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ANTIOXIDANT ACTIVITY & PHARMACOLOGICAL BENEFITS OF PUNICA GRANATUM- A REVIEW

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ABSTRACT

Punica granatum (pomegranate) is native to the region from northern India to Iran. It is also widely cultivated in parts of Southwest America, California, Mexico, Arizona and Africa. Pharmacological effects of pomegranate represent a long history and have been mentioned in the Greek and Egyptian documents. Studies in past have shown that pomegranate has many potential effects including: bacteriocidal, antifungal, antiviral, immune modulation, anti inflammatory, analgesic, anti diabetic, hypolipidemic, laxative, diuretic and antimutagenic. Ellagic acid is one of the main components of pomegranate with phenolic structure and antioxidant activity. This review article contains the recently published findings on various aspects of this plant, mainly focusing on its health benefits.

KEYWORDS: pomegranate, antioxidants, polyphenols, ellagic acid, traditional medicine

INTRODUCTION

Punica granatum L (pomegranate) belongs mostly to the regions of northern India to Iran. Pomegranate has extensively been used as a source of health benefits and for medicinal purposes. The fruit of pomegranate has shown anti-inflammatory and antibacterial activities. In recent past the plant had been studied extensively and its beneficial effects are seen in various bacterial, viral, fungal, digestive and immunological conditions.[1] The pomegranate seed oil has inhibitory effect on skin and breast cancers. The pomegranate seed oil has phytoestrogenic compounds and the fruit is rich in phenolic compounds with strong antioxidant activity. The fruit and bark of pomegranate are used against intestinal parasites, dysentery, and diarrhea.[2] The extract of fruits and seed is used to stop nose and gum bleeds and in treatment of hemorrhoids.[3]

Pomegranate is a rich source of cyaniding, delphinidin (both are anthocyanidins), caffeic acid, chlorogenic acid (both are phenolic acids), gallic acid, ellagic acid (tannic acids), luteolin, quercetin (flavones), kaempferol (a flavonol), naringenin (a flavanone) as well as 17-alpha-estradiol, estrone, estriol, testosterone, beta-sistosterol, coumesterol, gamma-tocopherol, punicie acid, campesterol and stigmasterol in its juice, peels and seed oil that are chemopreventive and therapeutic potentials of this plant.[4]

There are not enough studies performed on the scientifically proven health benefits of pomegranate. This review article presents the recently published findings on different aspects of this plant, with a focus on its medicinal properties.

History & Geographical Distribution of Pomegranate

Pomegranate (*Punica granatum* L.) is one of the first domesticated fruits that has been cultivated from past times. It is indigenous to Iran and neighbouring countries that gradually developed in central Asia regions to Himalaya, Eyalet of Anatolia, Middle East, and Mediterranean area. It also thrive in Arizona and California, and has been cultivated in the Mediterranean region, South Asia, and the Middle East countries; Kandahar in Afghanistan is famous for its high-quality pomegranate. Today, pomegranate is cultivated in most regions of the world, including Iran, Spain, Italy, Afghanistan, America, India, China, Russia, Uzbekistan, Morocco, and Greece.5 Iran is one of the biggest producers of pomegranate in the world. In Iran, Markazi, Yazd, Fars, Khorasan, and Kerman provinces have the highest production rates.[1]

Synonyms

- American English: pomegranate
- Arabic: Rumman
- Brazilian Portuguese: romã
- Croatian: nar
- Danish: granatæble
- European Spanish: granada
- French: grenade
- German: Granatapfel
- Italian: melagran
- Urdu: Anaar

Scientific Classification

Family: Lythraceae

Genus: Punica

Species: P. granatum

Kingdom: Plantae

Morphology of Pomegranate

Pomegranate is a shrub that reaches to 1.5 to 5 m in height, with more or less irregular and thorny branches and glossy leaves that appears as a deciduous shrub in temperate regions and as evergreen in frigid regions. The characteristics are:

- *Leaves:* Leaves are seen as reciprocal in newly grown branches and as integrated in spores.
- *Flowers:* 1-5 flowers, one of them terminal and the rest marginal, short or without peduncle, their color is red and rarely yellow or white, odorless, and two-sex.
- *Fruit:* Balausta in light red color to greenish yellow and rarely in some species dark purple. It is 5 to 20 cm in diameter and its weight varies from less than 200 g to more than 800 g.
- *Seed:* Seeds are produced in high amounts, are triangular, albumin free, and embedded in aril.[5]

