**Punica granatum** L. (Damim), Therapeutic Importance of World’s Most Ancient Fruit Plant

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**Introduction**

Medicinal herbs play a major role in our day to day life from providing food, shelter, clothes to medicines. The plants are being in use for medicinal purpose since ancient times. Medicinal plants have beneficial effects on overall health of the humans. As per the reports, Hippocrates used almost 400 different plant species at that times for the medical purpose. In the ancient era, medicinal preparations were primarily derived from plants. The plants play a vital role in traditional medication system like Ayurveda, Siddha, Unani, Chinese, Egyptian etc. Some plants are greatly promoted due to the associated ethnobotanical beliefs of different cultures. Many modern drugs in the present era have developed from the plant sources because these contain phytochemicals which exhibit various biological properties. Almost half of the modern drugs have the presence of plant contents in them. WHO is continually promoting the use of herbal drugs as these drugs are considered superior than the synthetic drugs because these are easily available, less expensive, have suitable, and compatible actions mechanisms inside the living system, multi-target actions, and produce negligible side effects. Herbal medicines are preferably considered in each and every corner of the world. These are used almost everywhere for the health maintenance purposes. One of the most ancient medicinal plants with significant value in many cultures is Punica granatum L. (figure 1) the pomegranate (anar) an ancient, mystical edible fruit and an ornamental tree. It is commonly known as grenade, granats, and pune apple. It is popular around the world as super food with super therapeutic properties. Previously the genus *Punica* was placed under monogenic Punicaceae family but after several analyses on molecular and morphological levels revealed that it has close relationship with the family named as Lythraceae. This family consists of one genus and two species only. The genus *Punica* is derived from Roman word called “carthage”. In French and Spanish, the species *granatum* is known as grenade and granada respectively which means seeded (granatus) apple (pomum). *Punica granatum* L. is a plant with rich ethnic history of its utilization in various cultures. It has a religious value in Zoroastrianism, Judaism, Buddhism, Christianity, and Islam. In an old testament of Bible, it was praised as “a sacred fruit conferring powers of fertility, abundance, and good luck”. In ancient Egypt, it was symbolized for prosperity and ambition. In the ancient paintings, the plant was depicted as the representation of life after death. Egyptians used this plant against parasitic infestation such as tapeworm. It is described as paradise fruit in the Holy Quran while in Christian Art it was symbolized as life. In Chinese art it was symbolized for fertility, posterity, abundance, numerous and virtuous offspring, and a blessed future. Persians used it as a sign of power during the battles. *Sefer ha Rimon: The Book of
the Pomegranate is an 800 years old Kabbalistic text which symbolizes pomegranate as Shekinah which is the female aspect of creation, and its creator. This plant has a significant value in Solomon's temple in Jerusalem. In ancient Rome it was known as "Phoenician Apple". Roman women use to wear its branches as a headband as the symbol of marital status. In Zoroastrian temples, pomegranates were used as a symbol for eternal life and fertility. In Buddhism, pomegranate is worshiped as a sacred plant. Plant holds a significant value in Hindu religion. It is related with the Goddess Earth and Lord Ganesha. The plant signifies prosperity and fertility. Vedas denoted this plant as the food of God. The plant indicated life, regeneration, and marriage in the Greek mythology. Besides its ethnic value, the plant has wide range of important therapeutic properties. The plant is widely used in folk remedies for numerous human ailments. Each part of the plant is utilized in various folk remedies of numerous diseases like skin diseases and wound healing, fever, diarrhea and microbial infection, ulcers, helminthiasis, acidosis, dysentery, haemorrhage and issues related to respiration. In Ayurveda, the plant holds significant place in the treatment of many diseases. It is entitled as "a pharmacy unto itself" in Ayurveda and mainly used as anti-parasitic agent. It is consumed as blood tonic and used in the treatment of aphthae, diarrhea, and ulcers. Each part of the plant is medically important due to its phytochemical constituents like alkaloids, tannins, flavonoids, polyphenols etc. The primary polyphenols found in the plant are anthocyanins (impart red color to the fruit) and hydrolysable tannins. This plant is majorly known for its high anti-oxidant properties which is mainly exhibited by polyphenols which contribute almost 90% of the total antioxidant property whereas 50% of this property is contributed by punicalagin alone. The characteristic features of the plant are soft seed, rich peel and aril color contributed by punicalagin alone. Aril is the edible part of this plant which also contain folate and Vitamin C, K are present in great amount in the seeds. The plant exhibits important biological properties like anti-microbial, anti-cancer, anti-inflammatory, immunomodulatory etc. Vernacular names and taxonomy of the Punica granatum L. are given in table no. 1 and 2.

