

# An Overview of Phytochemical and Pharmacological Potentials of *Punica granatum* L

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## ABSTRACT

Pomegranate (*Punica granatum*) is considered as "A pharmacy unto itself" in Ayurvedic medicine and also used in several other systems of medicine. The plant belongs to the family Lythraceae containing pomegranate as a predominant species. Various parts of the plant exhibits significant pharmacological activities due to its wide range of potential bioactive compounds. Many biological activities proved its antioxidant, anticancer, anti-inflammatory, antimicrobial, anti-atherosclerotic, antidiabetic actions and many more. This article provides a review of phytoconstituents of *Punica granatum* and its diverse array of biological properties.

**Key words:** *Punica granatum*, Phytoconstituents, Pharmacological activities, Traditional medicine, Lythraceae, Bioactive compounds.

## INTRODUCTION

Plants are thought to be a significant source of medicinal components.<sup>1</sup> Plants with medicinal values play a vital role in developing therapeutic drugs which are utilized in the indigenous system of medicine as described in ancient literature.<sup>2</sup> Plants are an excellent source of new bioactive compounds, because of which an interest for phytomedicinal sector is developing rapidly.<sup>3</sup>

As a result of phytochemical investigation, around 74% of drugs of plant origin were identified and isolated for their traditional medicinal use.<sup>4</sup> Being a potential source, natural products act as primary ingredient in drug development.<sup>5</sup>

Medicinal plants are the main source for traditional medicine, herbal medicine and various dietary supplements.<sup>6</sup> Currently, plants are considered to be the cheapest source of medicine used by the major population of the globe, considered as safe with less or no side effects.<sup>7</sup>

## CLASSIFICATION

**Kingdom:** Plantae

**Division:** Magnoliophyta

**Class:** Magnoliopsida

**Order:** Myrtales

**Family:** Lythraceae

**Genus:** *Punica*

**Species:** *P. granatum*

*Punica granatum* was formerly classified under a separate family Punicaceae and recently included in Lythraceae family. The family contains genus *Punica* with two species *Punica granatum*, commonly known as Pomegranate- the predominant species and *Punica protopunica* the less predominant species found typically in the island of Socotra.<sup>7</sup> The

plant is distributed throughout the world believed to be native to Iran and the Himalayan region.<sup>8</sup> The fruit of this plant is known as nature's power fruit. The plant is an evergreen shrub, with multiple tiny stems. It commonly grows up to 1.8 – 4.6 m height. *P. granatum* is found to have deciduous and shiny leaves which are around 7.6 cm long. The flowers are 5 cm long normally double trumpet-shaped orange-red ruffled petals and seen throughout the summer. The fruit is globose with a tough leathery skin with a diameter of around 5- 7.6 cm. The mature fruit has reddish or yellowish green shiny skin. The fruit is known as a berry which is composed of spongy membranous walls which contains reddish or whitish pulp with crunchy seeds. The seeds represent around 52% of the entire mass of the fruit.<sup>7-10</sup>

Anatomically, *P. granatum* can be divided into different parts like seed, juice, peel, leaf, flower, bark and root which exhibits significant pharmacological properties.<sup>11</sup>

*P. granatum* is used in different systems of medicine for treating a variety of ailments in humans. In the Ayurvedic system of medicine the plant is known as "A pharmacy unto itself" which is used as an antiparasitic agent, blood tonic and medicine for diarrhea and ulcers. In the Unani system of medicine, pomegranate is used in the treatment of diabetes and is practiced in the Middle East and India.<sup>12-14</sup>

*P. granatum* has a wide range of therapeutic properties against various illnesses and helps in the treatment and prevention of cancer, cardiovascular diseases, diabetes, dental conditions and offers protection against (UV) radiation. Its other significant applications include infant brain ischemia, Alzheimer's disease, male infertility, arthritis and obesity.<sup>15-19</sup>

In many countries pomegranate has been utilized in herbal remedies where the entire fruit, peels and roots and various other parts of the plants have been used. In the traditional system of medicine, the

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peels of pomegranate have been used in the treatment of diarrhea and dysentery.<sup>20-23</sup>