Phytoconstituents of Punica granatum

The main phenolic compounds reported in the literature include flavonoids (anthocyanins such as pelargonidin, delphinidin, cyanidin along with their derivatives and anthoxanthins such as catechin, epicatechin and quercetin), tannins (ellagitannins and ellagic acid derivatives such as punicalagin, punicalin and pedunculagin) and phenolic acids (such as chlorogenic, caffeic, p-coumaric, ferulic, ellagic, gallic and cinnamic acid).[6] The color of pomegranate is induced by its compounds, specially anthocyanin. Anthocyanin is a glycoside releasing a glucose molecule and a glycone ring (anthocyanidin).[7]

Pomegranate use in Traditional Medicine

Flowers, leaves, bark of young shoots and roots, fruit peel, and pomegranate juice have been traditionally used.[8] All components of *Punica granatum* fruit with abundant tannins show relatively strong astringent effects. Several infusions or decoctions of the plant flowers have been used in traditional medicine to treat simple diarrhea, vaginal discharge, and also this extract accompanied with pomegranate peel have usually been used to relieve pancreas

inflammation. Refreshing juice of *Punica granatum* fruit is recommended to heal gallbladder diseases. The fruit contains strong tannin considered as bitter nutrition. Its decoction appears to be helpful for treating diseases such as ordinary diarrhea, dysentery, and stomach disorders.[9] Tannin content of pomegranate seed, however, is not remarkable and it is usually used to treat women vaginal discharge and wound healing.[10] Fresh or dried root barks or ethanol extracts of pomegranate are used to remove intestinal parasites due to the alkaloid substances. It is also used in traditional medicine because of the antibacterial and anti-inflammatory properties.[8,9]

Pharmacological Benefits of Pomegranate

Steroidal activity

In addition to estrone and estradiol, testosterone and estriol as well as their precursor cholesterol had been isolated from petroleum ether extract of Punica granatum seeds. Beta-sitosterol and stigmasterol had also been isolated from the unsaponifiable fraction. The oily fraction of petroleum ether extract contains hormones with estrogenic-like action.[11] Watery parts of pomegranate can inhibit estrogen-dependent and estrogen-independent breast cancer cells. However, this inhibitory effect has been reported to be doubled for estrogen-dependent case.[12] Ellagic acid and gallic acid are among the constituents observed in pomegranate peels, and the former is a dimeric derivative of gallic acid and is found mostly in higher plants, such as fruits and nuts.[13]

Anti-Oxidant activity

Ellagic acid shows antimutant, antiviral, antioxidant, and skin-bleaching activity and has already been added to food as an antioxidant in Japan.[14] Antioxidant capacity of extracts derived from pomegranate peel in producing phospholipid complex has been measured. The base of method is established on the recovery of molybdenum(VI) to molybdenum(V) using antioxidant compounds and creation of green molybdenum(V) compounds with maximum absorption at 695 nm.[15] Antioxidant capacity of extracts from pomegranate peels is due to the presence of the phenols such as ellagic tannins, ellagic acid, and gallic acid.[16]

Anti-mutagenic activity

Antimutagenic and anticarcinogenic properties of the extracts were examined against the azide sodium by the Ames test. The experiment showed that juice extract of pomegranate peel can inhibit mutation and cancer using azide sodium in 2 species of salmonella.[17] The

results of the experiment showed that juice has the lowest antioxidant activity and the highest antimutagenic activity while methanol extract acts in the opposite way.[18]

Anti Bacterial, Viral & Fungal activity

Dahham et al. (2010) evaluated the antibacterial and antifungal activities of pomegranate peel extract (rind), seed extract, juice and whole fruit on the selected bacteria and fungi. The peel extract has shown highest antimicrobial activity compared to other extracts. Among the selected bacterial and fungal cultures, the highest antibacterial activity was recorded against Staphylococcus aureus and among fungi high activity against Aspergillus niger was recorded. Gram-positive cocci, and particularly Staphylococcus sp., are predominant among the organisms that are responsible for infective complications which have contributed significantly to the morbidity and mortality of hospitalized patients. He evaluated the antibacterial and antifungal activities of pomegranate peel extract (rind), seed extract, juice and whole fruit on the selected bacteria and fungi. The peel extract has shown highest antimicrobial activity compared to other extracts. Among the selected bacterial and fungal cultures, the highest antibacterial activity was recorded against Staphylococcus aureus and among fungi high activity against Aspergillus niger was recorded. Gram-positive cocci, and particularly Staphylococcus species, are predominant among the organisms that are responsible for infective complications which have contributed significantly to the morbidity and mortality of hospitalized patients.[19,20]