Table 1: Vernacular Names of Punica granatum L.

| Taxonomic Rank | Taxon                                      |
|----------------|--------------------------------------------|
| Kingdom        | Plantae                                   |
| Division       | Tracheophyta                              |
| Class          | Magnoliopsida                             |
| Order          | Myrtales                                  |
| Family         | Lythraceae                                |
| Genus          | Punica                                    |
| Species        | granatum                                  |
| Common Name    | Pomegranate/Anar                          |

Morphology of Punica granatum L.

Punica granatum L. is an evergreen deciduous spiny shrub or small trees which reach up to the height of 5-10m. It has multiple thorny branches with smooth stem having bark of dark grey color. The leaves are simple bright green and glabrous, glossy in appearance and present in opposite or sub opposite manner on the lateral shoots. The petiole is short. The leaves may be ovate or oblong. The flowers are 1-5 in number and all of them are marginal except the one which grows terminally. These are short in size and are present without peduncle. Flowers are funnel shaped, bisexual and actinomorphic. There is presence of a fleshy tubular calyx with 5-9 lobes. Imbricate and wrinkled 5-7 petals of orange red color are present in between the calyx lobes. There is presence of numerous filaments free stamens on the calyx tube. Dorsifixed anthers and aperturate pollens are present. There is presence of inferior ovary with the many locules. Punica granatum L. fruit are large sized and brownish yellow to red in color having round shape with 5-12 cm diameter with the presence of crown of tubular calyx. Fruit/berry is formed by two parts i.e, outer hard pericarp and inner mesocarp (albedo) of spongy nature. The mesocarp is divided into several chambers in non-
symmetrical manner where triangular soft/hard seeds usually of red or white colour, are contained. Seeds are entirely covered by arils which are the edible juicy portion 46-51.

**Geographical Distribution of Punica granatum**

*Punica granatum* is a known native plant of Central Asia mainly Iran, Afghanistan, India, Pakistan, China, Japan. It is also found in Mediterranean countries (Tunisia, Turkey, Egypt, Spain and Morocco) and U.S.A. California, Russia. It is believed that this plant has been spread to other regions of the world primarily from Iran, such as to from Iran to the Mediterranean region, Turkish European borders, American southwest, California and Mexico. In India, it is mainly found in Northern regions of the country. As per the reports, the total *Punica granatum* production in Turkey was around 100,000 tons in the year 2007. It grows well adapted plant that can grow in climate ranges as well as soils and often grows in poor soils 52-59.

**Phytochemistry of Punica granatum**

*Punica granatum* consists of wide range of bioactive compounds in it such as vitamins, polysaccharides, minerals, polyphenols, tannins, saponins, quinones, alkaloids, glycosides, coumarins, terpenoids, steroids, betacyaninetc. The major organic acids and phenolic acids in the plant are malic acid, fumaric acid, oxalic acid, succinic acid, citric acid, and tartaric acid, ascorbic acid, citric acid, fumaric acid, malic acid, oxalic acid, quinic acid, caffeic acid, chlorogenic acid, cinnamic acid, o-Coumaric acid, p-Coumaric acid, cis-p-coumaric acid, coumaric acid, 7,8-dihydroxy-3-carboxymethylcoumarin-5-carboxylic acid, ferulic acid, gallic acid, methyl gallate, neochlorogenic acid (5-O-Caffeoylquinic acid), protocatechuic acid, vanillic acid, coniferyl 9-O-[(β-D-apiofuranosyl)(1→6)]-O-β-D-glucopyranoside, Sinapyl 9-O-[(β-D-apiofuranosyl)(1→6)]-O-β-D-glucopyranoside.

