



A Review on Phytochemical and Pharmacological properties of Pomegranate (*Punica granatum*)

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ABSTRACT

Punica granatum L (pomegranate) belongs to the family *Lythraceae* (previously *Punicaceae*) is a fruit-bearing deciduous shrub growing within 5-8 meters (16-26 ft) in height. Among the species of *Punicaceae*, *Punica granatum* is the predominant one. Its medicinal importance has been scripted in various ancient literatures and nowadays more research is carried out on it. It has enormous clinical importance owing to its various phytochemical constituents like ellagitannins, punic acid, ellagic acid, flavonoids, anthocyanins, estrogenic flavonoids and flavones. These bioactive components are reported for treating various types of ailments like ulcer, hepatic damage, dysentery, acidosis, hemorrhage, snakebite, obesity, breast cancer, reproductive and respiratory problems. In spite of, pomegranate had been noted for its vast activity at cellular and enzymatic level particularly acting on the enzymes such as COX, CA, LOX, PLA2 and also on cell cycle, division and motility. Recent reports indicate that pomegranate fruits, flowers, seeds and peels describe therapeutic implications in health management by inhibition of free radical effect and modulation of enzyme activity bound with disease development and progression. In this review, we summarize the pharmaceutical importance of various parts of pomegranate in health management based on *in vitro* and *in vivo* studies.

Keywords: Pomegranate, Pharmacological properties, phytochemicals, antioxidants

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INTRODUCTION

Pomegranate under the family of *Lythraceae* is considered to be a superfood worldwide mainly cultivated in the Middle East, North and tropical Africa, the Indian Subcontinents, Asia and Latin America [1]. Pomegranate has been used in various regions as traditional medicine or as a food supplement due to its huge bioactive compounds with a lot of activity and no toxicity. Besides its edible use, almost every part of the plant is used therapeutically worldwide. For instance, flower is used as food supplement to cure diabetes mellitus in Unani Medicine; the pericarp is used to treat diarrhea, metrorrhagia, bellyache and metrostaxis by the Chinese; the bark and root of the plant are supposed to have anthelmintic and vermifugic properties in Ayurvedic medicine; the fruit is used by South Africa for the treatment of diarrhoea [2, 3]. Based on *in vitro* and *in vivo* studies, the report states that Pomegranate has a health enhancing effect mainly due to its Polyphenol content or antioxidant properties. The fruit of pomegranate has medicinal properties such as antibacterial and anti-inflammatory activities due to phenolic compounds. Pomegranate peel has a high content of tannins, flavonoids and other phenolic compounds. Its juice has various chemical constituents such as tannins, polyphenols, anthocyanins, vitamin C, Lipoic acid, Vitamin E and Punicalagin [4]. These constituents are responsible for the antioxidant activities of pomegranate juice.

Chief constituents of pomegranate

There are various constituents present in different parts of pomegranate fruits such as peels, arils, flowers and seeds. These constituents show therapeutic properties through modulation of many biological activities in the health management. Pomegranate peels contains various types of constituents such as ellagitannins, flavonoids and proanthocyanidin compounds as well as minerals like calcium, magnesium, phosphorus, potassium and sodium [5]. Anthocyanin is the major compound that induces colour in pomegranate. The peel and arils hold mainly flavonoids which include flavonols (luteolin, quercetin and kaempferol) [6, 7], flavanols, anthocyanins (pelargonidin-3-glucoside, cyanidin-3-glucoside, delphinidin 3-

glucoside, pelargonidin 3,5-diglucoside, cyanidin 3,5-diglucoside and delphinidin 3,5-diglucoside). The peel, membrane and pith contain hydrolysable tannins namely gallotannins (hydrolyzed to gallic acid) and ellagitannins (hydrolysed to ellagic acid). Pomegranate arils have a high level of sugars, vitamins, organic acids, minerals and polyphenols that show antioxidant activity. The pomegranate juice possesses water, sugar such as glucose, fructose and sucrose [8], pectin and organic acids such as citric, tartaric, succinic, fumaric, maleic and ascorbic acid [9]. Pomegranate flowers contain huge amounts of polyphenols which include gallic acid, ellagic acid and ethyl brevifolin-carboxylate. Moreover, seeds contain constituents like proteins, crude fibers, vitamins and minerals, sugars, polyphenols, the phytoestrogen coumestrol estrone [10-12].

Pharmacological activities of Pomegranate

Several epidemiological studies state that regular intake of foods and beverages containing polyphenols which includes tannins and flavonoids are related with reduced risk of several pathological conditions ranging from diabetes to coronary heart disease, atherosclerosis, stroke and dementia [13-14].

