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Polyphenols as Pomegranate dietary agent

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Pomegranate (*Punica granatum* L.) is a fruit that is grown in western Asia, although it is also grown in different parts of the world. Experimental studies have shown its useful physiological functions, in particular its anti-oxidant, anti-microbial and anti-inflammatory, anti-atherogenic and anti-hypertensive properties. Pomegranate potential as a beneficial agent for several diseases. It significantly reduces the atherosclerotic lesion in cardiac patients. Lipid peroxidation can also be reduced in patients with type 2 diabetes and systolic blood pressure and serum angiotensin conversion enzyme production in hypertensive patients. The goal of this review is to examine the possible health benefits of pomegranate that merit further clinical analysis, and research to date suggests that it may be wise to include this fruit in a healthier diet.

Keywords: Pomegranate, Polyphenol, Antioxidants, anti-obesity, anti-diabetes, anti-cancer

INTRODUCTION

Therapeutic plants are utilized by 80% of the total populace for their essential wellbeing needs. The connection between plants, people and medications got from plants depict the historical backdrop of humanity. Plants are the significant wellspring of characteristic medications. The plants are expected to contain mixes which can possibly be utilized in present day medication for the treatment of illnesses which are not reparable. During the previous decade, conventional frameworks of medication have become a subject of worldwide significance. Current evaluations recommended that in many countries, an enormous populace depends intensely on conventional expert and therapeutic plants to

meet the essential medical service needs, albeit present day medication might be accessible in these nations. Natural medications have regularly kept up prominence for historic and cultural reasons. Right now, numerous individuals in the created nations have started to go to option or corresponding treatments, including medication spices (Schippmann, 2002). Therapeutic plants have played major roles in the management of diseases all over the world since a long time ago. World Health Organization (WHO) has since distributed a critical arrangement for the turn of events and the progression of traditional prescriptions in four territories. Counting: Identification of traditional medicines, implementation of an effective approach and

schedule. Advancement of the production of the necessary spices to prevent the destruction of the characteristic properties.

Natural medicines are in very common use in the form of standardized extracts, partially due to their various side effects and the high cost of chemical medications. Therapeutic plants as oxidants for a wide assortment of regular cancer prevention agents and are utilized for the therapy of infections all through the world. A portion of these properties are antimicrobial, hostile to malignancy, against diabetic, hostile to atherosclerosis, immunomodulatory, or hepato-defensive impacts. As of late, because of helpful impacts of cell reinforcements, especially common cancer prevention agents, in the therapy and anticipation of sicknesses, there has been an extensive enthusiasm for discovering characteristic cancer prevention agents from plant sources. The investigations on restorative plants show that the vast majority of them have noteworthy cell reinforcement action (Rafieian, 2013).

It has been stated that 600 to 700 species are used for medicinal purposes. Significant research data on therapeutic plants are at reporting stage in Pakistan. The examination is carried out and also because plants are routinely essential to the adequacy of medicines, which should not be regarded as 'wonders' based on chemical compounds, but because of the soothing vitality that derives its restorative characteristics based on the relationship between plants and humans. (Jafri et al. 2000). Along with research activities, "medicinal plants from the wild resources are also exploited for commercial purposes which lead to the endangerment of species in their respective habitats. Though these medicinal plants are also important sources of income for poor people as well as for herbal dealers, and exporters but still no cultivation practices for these medicinal plants are observed in Pakistan. The aim of this current review paper is focus on issues of current status of medicinal plants in Pakistan, cultivation practices, conservation and their sustainable utilization as an income generation activities. These issues will provide a baseline to researchers, students, relevant institutes and conservation organization to plan or initiate research or activities related to income generation for poor farmers/collectors and for conservation of medicinal plants in Pakistan" (Murad et al. 2012).