Flavonoids present in the plant are luteolin, kaempferol, and nariginin found in glycoside forms. Glucose, fructose, sucrose are the simple sugars present in the juice. Polyphenols including ellagitannins, gallotannins (punicalin, punicalagin, pedunculagin, punigluconin, granatin B, and tellimagrandin I, punica cortein A-D, granatin A and B, punica folin, corilagin, gallothecins) are majorly present in the plant. Ellagitannins are majorly present in the root and bark. Six anthocyanins namely 3,5-diglucoside delphinidin, 3-glycoside delphinidin, 3,5-diglucoside cyanidin, 3-glycoside cyanidin, 3,5-diglucoside pelargonidin, and 3-glycoside pelargonidin are the compounds which impart a characteristic color to the plant. Pelargonidin is associated with orange and red colors, cyanidins imparts red and deep red color and delphinidins imparts blue and purple colors. Proline, valine, methionine are the major amino acids found in the plant. The plant has conjugated fatty acid like punicic acid and non-conjugated acids like linoleic acid, oleic acid, palmitic acid present in it. Plant consists of conidendrin, isohydroxymatairesinol, isolariciresinol, matairesinol, dihydroxy matairesinol, phylligenin, pinosinol, secoisolariciresinol, syringaresinol, pomegralignan, punica gain C as lignans. The seeds contain sex steroids like 17-Estradiol, testosterone. Other compounds like catechol, coumestrol, phenyl alphatic glycosides (icariside D1), phenylethyl rutinoside, syringaldehyde, sitosterol have also been isolated from the plant 65-72.

![Chemical Structures of Some Phytochemical Constituents of Punica granatum L.](image-url)
Traditional and Modern View of Punica granatum L.

Ayurvedic View of Punica granatum L.

As per Sushruta Samhita (surgical compendium of Ayurveda), health is a balanced state of Doshas (three biological humors i.e kapha (water & earth), pitta (fire) and vata (space & air), dhatus (seven body tissues), digestion, peace of soul, mind and senses. 73-75. *Punica granatum* is a plant of great significance in Ayurveda commonly known as "dadim". It balances the three Doshas of the body. It is considered as Rasayanay which consists of properties like Dhatus (seven body tissues), digestion, cardiaco tonic, stomachic. It is used in the treatment of chronic diarrhoea and dysentery, dyspepsia, colitis, piles and uterine related disorders. 76 It is helpful in treating anemia and other blood related disorders.

Properties and uses of *Punica granatum* L. 80,81

Sansthanik karam wah: It has anthelminthic properties and helpful in treatment of throat and buccal cavity diseases. It is useful in edema due to its healing properties.

Abhyastra naadi sansth: It works as brain tonic.

Pachansansth: It works as an appetizer. It relieves thirst and have soothing properties. It is used in diarrhoea, dysentery and hyper acidity. It has anthelminth property which is specifically effective against tapeworms.

Rakat wah sansth: It works as a cardiac tonic. It is helpful in treating anemia and other blood related disorders.

Sawansansth: Due to the astringent property of flowers it balances the vitiated kapha dosh. It reduces cough and bronchi dryness.

Mootarwah sansth: Due to its diuretic property it is used in oliguria.

Prajannan sansth: It enhances the spermatogenesis.

Taapkram: It has antipyretic property. It subsides the further fever related complications.

Saatmikaran: It helps in reducing general body weakness.

Ayurvedic formulations of *Punica granatum* L. 82

*Punica granatum* L. is present in many Ayurvedic formulations like dadimashtak choorna, dadimadi choorna, dadimadi ghrut, dadimadya taila, dadim chatusama.