## CHEMICAL CONSTITUENTS AND COMPONENTS

The chemical composition of the fruit and other plant parts is influenced by climate, geographical area, storage and cultivars. Punicalagin, punicalin, ellagic acid and ellagic acid derivatives such as 3,3'-di-O-methylellagic acid, 3,3'-tri-O-methylellagic acid, 3'-O-methyl-3,4-methylene, flavonoids like luteolin, quercetin, kaempferol and anthocyanins (delphinidin, cyanidin and pelargonidin), phenolic compounds such as pedunculagin, punicaortein A-D, granatin A and B, punicafolin, puniguconin, corilagin, gallo catechins, several fatty acids, sterols, triterpenes and other tannins have been identified and isolated from various parts of the plant which possess an array of therapeutic properties.<sup>24-34</sup>

*P. granatum* juice contains anthocyanins, glucose, ascorbic acid, ellagic acid, gallic acid, caffeic acid, catechin, epigallocatechin gallate, quercetin, rutin, iron and amino acids. Punicic acid and sterols are also found in the seed oil of pomegranate. The fruit rind of the plant contains punicalagin, flavones, flavonones and other flavanols. The leaves are found to contain tannins such as punicalin and punicafolin and flavone glycosides like luteolin and apigenin, considered to be the important constituent of *P. granatum*. The flowers of pomegranate contain Ursolic acid, triterpinoids and Asiatic acid, the roots and barks ellagitannins and piperidine alkaloids.

Around 16% of an individual's daily requirement such as vitamin C, vitamin B5, potassium and natural phenols like ellagitannins and flavonoids are also present in the aril juice of pomegranate.<sup>35</sup>

## PHARMACOLOGICAL ACTIVITIES

### Antioxidant activity

Four different *in vitro* testing methods were used to demonstrate that the juice and seed extracts of pomegranate exhibited 2 to 3 times the antioxidant activity of either green tea or red wine.<sup>30</sup> Free radical scavenging, decrease in macrophage oxidative stress and lipid peroxidation in animals were shown by the extract of *P. granatum* including plasma antioxidant capacity in elderly humans.<sup>36</sup> Pomegranate possessed the best antioxidant activity, independent of the antioxidant between phenolics concentration and antioxidant capacity.<sup>37</sup> Research on rats and mice showed that by-product extract of pomegranate whole fruits reduced 19% oxidative stress in peritoneal macrophages, 42% decrease in cellular lipid peroxide content and 53% increase in reduced glutathione levels.<sup>36</sup>

A study confirms that the juice of pomegranate pulp shows higher antioxidant capacity in comparison with apple juice. An increase in plasma antioxidant capacity from 1 to 1.46 mmol was observed when using Ferric Reducing Antioxidant Power assay (FRAP assay), when 250ml of juice of pomegranate pulp given daily for a period of 4 weeks to the elderly healthy subjects.<sup>38</sup>

The results of DPPH test, 5-lipoxygenase assay and luminal/xanthine/xanthine oxidase assay reveal that arils, juice and rinds of pomegranate show higher antioxidant activity when compared to aqueous and ethyl acetate extracts.<sup>39</sup>

### Anticancer

Different plant parts of *P. granatum* like fruit, juice, seed and seed oil works on prostate, blood, skin, colon, lung, oral and leukaemia cancers. Ellagic acid is an important Phytochemical in pomegranate and the seed oil is effective against various cancers including prostate, blood, skin, colon, lung, oral, oesophagus, bladder and leukaemia

cancers.<sup>40</sup> The results of *in vitro* cell cultures and animal studies, as well as the existing data, show that breast cancer can be prevented by the anticancer activity of pomegranate.<sup>41</sup> Organ culture model of mouse breast cancer demonstrates that the pomegranate seed oil is capable of blocking the development of breast cancer<sup>[43]</sup>. Pomegranate seed oil helps in inhibiting the proliferation of prostate cancer lines by changing the cell growth cycle.<sup>42</sup>

### Antimicrobial

The alcohol extracts of the fruits of *P. granatum* exhibited significant antibacterial activity against *S.aureus*, *E.coli* and *Shigella dysenteriae*.<sup>20</sup> Results of studies reveal that punicalagin, major hydrolysable tannin found in the pomegranate possesses antimicrobial activity against *Candida albicans*.<sup>43</sup> The fruit rind of pomegranate inhibits the growth of *Penicillium citirnum*, *P. patulum*, *P. ruqfortii* and *Aspergillus achraceous* with various test organisms when tested for its fungistatic activity.<sup>44</sup>