Pomegranate is straight spreading tree, almost 8 to 10 meters high; light yellowish woody

stem. Leaves, opposite, lanceolate. "Leaves shed in December, new light red leaves appearing in the middle of March, the plant is very ornamental, Flowers, bisexual. Fruits, globular, possess a hard outer rind, with a red tinge. Seeds with a fleshy aril which constitutes the edible part. The number of seeds in a pomegranate can vary from 200 to about 1400 seeds. The flowering season of the wild pomegranate, in the Northern Hemisphere, is typically in season from September to February, and in the Southern Hemisphere from March to May. Pomegranate grows easily from seed, but is commonly propagated from 25–50 cm hardwood cuttings to avoid the genetic variation of seedlings" (Sultana and Rahman, 2013). The pomegranate has been grown in "India, Mesopotamia Persia, Turkey, Arabian Peninsula, America, Southern Europe, Middle East, Northern Africa, Tropical Africa, Indian Subcontinent, Central Asia, Asia, California, and Arizona". In Pakistan Pomegranate is very common fruit (Abrams and Gray, 1993).



Figure 1: Images *P. granatum*

Table 1: Organic acids and phenolic compounds in *P. granatum* (Chidambara 2002)

Punicalagin	Punicacortein	Oxalic acid	O-coumaric acid
Tellimagrandin	Delphinidin	Tartaric acid	Gallic acid
Pedunculagin	Quercetin	p-coumaricacid	Proto-catechuic acid
Punicic acid	Melatonin	Punicacortein	Catechin
Caffeic acid	Ellagic acid	Quinic	Chlorogenic acid
Citric acid	Tellimagrandin	Malic acid	Ferulic acid
Corilagin	Phloridzin	Succinic acids	Malic acid
Epicatechin	Apigenin	Luteolin	Naringin

Pomegranate medicinal properties (*Punica granatum* L.)

The pharmacological properties of pomegranate have a long tradition. In recent times, studies have shown that "pomegranate has many impending effects including: bacteriocidal, antifungal, antiviral, immune modulation, vermifuge, stimulant, stomachic, styptic, diuretic and moreover, it serves to decrease the adverse effects of cardiovascular diseases, diabetes, asthma, bronchitis, cough, bleeding disorders, fever, inflammation, acquired immune deficiency syndrome, dyspepsia, ulcers, sores, malaria, prostate cancer, atherosclerosis, hypertension, periodontal diseases, hyper lipidemia, male infertility, alzheimer, obesity and infant brain ischemia" (Rose et al. 2001). The flower-buds are astringent, and are given in chronic diarrhea. "The bark contains an alkaloid, punicine, which is highly toxic to tapeworms. It is a specific remedy for tapeworm infestation. The dried pericarp is decocted with other herbs and used in the treatment of colic, dysentery, leucorrhoea etc" (Al-Maiman and Ahmad, 2002).

Antifungal property of pomegranate (*P. granatum*) peel extract against dermatophytes

Dermatophytes are species that use keratin for their nutrition and may cause diseases of the nails, skin, and hair, such as dermatophytosis. Dermatophyte organisms infect the epidermis and limbs annually with real social and well-being monetary effects. Movement against the dermatophyte parasites *Trichophyton mentagrophytes* and *Microsporum canis* has been suggested for the hydroalcoholic concentrate of the pomegranate natural product strip. Results found that the focus and the punicalagin had a more influential anti-dermatophyte movement toward *T. rubrum*, showing that *P. granatum* was a decent research target with another anti-dermatophyte drug (Jafri et al. 2000). Consequences of this investigation showed that

the rough concentrate of pomegranate had a more noteworthy antifungal movement against *T. rubrum*, demonstrating that the pomegranate is a decent objective for study to acquire another anti-dermatophyte medication. Spectroscopic investigations uncovered punicalagin as the dynamic substance. The anti-dermatophyte examine, utilizing "*Trichophyton rubrum*" as a model, proved that the rough concentrate follows up on conidial and hyphal structures. In addition, cytotoxicity examination has shown that punicalagin is more specific to infectious than warm blood cells in animals, suggesting that it is likely to be better used in therapeutic applications. These results have shown that punicalagin has a more influential antifungal movement against *T. rubrum*, showing that pomegranate is a good target for concentration due to its potential future use as another restorative tool against dermatophytosis. (Foss et al.2014).