Folk View

There are many social and cultural beliefs associated with some plants representing their rich ethnomedicine. One of the plants with rich ethnomedicine found many countries is *Punica granatum* L. It is the most beloved plant since the ancient times. Greek and Romans used the plant as remedy for many diseases. In Dir district Pakistan, the plant is used in medicinal folk practices for treating several diseases like cough, stomach and urine related issues, diarrhoea, bone and chest pain, dysentery, diabetes, throat infection. People used the plant as anthelminthic, refrigerant, astringent, and as expectorant. 84. The fruit skin infusion is used to treat dysentery, vomiting, food poisoning in coastal areas of Pakistan 85. Tribal people of lesser Himalayas, Pakistan, use fruit of the plant diabetes, diarrhoea, piles, and dysentery 86. In the Altiplano region of Mexico, people use plant pericarp syrup to get relief from gum diseases, aphous ulcers and mouth sores. 87. In Lorestan province of Iran, people treat peptic ulcers traditionally with the pomegranate seeds 88. *Punica granatum* fruit, seed and flower is used traditionally in Kerman Province, Iran for treating skin blisters, skin tissue integrity, diarrhoea in children, hypertension, strengthening and bleeding gums 89. People in Fars Province of Iran, use fruits of *Punica granatum*, in jaundice and use as an appetizer. 90. Pericarp is used against renal diseases in the North center region of Morocco 91. In Agadir Ida Ou Tanane Province (Southwest Morocco), the infusion, powder and decoction of leaf, fruit, seed, bark is used orally or externally to enhance digestion. 92. The Brazilian community Sobradinho, use the plant traditionally to get relief from sore throat. 93. The local people of Turkey use flower decoction to treat asthma. 94. People use roots of *Punica granatum* to treat diabetes mellitus in Limpopo Province, South Africa. 95. In Boheratoli & Menkifanda, Netrokona ares of Bangladesh, people traditionally use root bark decoction to expel out the human worms. 96. In some areas of Dhaka Bangladesh, the plant is used in the anemia treatment. 97. The Garo tribal people of Bangladesh use the leaf paste of the plant to treat fungal infection of the nail called onychomycosis. 98. In Sulawesi (Makassarrese, Buginese), Java (Javanese, Sundanese), Madura, Vietnam the pericarp is used in many formulations to get relief from teeth blackening. 99. In the southeast of the capital of Hodna (Algeria) the bark decoction is used to get relief from stomach ache, diarrhoea, ulcer. 100. In Jammu and Kashmir, seeds are used against anemia and jaundice. Seeds are used to recover from weakness. Whereas they consume juice as an appetizer. 101. In Parinche valley of Pune Maharashtra, fruit rind is traditionally used to treat diarrhoea. 102. The plant is used for various therapeutic purposes like treatment of fever, cardiac and throat problems in Satpura region of Maharashtra. The plant is also used as anthelminthic, laxative, astringent and to enhance memory. 103. The fruit powder is consumed orally to treat stomachache in Kani tribals in Tirunelveli hills of Western Ghats. 104. In the in Southern part of Tamil Nadu, the plant made up of whole plant is used topically as an anti-venom. 105.

Modern View

Herbal medicines are primarily known for their negligible adverse impacts and least toxicity than allopathic medicines around the world. 106. But over the past few years some deliberate practices have been noticed which are majorly responsible for the gradual fall in quality of herbal products for example adulteration, contamination etc. The definition of adulteration as per the quality control (QC) guidelines of WHO is “herbal material, an herbal constituent or other substance that is either deliberately or non-intentionally (through cross-contamination or contamination) added to...
an herbal material, herbal preparation, or finished herbal product. The authenticity and quality of these drugs must be checked carefully as adulterated herbal products have so many health risks associated with them. More checkpoints need to be placed during the whole process from the processing of the raw material to the formulation of the end product so that authenticity and quality are ensured.

**Therapeutic Properties of Punica granatum L.**

*Punica granatum* L. is associated with many important therapeutic properties. Some of the reported studies on therapeutic properties are discussed below:

**Antioxidant**

The anti-oxidant potential of *Punica granatum* L. was evaluated by Hossain et al., in an in-vitro study. The crude ethanolic extract of the plant was tested for its anti-oxidant activity by using tests like 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging, nitric oxide scavenging, reducing power, Fe³⁺ ion chelating ability and total phenolic content. The findings revealed that IC₅₀ values of crude ethanolic extract in each test were significant different from the IC₅₀ values of reference standards. This study supports the use of *Punica granatum* as an anti-oxidant agent. In-vitro antioxidant analysis of *Punica granatum* L. by Boggula et al., suggested that the leaf extract of the plant is associated with anti-oxidant activities. They subjected the extract to reducing power, hydrogen peroxide scavenging assay, DPPH methods. Results confirmed the significant anti-oxidant behavior of the plant. Singh et al., carried out an in-vitro study to investigate the anti-oxidant potential of *Punica granatum* fruit and peel. Methanol extract of both peel and fruit showed anti-oxidant in beta-carotene-linoleate and DPPH model systems. Extract exhibited inhibitory actions at 100 ppm using thiobarbituric acid method, hydroxyl radical scavenging activity, and LDL oxidation at the rate 56, 58, and 93.7% respectively.