Antioxidant activity

In pomegranate, the leaves and the fruits including seed, juice and pericarp possess antioxidant substances. Polyphenols are the main secondary metabolites of pomegranate juice [15]. The major antioxidant polyphenol is punicalagin that is widely recommended for its potential activity [16]. All antioxidant activities may be associated with various phenolic compounds present in pomegranate including the isomers of punicalagin, tannin derivatives and anthocyanins (delphinidin, pelargonidin 3-glucosides, cyanidin and 3,5- diglucoside) [17]. Antioxidants properties exhibited by these compounds scavengers' free radicals and inhibit lipid oxidation in vitro. Another report suggests that punicalagin derived from peels of pomegranate is one of primary bioactive constituents contributing to the total antioxidant capacity of pomegranate juice [18]. To study the antioxidant effects of peel, seed, leaf and flower extracts of pomegranate, their ethanolic extracts are added to soybean oil analyzing the peroxide value (POV) and malondialdehyde (MDA) with Schall heating oven method and also the ability of scavenging free radicals was measured by 1,1-diphenyl-2-picrylhydrazyl free radical (DPPH) elimination method [19]. Experimental results suggest that peel has the strongest antioxidant activities and high polyphenol content when compared with flowers and seeds. The antioxidant activity of pomegranate is also contributed by flavonoids by free radical elimination. Antiperoxidative activity is possessed by the flavonoids present in the pomegranate. It was reported that malondialdehyde, hydroperoxides and conjugated dienes concentration in the liver, heart and kidney were notably reduced and the enzyme activities of catalase, SOD, glutathione peroxidase, glutathione reductase and the tissue glutathione concentration were significantly increased after the rats were orally administered with total flavonoids from pomegranate. Atechin, quercetin, kaempferol and equol are the major flavonoids in pomegranate play an important role in photoprotective effects on UVB-induced skin damage that is illustrated by enhanced expression level of procollagen type I and reduced expression of matrix metalloproteinase-1 (MMP1S) [20].

Antimicrobial activity

Antibiotics are effective in inhibiting growth of bacteria or microorganisms. On the other hand, the major problem associated with antibiotics is antibiotic resistance against microorganism. The bioactive ingredients of *Punica granatum* shows a very effective role in the inhibition of microorganisms growth which includes tannins and flavonoids [21-22].

Antibacterial activity

Earlier studies on pomegranate peel suggest that peel has an antibacterial effect [23]. Experimental results indicated that methanolic extract of peels was a potent inhibitor for *S.aureus*, *Listeria monocytogenes*, *Yersinia enterocolitica* and *Escherichia coli* [24]. In vitro studies of antibacterial activities of different extracts of fruit peels and arils reported that all pomegranate extracts contained high levels of phenolic compounds and exhibited antibacterial activity against all food related bacteria [25]. Aqueous and methanolic extracts of pomegranate exhibited good antibacterial activity against *S. aureus* and *P. aeruginosa*. [26] The bioactive constituents that exhibited antibacterial activity were reported to be tannins such as ellagitannins and flavonoids.

Antiviral activity

Previous studies based on pericarp of pomegranate reported that tannin is a very effective constituent against genital herpes virus (HSV-2) and effectively kills the virus by blocking its absorption in cells²⁷. Another investigation demonstrated that acidity of juice and aqueous extract contributed to rapid anti influenza activity [28]. The four important polyphenols exhibited anti influenza effects are caffeic acid , Luteolin , ellagic acid and punicalagin among which punicalagin was the most effective one. Punicalagin prohibited replication of virus RNA, inhibited agglutination of chicken RBC induced by virus and had a virucidal property [29].

Antifungal activity

Investigation related to the antifungal activities of pomegranate extracts of peels, seeds, juice and whole fruit was conducted. The result suggests that among the selected bacterial and fungal culture, the highest antibacterial activity was exhibited against *Staphylococcus aureus* and among fungi the highest activity was noticed against *Aspergillus niger*. [30]

Hepatoprotective activity

The commonly used model system for screening hepatoprotective activity of plant extract is by inducing hepatotoxicity by CCl₄. Administration of CCl₄ to rats significantly increases serum AST, ALT, ALP, GGT and TB levels which indicate the severity of liver damage [31-32]. Treatment with *Punica granatum* significantly reduced the increased level of these enzymes demonstrating that the juice prevented hepatic damage which was further confirmed by the reduced amount of histopathological injuries. The radical scavenging antioxidant constituents prevented lipid peroxidation by treating with pomegranate juice [33]. Additionally, it increased hepatic GST activity and maintained GSH level even after treatment of CCl₄. After CCl₄ injection, the ROS production was highly elevated in the livers of rats thus confirming that free radical and oxidative damage plays an important role in the pathogenesis of acute liver injury, which indicates a strong evidence for natural antioxidants used in the curing of toxic hepatopathy effects.