Changes in physical and chemical properties during maturation of *P. granatum* fruit

Physicochemical tests of *P. granatum* variety fruit have been conducted, including complete seed juice from unripe, semi-ripe and full-ripe levels. "Edible portion of pomegranate (57.51% of total fruit wt.) comprised 63.58% of juice and 36.21% of seeds. Fresh juice contained 84.57% moisture, 14.1% sugar, 1.05% protein and 0.33% ash. Total proteins, ascorbic acid, fat and phenolic compounds in seeds were 4.06, 0.23, 0.15, 2.92%, respectively". Polyphenols were lower in full-ripe fruits than unripe. "The amounts of K, Na, Mg and Ca were highest among other minerals in the fruit. Cu, Zn and Ca contents were higher in seeds, whereas K, Na and Fe were higher in juices" (Poyrazoğlu et al. 2002).

From an examination, "it is obvious that potassium is the most abundant element in fruit, followed by Na and Ca. The other elements, in descending order by quantity (mg/100 g) were Mg, P, Zn, Fe and Cu and their respective values in the fruit. The exception was iron, which was

reported to be 21.1 mg/100 g as compared to 1.33 in seeds and 2.91 mg/100 g in juice. The study provides important data for calorific and compositional changes of the fruits (e.g. sugars, ascorbic acid and minerals, respectively) at different stages of ripening, emphasizing that pomegranate fruit can be a good source of nutrients" (Katz et al. 2007). More work on the physical and chemical interaction between different varieties need to be done.

Effect of *P.granatum* (flowers) on diabetes and obesity

The emergence of diabetes as a global problem necessitates the development of timely, efficient treatments or strategies. Indian traditional medicinal society observed the hypoglycemic activity of Pomegranate's flowers, seeds and extracts. Systems for such impacts are usually unclear, but the ongoing review advises that pomegranate blossoms and extracts can prevent diabetics by means of peroxysome proliferator-actuated receptors – both official and nitric oxides. Pomegranate mixtures linked to anti-diabetic effects include: oleanolic, ursolic and gallic acids. It's portions and their complex mixtures carry promise and deserve further review as a safe and viable therapeutic medication for diabetes mellitus and its obsessed effects (Katz et al. 2007). As suggested by the 'Gulnarfarsi' investigation, male fruitless blossoms of *P. granatum* have been used for the cure of diabetes mellitus in Unani medicines. Oral organization of the ethanolic fluid (half, v:v) separately induced essential blood glucose, which had a normal effect on glucose, took care of hyperglycaemic and alloxan-actuated diabetic rodents. (Lee et al. 2016).

Pomegranate and, in particular, its concentrates have various medicinal benefits, some of which are related to body weight. A few researches considered that pomegranate can control irritation and serum LDL (low-density lipoprotein) cholesterol in "high-fat" eating routine active corpulent mice and may decrease hepatic lipid peroxidation and glucose levels in solid rodents, despite improved glycemic control and increased relative beta cell count in alloxan-installed diabetic rodents (Banihani et al. 2013). In this study, the combination of pomegranate extract and inulin resulted in enhanced cholesterol-lowering effects. Also, the pomegranate concentrate action mechanism was discovered in a related report—more specifically, by extending the corrosive bile bond, cholesterol was lowered. Various tests have shown that

pomegranate leaf concentrates can inhibit lipid absorption and reduce blood fatty oils and absolute cholesterol in hyperlipidemic mice by limiting lipase movement.(González-Ortiz et al. 2011).

Antibacterial activity of *P. granatum* peel ethanol extract against *Salmonella*

Salmonella typhimurium affected mice who did not get *Punicagranatum* peel ethanol extract were lethargic and displayed symptoms of histological damage to the liver and spleen. Conversely, clinical symptoms and histological disruption have rarely been seen in *S. Typhimurium* contaminated mice fed with *Punicagranatum* peel ethanol extract (Uddin and Rauf, 2011).