**Anti-microbial**

Duman et al., studied the anti-microbial activity of arils of six *Punica granatum* L. varieties from Mediterranean region of Turkey. In this in-vitro study they used seven bacterial strains viz. (*Bacillus megaterium* DSM 32, *Pseudomonas aeruginosa* DSM 9027, *Staphylococcus aureus* Cowan 1, *Corynebacterium xerosis* UC 9165, *Escherichia coli* DM, *Enterococcus faecalis* A10, *Micrococcus luteus* LA 2971) and three fungal strains namely *Klavuyromycyes marxianus* A230, *Rhodotorula rubra* MC12, *Candida albicans* ATCC 1023. It was observed that the aril extracts showed potent inhibitory actions against all the microbial strains which confirms its anti-microbial property. Bassiri-Jahromi et al., studied the anti-fungal behavior of peel and pulp extract of this plant against *Candida* species viz. *Candida albicans* (ATCC 10231), *Candida parapsilosis* (ATCC 22019), *Candida tropicalis* (ATCC 750), *Candida glabrata* (PTCC 5297) and *Candida krusei* (PTCC 5295). Results revealed that the peel extract showed the maximum inhibitory actions against the *Candida* species. This study supports the use of peel extract of *Punica granatum* L. in the effective treatment of candidiasis.

**Anti-diabetic**

The reported *in-vivo* study conducted by Gharib et al., in alloxan-induced diabetic rats for the evaluation of anti-diabetic potential of *Punica granatum* suggested that the aqueous extract of the fruit is associated with significant anti-diabetic activity. Plasma insulin, free fatty acids, and triglycerides levels and tissues contents of glycogen and triglycerides were compared with the control groups i.e. diabetic control (DC) and healthy control (NC). Insulin receptor substrate 1 (IRS-1), Protein kinase B (Akt), Glucose transporter 2 and 4 (Glut-2, 4) mRNAs expression levels were also analyzed. A significant reduction fasting blood glucose (FBG) was noticed in pomegranate fruits aqueous extract (PE) + Dc group.

**Anti-peroxidative**

Sudheesh et al., conducted an experimental study to evaluate the anti-peroxidative potential of *Punica granatum*. Oral administration of flavonoid fractions (B and C) to the rats showed effective decrease in malondialdehyde, Gastro Intestinal Tract (GIT) infection viz. *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *S. paratyphi A*, *S. paratyphi B*, *S. typhimurium*, *Shigella dysenteriae* Serotype 1, *Shigella flexneri* Serotype 2 and *Vibrio cholera*. The pericarp extract namely crude, methanol and acetone extracts were screened out against the above mentioned bacterial strains. It was observed that methanol extract showed highest inhibitory actions against the used strains as compared to the selected other extracts. The maximum inhibition was seen against *Salmonella typhimurium*, *Salmonella typhi* and *Shigella dysenteriae* Serotype 1. Choi et al., studied, in-vitro as well as in-vivo anti-bacterial property of this plant. The ethanol extract of peel was investigated against 16 *Salmonella* strains. The minimal inhibitory concentrations (MIC) of ethanol extract against all the used strains revealed its anti-bacterial potential. Whereas in the *in-vivo* *S. typhimurium* growth was effectively inhibited by ethanol extract of peel in the mice models. This study confirms that *Punica granatum* is associated with potent anti-bacterial property.

**Anti-hypertensive**

Wang et al., conducted an *in-vivo* study on pregnant female rat models to investigate the anti-hypertensive activity of *Punica granatum* L. Pre-eclampsia (PE) is a term used for pregnancy hypertension. Hypertension was induced artificially in the models. NG-nitro-L-arginine methyl ester (L-NAME) at the dosage of 50 mg/kg/day were administered orally in the models on days 14-19 of pregnancy for inducing hypertension. The polyphenol named as punicalagin present in the plant was showed effective results by reducing diastolic, systolic, and mean arterial blood pressure and it significantly helped in restoring angiogenesis as well as the levels of placental nitric-oxide were increased. The reduction in levels of oxidative stress was observed. It also enhanced the antioxidant capacity of placenta.
hydroperoxides and conjugated dienes concentration in the liver, heart and kidney and significant elevation in the levels of enzymes such as catalase, superoxide dismutase (SOD), glutathione peroxidase and glutathione reductase was noticed 120.

