

PHARMACOLOGICAL ACTIVITIES OF LEAF EXTRACT OF *Punica granatum*: A REVIEW ARTICLE

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Abstract

Punica granatum L (pomegranate) is a deciduous shrub, native to Iran. Nowadays, besides its use as a fruit, its medicinal properties have attracted the interest of researchers of many countries. Pomegranate fruit has medicinal properties such as anti-inflammatory and antibacterial activities. The pomegranate seed oil has inhibitory effect on skin and breast cancers. This plant shows good antioxidant properties and hence it seems a very promising contender in future of Medicine. This Review Aimed to summarize different Pharmacological activities that has already been explored in the Leaf extract of *Punica granatum*. We found that the leaf extract of *Punica granatum* shows number of Pharmacological activities such as, Anticancer, Antidiabetic, Antiemetics, Anti-inflammatory, Antiulcer, Antiviral, Anxiolytic, Hepatoprotective, Neuroprotective and Nephroprotective.

Keywords: Anticancer, Antidiabetic, Antiemetics, Anti-inflammatory, Antiulcer, Antiviral, Anxiolytic, Hepatoprotective, Neuroprotective and Nephroprotective

1. INTRODUCTION:

1.1 *Punica granatum L.* :

It is a deciduous shrub, native to Iran. Pomegranate has extensively been used as a source of traditional medicine. It is one of the first domesticated fruits that has been cultivated from past times. It is indigenous to Iran and neighboring countries that gradually developed in central Asia regions to Himalaya, Eyalet of Anatolia, Middle East, and Mediterranean area. It also thrives 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. Iran is one of the biggest producers of pomegranate in the world.¹

In the ancient Ayurveda system of medicine, the pomegranate has extensively been used as a source of traditional remedies for thousands of years. The rind of the fruit and the bark of the pomegranate tree is used as a traditional remedy against diarrhea, dysentery and intestinal parasites. The seeds and juice are considered a tonic for the hear, throat, eyes and for a variety of purposes, such as stopping nose bleeds and gum bleeds, toning skin, firming-up sagging breasts and treating hemorrhoids.²

1.2 Plant Profile:

Kingdom: Plantae

Order: Myrtales

Family: Punicaceae

Genera: *Punica*

Species: *P. granatum*

1.3 Vernacular names:

Common name: Pomegranate

Hindi: Anar

Urdu: Anar

Tamil: Madulai

Marathi: Dalimb

Kannada: Dalimbe

Telugu: Danimma



Fig.1: Leaves of *Punica granatum*.

1.4 Morphological Characters:

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. *Punica granatum* L belongs to the Punicaceae family and is the smallest plant family that includes 1 genus and 2 species, including the following: *Punica granatum* (edible pomegranate) is indigenous to Iran and Mediterranean regions, and *Punica protopunica* (inedible) is endogenous to Socotra islands in Pacific Ocean.³ The other characteristics are:



Fig. 2: Fruit of *Punica granatum*.

- **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.



Fig. 3: Flower of *Punica granatum*.

1.5 Chemical Constituents:

It contains numerous valuable ingredients such as flavonoids, ellagitannin, punicalagin, ellagic acid, vitamins and minerals. The principal constituents including punicalagins and ellagitannin are responsible for immeasurable health benefits due to its strong antioxidant activity.⁴

1.6 Traditional uses:

Heart problem:

It is said that Frequent intake of pomegranate juice can maintain good flow of the blood in the body. Along with this, it decreases the risk of heart attack and heart strokes.

Stomach disorder:

Peel and bark of Pomegranate are used to calm the stomach disorder or diarrhea due to any kind of digestive problems.

Drinking tea made from the leaves of *Punica granatum* helps in curing digestive problems.

Dental care:

It is also said that the juice of *Punica granatum* shows relief from the effects of dental plaque.

Cancer:

Punica granatum said to contain advanced level of antioxidants called Flavonoids. These are thought to be very useful against cancer radicals. The individuals that face high risk of prostate and breast cancer should start drinking the juice of this fruit, as this will help them to reduce further risk of developing cancer.

Osteoarthritis:

This plant seems to minimize the illness in various forms, like atherosclerosis and osteoarthritis. The loss that is triggered due to the thickening and solidifying of the arterial walls and in cartilage and joints can be cured by consuming this fruit. Also, pomegranate is capable of preventing the creation of minerals that are liable for breaking down the connective tissues.

Diabetes:

Coronary illness seems to be prevented due to the consumption of the *Punica granatum* fruits. Along with this, there is a slowdown in solidifying of the bloodstream, which can fuel non-occurrence of various heart diseases.

Anemia:

In any form the consumption of this fruit causes healthy blood flow in the body. Seed extract of *Punica granatum* supplies iron to the blood and thus, helps to decrease the anemic symptoms including fatigue, wooziness and weakness and hear loss.

