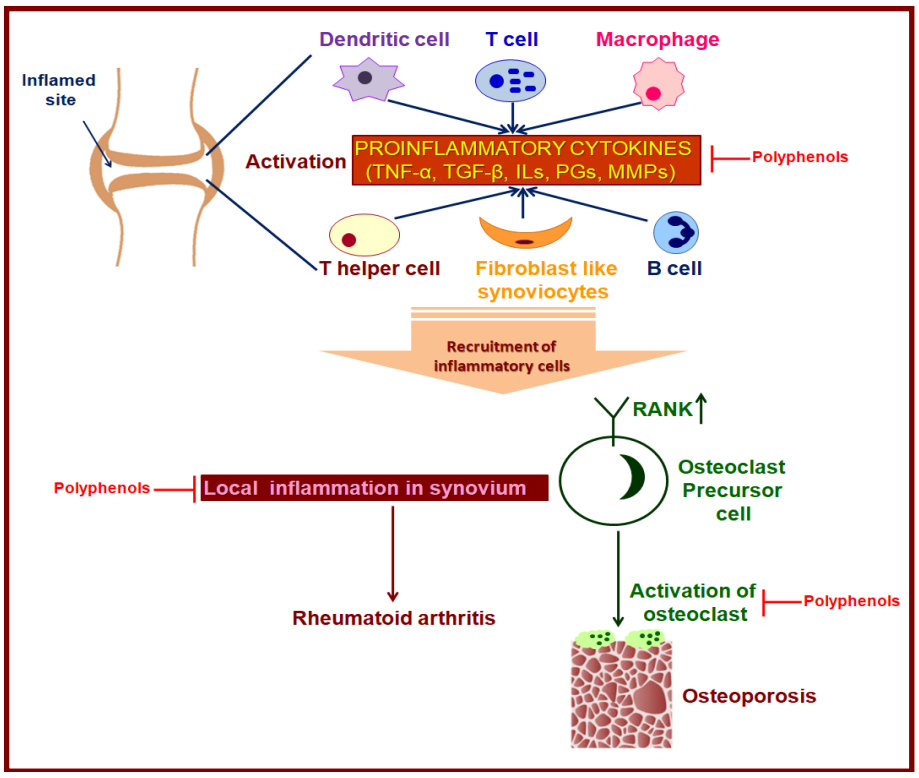

Fig 7: Scheme representing the mechanistic aspect of inflammation-associated pathogenesis in rheumatoid arthritis and osteoporosis. In a rheumatoid synovium and bone tissue proinflammatory cytokines are produced by recruited inflammatory cells (macrophages, T-cells and B- cells), endothelial cells and synovial fibroblasts inducing inflammatory processes and osteoporosis. The proinflammatory cytokines results in activation of synovial fibroblasts and produce proteases leading to tissue destruction. Cytokines also trigger activation and differentiation of osteoclasts which are associated with bone loss [44].

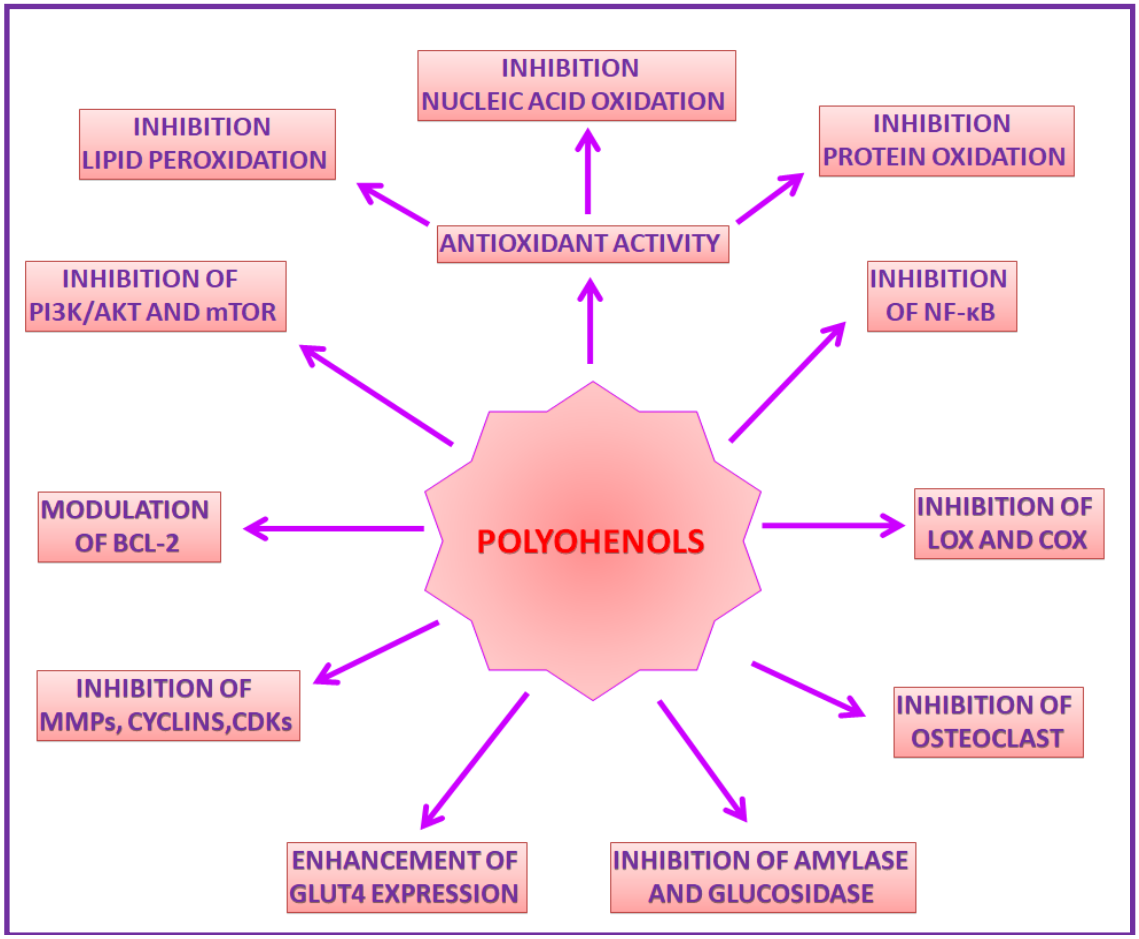

Figure 8: Schematic representation of various pharmacological actions of polyphenols

CONCLUSION

Presently, though a lot of research has been done of polyphenols and it's medicinal and antioxidant properties, a large proportion of them have been done on cell cultures or on animal model with comparatively a smaller number of clinical trials. Thus, in order to effectively exploit the medicinal properties of polyphenols, it is also equally important to stress upon clinical trials of the polyphenols and proceed towards development of plant-based drugs. India is a country with rich biological diversity and thus impetus on exploration of plants as source of natural antioxidants needs active consideration and successful implementation. These biodiversity regions can thus act as a source for pooling of plant materials for onward extraction and bio prospection of plant-based drugs and health supplements. The Plant based drugs supported by nutraceuticals would then emerge as a wonderful tool of antioxidant therapy to restore the disruption in balance between oxidants and antioxidants amongst the population suffering from harmful industrial pollution.

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