Therapeutic potential of *P. granatum* for human breast cancer

Pomegranate was also found to have beneficial effects in different cancers, including "interference with tumor cell proliferation, cell cycle, invasion and angiogenesis. Polyphenols from pomegranate were found to inhibit at least 2 enzymes involved in breast carcinogenesis: aromatase, which converts androgen to estrogen, and 17- β -hydroxysteroid dehydrogenase, which is involved in estrogen biosynthesis. In vitro studies have demonstrated inhibition of proliferation and cell growth in two breast cancer cell lines MCF-7 and MB-MDA-231". "Anti-proliferative and anti-aromatase activities have also been revealed for pomegranate ellagitannin derived compounds (ellagic acid, gallic acid, and urolithins A and B) in breast cancer cells" (Noreen et al. 2020). In addition to these compounds, "urolithin B has demonstrated the most potent aromatase inhibition activity, followed by gallic acid". It induced cell proliferation, indicating that the use of pomegranate can contribute to the prevention of breast cancer (Kim et al. 2002).

Effect of *P.granatum* on Skin Health

Pomegranate phenolics can be used as a standard cancer prevention agent for cosmetic skin safety applications. A vitro research showed their guarded effects in human keratinocyte HaCa T cells against oxidative pressure and cytotoxicity caused by H₂O₂. In addition, pomegranate products (extract, concentrate and oil) derived from the organic pomegranate crushing material for the production of juice have added photographic chemopreventive effects. More specifically, pomegranate objects tend to have

repressed “UVB-interceded DNA and protein destruction”, increased cell-multiplying atomic antigen and tropoelastine levels along with extracellular degradation matrix proteins in human reconstituted skin (Viuda-Martos et al. 2010).

Antioxidant activity of *Punicagranatum* peel extracts using in vivo models

Punicagranatum peel extracts have antioxidant efficacy in multiple in vitro models. “Histopathological studies of the liver were also carried out to determine the hepato-protection effect exhibited by the pomegranate peel extract against the toxic effects of CCl₄. Histopathological studies of the liver of different groups also support the protective effects exhibited by the MeOH extract of pomegranate peel by restoring the normal hepatic architecture” (Katz et al. 2007).

Other Benefits of pomegranates

Pomegranates in dietary regimens can slow the progress of intellectual and social weaknesses in Alzheimer's disease, whereas its juice has a calming effect on cancer prevention agents for cecal ligation and severe liver injury; additionally, it has the property to defend against arsenic-induced irritation and apoptosis in male Swiss pale-skinned liver cells (Mubarik et al. 2020). Another significant result of pomegranate with a few medical advantages is the polysaccharide pomegranate strip, which may be used in useful adjacent safe potentiation treatment or in elective methods to reduce chemotherapy-prompted immune suppression. A few researches have shown that pomegranate strip polysaccharides may upgrade the immunomodulatory impact, instigated by cyclophosphamide, of immunosuppressed mice, display a solid defensive impacts against CCl₄-initiated liver injury in creature study, and, at low dosages, mitigate contact extreme touchiness indications, proposing that they may give helpful consequences for unfavorably susceptible contact dermatitis at physiologically relevant doses in humans in people (Viuda-Martos et al. 2010).

CONCLUSION

Pomegranate is a best source of a wide range of mixtures of positive physiological functions, especially antioxidant and anti-inflammatory properties. A significant number of these properties can be attributed to corrosive ellagic and ellagitanin. Mixing of these compounds involves synergistic effects that are especially higher than the influence of a single compound.

Future research should reveal the concept of these relations almost as central to the structures of these exercises. The use of this organic food or its juice protects against some of the most basic diseases and can also change the course of illness, essentially obesity, diabetes, coronary disease, inflammatory infections and even a few types of disease. It is worth noting the intestinal microbiota plays a major role in the beneficial effects of pomegranate, as its metabolites increase the well-being of the pomegranate.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

AUTHOR CONTRIBUTIONS

TN: Conceptualization and methodology. MI, SA, SN and HA: Writing original draft. TN, BR, HAJ and AC: Visualization and investigation. SB and MA: Data validation. SF, SK, SN and MIA: Writing reviewing and editing. All authors read and approved the final version.

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