2. REPORTED PHARMACOLOGICAL ACTIVITIES:

2.1 Anticancer activity:

Punica granatum (pomegranate) leaves extract induces apoptosis through mitochondrial intrinsic pathway and inhibits migration and invasion in non-small cell lung cancer in vitro is a study published by yali Li and co-wrokers, and they found that *Punica granatum* leave extract can suppress the proliferation of Non-small cell Lung cancer in vitro and can induce cell apoptosis through mitochondrial pathway associated with loss of mitochondrial transmembrane potential and the down regulation of ROS accumulation. They even mention that *Punica granatum* Leaf extract can arrest cell cycle in G2/M phase.⁵

2.2 Antidiabetic activity:

Antidiabetic and antihyperlipidemic effects of ethanolic extract of leaves of *Punica granatum* in alloxan-induced non-insulin-dependent diabetes mellitus albino rats was a study carried out by Swarnamoni Das and Sarajita Barman and they found that the ethanolic extract of leaves of P. granatum at the dose of 500 mg/kg body weight produced significant antidiabetic activity in alloxan-induced NIDDM albino rats. It is also found to be highly effective in managing the complications associated with diabetes mellitus, such as hyperlipidemia, and prevents the defects in lipid metabolism.⁶

2.3 Anti-emetics activity:

Phytochemical screening and evaluation of anti-emetic activity of *Punica granatum* leaves was the study done by Jainendra Kumar B and co-workers and they found that the ethanol extracts of *Punica granatum* (200 mg/kg) have protective effect against copper sulphate induced-retching in young chickens, possibly by peripheral and central mechanisms. The potential of this extract as antiemetic activity may be due to the presence of phytoconstituents like alkaloids and terpenes and might be responsible for its activity.⁷

2.4 Anti-inflammatory:

Punica granatum L. Leaf extract attenuates lung inflammation in mice with acute lung injury was the study done by Aruna Joaquim et al. and they found that Hydroalcoholic extract of *Punica granatum* may be used as food supplements, like tea, to prevent inflammatory disorders in which neutrophils play an essential role, such as ALI (Acute lung injury).⁸

2.5 Anti-ulcer activity:

Antiulcer activity of Ethanolic extract of *Punica granatum* against stress induced ulcer albino rats' study was done by V. Ramamurthy and J. Antoniaaaxi marueen and they found that leaf extract of *Punica granatum* have significant antiulcer activity in animal models. It has gastric antisecretory when compared with that of reference drugs omeprazole. The extract is non-toxic even at relatively high concentrations. The anti-ulcer activity is probably due to the presence of flavonoids.⁹

2.6 Antiviral activity:

Antiviral study on *Punica granatum* L., *Momordica charantia* L., *Andrographis paniculata* Nees, and *Melia azedarach* L., to Human Herpes Virus-3 was published by Divyadarshini Angamuthu and co-workers, and they found that Aqueous extract from the leaves of *Punica granatum* L. was superior in exhibiting its antiviral efficacy to HHV-3 whose in vitro activity was comparable with acyclovir. As the leaf phytochemicals interacted with the HHV-3 protease, the antiviral activity of the *Punica granatum* L., leaves may interfere with the capsid assembly of the HHV-3.¹⁰

2.7 Anxiolytic activity:

Assessment of anti-oxidant, anti-epileptic and anti-anxiety activities of pomegranate leaf (*Punica granatum*) in mice was a study published by Keshav Dhakal and co-workers and they found that the flavonoids contained in *Punica granatum* possesses significant anti-epileptic, antioxidant and antianxiety activity in mice which is supported by the phytochemical screening. They also state that the Methanolic Flavonoid has shown better results in all assessed activities than Ethanolic acetate flavonoid which suggests that the flavonoid content was more in Methanolic extract.¹¹

2.8 Hepatoprotective activity:

Hepatoprotective activity of *Punica granatum* leaf extract against Carbon Tetrachloride induced Hepatotoxicity in Rats was a study done by Mnojkumar and his colleagues in 2018 and they found that the group of animals which was administration with *Punica granatum* leaf extract shows relatively lower surge in Marker enzymes (AST, ALT and ALP) compare to the group of animals given only CCl₄. Hence study concludes the aqueous leaf extract of *Punica granatum* to possess Hepatoprotective activity.¹²

2.9 Neuroprotective activity:

Effect of pomegranate extracts on brain antioxidant markers and cholinesterase activity in high fat-high fructose diet induced obesity in rat model was a study published by Zahra Amri et al. in 2017 and their study suggests that chronic intake of pomegranate extracts prevents against HFD (High fructose diet) complications such as hyperlipidemia and cerebral oxidative stress. In fact, they also stated that, the administration pomegranate juice, peel and seeds oil to HFD-fed rat decreased body weight, restored serum lipid levels, and attenuated oxidative stress in brain. Hence, they conclude that Leaf extract of *Punica granatum* has got Neuroprotective potential.¹³