Wound Healing
An in-vivo study was conducted by Nasiri et al., for the evaluation of wound healing property of Punica granatum in the treatment of thermal injuries in rat models. Study revealed that tannin content in the extract effectively helped in decreasing the wound size and the healing of wound 121.

Cardioprotective
Sumner et al., conducted a clinical study in patients suffering from ischemic coronary heart disease (CHD). They observed that consumption of pomegranate juice for 3 months at regular basis effectively helped in reducing the stress-induced ischemia which indicates the use of Punica granatum as a cardioprotective agent 122.

Effect on Male Reproductive system
Turk et al., evaluated the effect of pomegranate juice on sperm quality, spermatogenic cell density, testosterone level in male rats. The observations of the study stated that the consumption of pomegranate juice had positive results by increasing epididymal sperm concentration, sperm motility, spermatogenic cell density, diameter of seminiferous tubules, and germinal cell layer thickness. It significantly lowered down the rate of abnormal sperms 123. Forest et al., evaluated the effect of pomegranate juice in the treatment of erectile dysfunction in 53 men. Subjects were administered with pomegranate juice, or placebo, for four weeks. The treatments were switched after washout period of two-week. The result stated that pomegranate juice consumption was associated with improved scores 124.

Anti-cancer
Joseph et al., studied the anti-cancer behavior of Punica granatum in in-vitro and in-vivo. Galactomannan polysaccharide (PSp001) a compound isolated from the fruit has proved to be an anti-cancer agent. Its cytotoxic impact was studied on human cancer cell lines A375, HCT116, and HepG2 as well as the murine cancer cell lines DLA and EAC. Compound showed significant cytotoxic activity against these cancer cell lines. In EAC and DLA bearing mice models the compound effectively reduce the volume of tumor. This compound improved the survival of the models which suggested that Punica granatum has anti-cancer properties 125.

Anti-inflammatory
Houston et al., carried out an ex-vivo study to investigate the anti-inflammatory activity of Punica granatum. Pomegranate rind extract (PRE), total pomegranate tannins (TPT) and zinc (II) were evaluated for anti-inflammatory actions. When PRE alone and in combination with ZnSO4 topicaly applied to the skin, they downregulated the expression of COX-2 while the downregulation of COX-2 on the application of TPT was comparatively less than that of PRE. This study concluded that Punica granatum can be a good source of anti-inflammatory drugs 126.

Immunomodulatory
Ross et al., evaluated the immunomodulatory property of the plants in rabbit models. Punica granatum fruit rind powder (PGFRP) is associated with this property. The administration of aqueous suspension of (PGFRP) significantly helped in the stimulation of cell-mediated components and humoral components of the immune system of the models. A significant boost in the inhibition of leucocyte migration was observed. A noticeable increase in the thickness of skin was seen in the PGFRP group. These findings of the study suggested that Punica granatum is associated with immunomodulatory effects 127.

Anti-anemic
The study reports of Riaz et al., confirms the anti-anemic property of Punica granatum. They conducted the study on healthy rabbit models. The pomegranate juice effectively worked on erythrocytes, hemoglobin, and mean corpuscular hemoglobin concentration. It also reduced the platelet aggregation and fibrinogen concentration whereas protein C, thrombin antithrombin complex levels were increased which showed the anti-anemic behavior of the juice 128.

Conclusion
The present study is an attempt to provide the detailed information about the most ancient medicinal fruit plant, Punica granatum L. The reported pharmacological studies indicated that this plant has extraordinary biological potential. It is strongly believed that the present review on the phytomedicinal value of Punica granatum, might draw the attention of researchers to use this plant in modern medicines. From the present review, it can be concluded that plants are the promising source of anti-oxidant and anti-microbial compounds.

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Conflict of Interest
None

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