Effect on Reproductive system

Many medicinal plants have confirmed their role in the reproductive system via elevation of hormones and maintenance of spermatogenesis. In this phenomenon, pomegranate also shows vital role in elevation of reproductive linked hormones. Result studies indicated that pomegranate juice showed elevation in testosterone, luteinizing hormone and follicle stimulating hormone depleted after the administration of CCl₄. In addition to it, the report also illustrated that degeneration of germ and Leydig cells along with deformities in spermatogenesis due to CCl₄ injections were retained with pomegranate juice treatment [34]. Another report demonstrated that extract and ascorbic acid injection decreased the deleterious effect of lead acetate on daily sperm production and epididymal sperm number [35]. Study on effects of pomegranate juice on sperm quality and spermatogenic cell density confirmed that juice consumption increased epididymal sperm concentration, sperm motility and spermatogenic cell density [36]. A decrease in malondialdehyde (MDA) level and marked elevation in glutathione (GSH), glutathione peroxidase (GSH-Px) and catalase (CAT) activities and vitamin C were estimated on treatment with pomegranate juice. Long term intake enhanced intracavernous blood flow, improved erectile response and smooth muscle relaxation in erectile dysfunction [37].

Antidiabetic activity

The mechanism of pomegranate affecting type2 diabetic conditions is by declining oxidative stress and lipid peroxidation. The reduction is done by directly neutralizing the reactive oxygen species generated, increasing some antioxidant enzyme activities, inducing metal chelation activity and inhibiting or activating certain transcriptional factors such as nuclear factor κB and peroxisome proliferator activated receptor γ. The significant reduction of fasting blood glucose level was by punicalic acid, methanolic seed extract and pomegranate peel extract. The active constituents in pomegranate identified having anti-diabetic actions are punicalagin and ellagic, gallic, oleanolic, ursolic and uallic acids. Moreover, the pomegranate juice was known to possess unique antioxidant polyphenols such as tannins and anthocyanins which could be beneficial to control type 2 diabetes conditions. Some report revealed that aqueous peel extract of pomegranate markedly decreased blood glucose and significantly raised insulin levels in normal and diabetic treated rats. A significant increase in number of beta cells was shown in pancreas in normal and diabetic treated rats. Another result revealed that aqueous aril extract exhibited the highest α-amylase inhibition compared to all other extracts. Inhibiting α-amylase, the first enzyme involved in starch hydrolysis, can delay the digestion of carbohydrates thereby, reducing the speed of glucose release in blood. Oral administration of pomegranate aqueous-ethanolic (50%,v:v) flower extract found to significantly reduce blood glucose level by increasing peripheral glucose utilization [38].

Anti-Obesity effect

One of the key factors for numerous diseases is obesity. Experimental studies carried out to evaluate anti-obesity effects of pomegranate leaf extract revealed that pomegranate extract significantly reduced body weight, energy intake and various adipose pad weight percents and Serum TG, glucose levels [39].

Anti-inflammatory effects

The pomegranate oil extract can effectively block the production of prostaglandin or leukotriene through cyclooxygenase and lipoxygenase eicosanoid enzymes inhibition so that it may increase the application of oil or its derivatives as internal or external anti-inflammatory substances [40].

Anti-tumor activity

Cancer is a multifactorial disease and a process involving numerous factors. In this phenomenon, pomegranates fruits, seed and peels possess cancer preventive role seems due to rich source of

antioxidants. Pomegranate oil contains 80% conjugated fatty acids, especially punic acid and octadecatrienoic acid [40-41]. Punic acid inhibits prostaglandin biosynthesis (stimulate ornithine decarboxylase enzyme activity at lower concentration) as well as act as a cytotoxin for cancer w2a cells; such activity is possibly due to inhibitory effect against lipid peroxidation [42]. In addition, this oil can prevent DMBA and TPA induced skin cancer [43]. In vivo reveals the inhibitory impact of aqueous and oily parts of pomegranate fractions on breast cancer cells. Such parts inhibit the enzyme activity responsible for active estrogen biosynthesis(17- β -estradiol). In vitro assays using various extracts of *Punica granatum* studied in three different cancer cell lines demonstrated anticancer activity [44]. Moreover, it is revealed to exhibit inhibitory effects on motility, cell cycle, cell division or cell growth, apoptosis.

CONCLUSION

The health promoting effect of pomegranate has been described in traditional medicines in various regions. Pomegranate leaves, fruits, seeds and peel contain enormous phytochemicals that have wide therapeutic importance. *Punica granatum* possesses a wide range of constituents such as polyphenols, alkaloids and vitamins with potent free radical scavenging properties. Preclinical and clinical research has revealed that pomegranate antioxidant properties are effective against free radical induced complications including diabetes, cancer, LDL oxidation, cognition problem and infectious diseases. Because of its wide potential, *Punica granatum* is regarded as “nature’s power fruit” [45].

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