Extracts of *P. granatum* act as an antagonist against the microorganisms that are responsible for the urinary tract infection. Methanol extract shows activity against the multidrug resistant bacterial strains of the urinary infection samples.<sup>45-48</sup> Research results show that the hydroalcohol extract of pomegranate may be used as a substitute for treating the dental plague bacteria by decreasing the number of colony-forming units per milliliter by 84% compared to control groups that offer only 11% reduction.<sup>49</sup>

### Anti-inflammatory

An *in vivo* study shows that the extract of *P. granatum* effectively inhibits the inflammatory cytokine-induced production of PGE2 and nitric oxide.<sup>50</sup> An *in vitro* study results exhibit that the Cold pressed seed oil of *P. granatum* (CPSO) inhibits both cyclooxygenase and lipoxygenase enzymes. The enzyme Cyclooxygenase which is responsible for the conversion of arachidonic acid to prostaglandins is inhibited by the Cold pressed seed oil of *P. granatum* by 37% and helps by 75% in the inhibition of Lipoxygenase, which acts as a catalyst in the conversion of arachidonic acid.<sup>9</sup>

Cold pressed seed oil of pomegranate seeds is found to contain significant anti-inflammatory constituents such as polyphenols and fatty acids. These chemical constituents exhibit an inhibition of 31- 44%, 69- 81% and 21- 30% of sheep cyclooxygenase, soyabean lipoxygenase and soyabean lipoxygenase from fermented juice of the extract respectively. The polyphenols also is reported to suppress the inflammatory cell signaling in colon cancer cells.<sup>51</sup>

### Anti-atherosclerotic activity

Atherosclerosis may be prevented and suppressed by pomegranate-derived products which possess anti-atherogenic effects.<sup>52-56</sup> Anti-atherogenic effects have been observed when pomegranate is taken for longer as well as shorter periods. Enhancement of oxidative status and reduction in lipid peroxidation were exhibited in the study when pomegranate juice was administered for a week with various dose levels.<sup>12,53,57</sup>

An attempt was made to identify the constituents of various parts of pomegranate which possessed anti-atherosclerotic activity. Results reveal that the juice of pomegranate and the extract of the aerial parts are found to contain excellent content of anthocyanins and hydrolysable tannins act in the reduction serum oxidative stress in contrast peel extract of pomegranate which is effective on the extent of Ox-LDL uptake of macrophages and their oxidative status.<sup>56</sup>

Reduction in cholesterol level was found more effective by the juice of pomegranate when compared to the extracts of fruit peel.<sup>54</sup>

## Alzheimer's disease

Polyphenols present in pomegranate possess neuroprotective properties and were tested for Alzheimer's disease in an animal model. Pomegranate juice when given to transgenic mice with Alzheimer's kind of pathology, were observed to have 50% less accumulation of soluble amyloid-beta and hippocampal amyloid deposition that consumed sugar water. This study proves that pomegranate juice has neuroprotective activity.<sup>58</sup>

Cognitive disorders like dementia and Alzheimer's disease may be effectively treated with pomegranate. Ethanol extract of the seeds of pomegranate showed a significant cognitive activity on aged and scopolamine treated mice. Upon the chronic administration for 21 days of extract of *P. granatum* and vitamin C, a significant reverse was observed in the age induced or scopolamine induced retention deficits in both the paradigm. A significant reduction of lipid peroxidation level and increased antioxidant glutathione level were found in the tissues of the brain with the treatment of pomegranate extract.<sup>59</sup>

## Anti-diabetic activity

The fruit rind extract of pomegranate exhibits an excellent-blood-sugar-lowering effect. It is suitable for prolonged use with low toxicity for metabolic syndrome and its related pathologies, obesity, type 2 diabetes and cardiovascular diseases.<sup>60</sup>