Anti-inflammatory and analgesic activities

Anti-inflammatory and analgesic activities of of fruit rind, flower, and leaves was measured and it was observed that pretreatment with the dried extracts produced significant and dose dependent inhibition of edema when compared to the control groups.[21] Topical anti-inflammatory and analgesic activities of a standardized pomegranate rind extract of which ellagic acid (EA) was assessed and finding reported that rind extract and the equivalent ellagic acid dose-dependently reduced the ear edema.[22]

Liver protective effects

The effect of chronic administration of pomegranate peel extract on liver fibrosis was examined and results confirmed that plasma AOC and hepatic GSH levels were considerably depressed by bile duct ligation whereas increased back to control levels in the peel extract treated bile duct ligation group.[23]

Anti Diabetic and hypolipidemic effects

Ethanolic extract of leaves showed noteworthy antidiabetic activity and it is also found to be highly effective in managing the complications associated with diabetes mellitus.[24] Another research was carried out to investigate the anti-diabetic, hypolipedimic and antioxidant activity and study results concluded that fruit peel and LPG has shown anti-diabetic and hypoglycemic activity.[25] Administration of crude powder of Punica granatum husk decreased the concentration of glucose, triglycerides, cholesterol, LDL cholesterol and raised the level of HDL cholesterol and hemoglobin content in the blood of normal group and alloxan diabetic group treated rats.26 Study finding revealed that seed and rind extracts showed significant reduction in the rise in blood glucose.[27]

Photo protection effect

Other findings revealed that pomegranate extract showed effective at protecting human skin fibroblasts from cell death after UV exposure.28 Pretreatment of epiderm with pomegranate-derived products showed inhibition of UVB-induced cyclobutane pyrimidine dimers.[29]

Immune system booster

Pomegranate fruit has been recommended as a pharmaceutical and food ingredient in treatment of acquired immune deficiency syndrome (HIV/AIDS) due to the enrichment of divers bioflavonoids, inhibition of free radicals, as well as lipooxygenases inhibition (the enzymes that transform arachidonic acid to leukotrienes).[30]

Cardiovascular effects

Punica Granatum Juice extract showed reduction in the mean arterial blood pressure and vascular reactivity changes to various catecholamines.[31] Study research suggests that pomegranate juice exert beneficial effects on the evolution of clinical vascular complications, coronary heart disease, and atherogenesis in humans.[32] Consumption of pomegranate juice hold anti-atherosclerotic properties which might be associated to its powerful anti-oxidative characteristics.[33]

Neuro-protective effects

Membrane-bound enzymes were altered in the brain regions of Tg2576 mouse treated with control diet, and pomegranate supplementation restore the activities of enzymes to comparable values noticed in the controls.[34]

DISCUSSION

Pomegranate's uncountable beneficial pharmacological properties encourage more and more studies to discover other secrets for solving mankind health problems. Presence of a wide range of compounds, including polyphenols, alkaloids, and vitamins with potent free radical scavenging properties is responsible for the pharmacological benefits. It reduces the oxidative stress, which may induce damage to biomolecules, leading to many chronic diseases, such as cancer,[34,35] diabetes,[36,37] atherosclerosis,[38,39] Alzheimer's disease,[40] nephrotoxicity,[41] hepatotoxicity,[42] pain,[43] and other degenerative diseases. The red color of pomegranate juice has been attributed to anthocyanins, such as cyanidin, pelargonidin glycosides, and delphinidin, which have potent antioxidant activity.[33]

Preclinical and clinical researches have revealed that plants antioxidants are effective in prevention and treatment of free radical–induced complications such as low-density lipoprotein oxidation, heart disease, diabetes, cancer, cognition problem, and infectious diseases. Therefore, the medicinal properties of pomegranate, at least in part, can be attributed to its components with antioxidant activities. If it is true, other medicinal plants with antioxidant activity might have the same properties.

Pomegranate can induce its beneficial effects through the influence of its various bioavailable constituents and metabolites on gene expression. Although many in vitro, animal and clinical trials have been carried out to examine and prove the therapeutic effects of these compounds, further human trials and studies are necessary to understand the therapeutic potentials of pomegranate.

Declaration of Conflicting Interests

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