2.10 Nephroprotective activity:

Punica granatum improves renal function in gentamicin-induced nephropathy in rats via attenuation of oxidative stress named study was published by Snehal N. Mestry and co-workers and they conclude that the protective effect of MPGL(Methanolic *Punica granatum* Leaf extract) was associated with its ability to ameliorate renal function parameters; prevent the increase in lipid peroxidation and the fall in the antioxidant enzymes activity observed in the kidney of rats with gentamicin-induced nephropathy. Taking together these studies attribute the protective effect of MPGL in gentamicin induced nephropathy to the attenuation of inflammatory response, preservation of antioxidant enzymes and prevention of oxidative stress. Hence, they stated that their present study work identifies MGPL as a promising renoprotective agent against renal injury.¹⁴

3. CONCLUSION:

Based on the previous discussed reviews on various articles, it can be said that *Punica granatum* has got a wide spectrum and potential as a medicinal plant, as some addresses this fruit as the “Fruit from Heavens”, so the other parts can also be used for medicinal development. The leaf of *Punica granatum* promisingly shown to have Anticancer, Antidiabetic, Antiemetics, Anti-inflammatory, Antiulcer, Antiviral, Anxiolytic, Hepatoprotective, Neuroprotective and Nephroprotective, so further exploration on this wonderful plant is highly encouraged.

4. REFERENCES:

1. Erfaneh Shaygannia et al. A Review Study on *Punica granatum* L. Journal of Evidence-Based Complementary & Alternative Medicine. 2016; 21(3): 221-227
2. Debjit Bhowmik et al. Medicinal Uses of *Punica granatum* and Its Health Benefits. Journal of Pharmacognosy and Phytochemistry. 2013;1(5): 28-35
3. Syed Zameer Hussain et al., Fruits Grown in Highland Regions of the Himalayas. Page no. 131-143.
4. Arshad Husain Rahmani et al. Active constituents of Pomagranate (*Punica granatum*) as potential candidate in the management of health through modulation of biological activities. Pharmacognosy journal. 2017;9(5):689-695
5. Yali Li et al. *Punica granatum* (pomegranate) leaves extract induces apoptosis through mitochondrial intrinsic pathway and inhibits migration and invasion in non-small cell lung cancer in vitro. Biomedicine and pharmacotherapy. 2016;80:227-235
6. Swarnamoni Das, Sarajita Barman. Antidiabetic and antihyperlipidemic effects of ethanolic extract of leaves of *Punica granatum* in alloxan-induced non-insulin-dependent diabetes mellitus albino rats. Indian journal of Pharmacology. 2012 April;44(2):2019-224
7. Jainendra Kumar Battineni et al. Phytochemical screening and evaluation of anti-emetic activity of *Punica granatum* leaves. European journal of pharmaceutical and medical research. 2017;4(4):526-532.
8. Aruana Joaquim Matheus costa et al. *Punica granatum* L. Leaf Extract Attenuates Lung Inflammation in Mice with Acute Lung Injury. Hindawi Journal of Immunology Research. 2018;11 pages.
9. V. Ramamurthy and J. Antoniaauxi Marueen. Antiulcer activity of ethanolic extract of *Punica granatum* against stress induced ulcer in albino rats. International journal of basic and applied research. 2018; 8(10):461-469.
10. Divyadarshini Angamuthu et al. Antiviral study on *Punica granatum* L., *Momordica charantia* L., *Andrographis paniculata* Nees, and *Melia azedarach* L., to Human Herpes Virus-3. European Journal of Integrated Medicine. 2019;28:98-108.
11. Keshav Dhakal et al. Assessment of anti-oxidant, anti-epileptic and anti-anxiety activities of pomegranate leaf (*Punica granatum*) in mice. Asian Journal of Pharmacy and Pharmacology. 2021;7(2):58-62.
12. Manoj Kumar et al. Hepatoprotective activity of *Punica granatum* leaf extract against Carbon Tetrachloride induced Hepatotoxicity in Rats. Balneo Research Journal. 2018;9(1):24-27.
13. Zahra Amri et al. Effect of pomegranate extracts on brain antioxidant markers and cholinesterase activity in high fat-high fructose diet induced obesity in rat model. BMC Complementary and Alternative Medicine. 2017; 17:339.
14. Snehal N. mestry et al. *Punica granatum* improves renal function in gentamicin-induced nephropathy in rats via attenuation of oxidative stress. Journal of Ayurveda and Integrative Medicine. 2020;11:16-23.