Research studies show that the increase in the blood sugar level is prevented when the Flower extract of *P. granatum* is supplemented for 6 weeks to the obese diabetic rats following a glucose- laden meal. There was no such activity found in normal rats. The extract of pomegranate flower also exhibits an enhancement in the gene expression of the vital transcription factor PPAR- gamma. This in turn helps in regulating the cellular responses enabling the heart of a diabetic animal to use the sugar energy better by its normalized expression of a glucose transporting protein in the heart muscle.<sup>61,62</sup>

In Unani and ayurvedic systems of medicine pomegranate flowers have been used for the diabetic treatment. Researchers conducted studies on the extract of pomegranate flowers investigated on serum lipid profile.<sup>63,64</sup>

## Dermatology

Studies reveal that the fruit extract of *P. granatum*, standardized with punicalagins, shows significant protective effects against UVA and UVB induced damage in human skin fibroblast cells. The fruit extract of *P. granatum* is capable of protecting human skin fibroblast against UV exposure by decreasing the induction of the proinflammatory transcription factor NF-KappaB, a down regulation of pro-apoptotic caspase-3 and increasing G0/ G1 phase associated with DNA repair.<sup>65,66</sup>

## Other biological activities

Tannins present in the pomegranate play a vital role in protecting people against gastric ulcer.<sup>67</sup> Hydro alcoholic extract of *P. granatum* fruit which possesses antibacterial activity may be considered as an alternative in the treatment against dental plague bacteria.<sup>49</sup>

Aqueous and alcohol extract of the fruit peel of the plant has been reported for anti-diarrheal activity. Reports reveal that the extracts show remarkable activity in rats, when compared to loperamide hydrochloride which is used as an anti-diarrheal drug.<sup>68</sup>

## CONCLUSION

*Punica granatum* is an ancient fruit with an illustrious medical history and has been the subject of classical review for over 100 years. Pomegranate contains a lot of potential therapeutic properties due to the presence of various classes of chemical constituents like tannins,

alkaloids, glycosides, volatile oils, flavonoids and resins, gums. *P. granatum* has been reported with various pharmacological activities like antioxidant, antimicrobial, antiviral, antidiabetic, anticancer, Alzheimer's disease, etc., due to the presence of bioactive compounds.

The indigenous or traditional system of medicine has become important in the field of medicine. The practitioners relying on medicinal plants for their primary healthcare needs. Herbal medicines are still being used primarily for historical and cultural reasons. This attempt is made to present an overview of phytochemical and pharmacological activities of plant *Punica granatum*.

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## CONFLICTS OF INTEREST

None.

## ABBREVIATIONS

UV: Ultra violet; DPPH: 2,2-diphenyl-1-picrylhydrazyl; Ox-LDL: Oxidized low-density lipoprotein; UVA: Ultra violet A; UVB: Ultra violet B; DNA: Deoxyribonucleic acid.

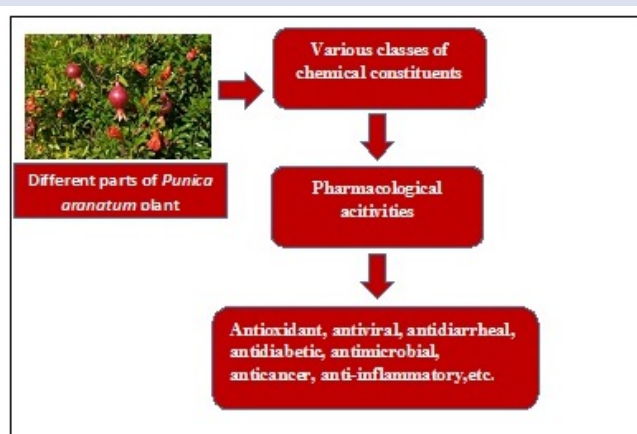
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## GRAPHICAL ABSTRACT



## SUMMARY

- This attempt is made to present an overview of phytochemical and pharmacological activities of plant *Punica granatum*.
- In the Ayurvedic system of medicine, *Punica granatum* is known as "A pharmacy unto itself"
- *P. granatum* is used in different systems of medicine for treating a variety of ailments in humans.
- The chemical composition of the fruit and other plant parts possess an array of therapeutic properties.
- *P. granatum* has been reported with various pharmacological activities like antioxidant, antimicrobial, antiviral, antidiabetic, anticancer, Alzheimer's disease, etc., due to the presence of bioactive compounds.

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