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Review Article

Punica granatum L. (Dadim), Therapeutic Importance of World's Most Ancient Fruit Plant

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Abstract

The custom of using plants for the therapeutic and dietary practices is as old as origin of humanity on the earth. One of the most ancient fruit plant is *Punica granatum* L., pomegranate belongs to Lythraceae family. The plant has a very rich ethnic history of its utilization around the world. The plant was used to symbolize prosperity, life, happiness, fertility etc. Apart from the ethnic beliefs associated with the plant, it is a well-considered plant based remedy used in treatment of many diseases in traditional system like Ayurveda and folk system of medicine. In Ayurveda it is esteemed as a Rasayana. It is used in many Ayurvedic polyherbal formulations which are used against many diseases. The plant consists of numerous phytochemical constituents in it such as polysaccharides, minerals, polyphenols, tannins, saponins, quinones, alkaloids, glycosides, coumarins, terpenoids, steroids etc. Each of the phytochemical constituent is associated with important therapeutic properties. This supper food is globally known for its high anti-oxidant potential. Other associated properties of this medicinal fruit plant are anti-microbial, hepatoprotective, cardioprotective, anti-diabetic, anti-cancer, immunomodulatory, anti-inflammatory, anti-hypertensive, anti-anemic etc. The aim of present review is to provide information related to phytochemistry, traditional uses in Ayurveda and folk medicinal system and therapeutic properties of *Punica granatum* L.

Keywords: Dadim, Rasapanchak, Punicalagin, Punicic acid, Anti-oxidant.

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 [1,2]. In the ancient era, medicinal preparations were primarily derived from plants [3]. The plants play a vital role in traditional medication system like Ayurveda, Siddha, Unani, Chinese, Egyptian [4]. Some plants are greatly promoted due to the associated ethnobotanical beliefs of different cultures [5]. Many modern drugs in the present era have developed from the plant sources because these contain phytochemicals which exhibit various biological properties [6,7]. Almost half of the modern drugs have the presence of plant contents in them [8,9]. 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 [10-14]. Herbal medicines are preferably considered in each and every corner of the world. These are used almost everywhere for the health maintenance purposes [15]. 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 [16,17,18]. It is commonly known as grenade, granats, and punica apple [19]. 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 [20,21]. This family consists of one genus and two species only [22]. 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) [23,24]. *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" [25]. 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 [26,27]. 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 [28,29]. "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 [30]. This plant has a significant value in Solomon's temple in Jerusalem. In ancient Rome it was known as "Phoenician Apple". Romanian 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 [31]. 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 [32]. 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 [33-36]. 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. Aril is the edible part of this plant [37,38]. folate and Vitamin C, K are present in great amount in the seeds [39]. The plant exhibits important biological properties like anti-microbial, anti-cancer, anti-inflammatory, immunomodulatory etc. [40-43]. Vernacular names and taxonomy of the *Punica granatum L.* are given in table no. 1 and 2.

Figure 1: *Punica granatum L.*

Table 1: Vernacular Names of *Punica granatum L.* [44]

India	Dadima, Dalima, Dalim , Anar
Persian	Dulim, Dulima
Guatemala	Granad
Indonesia	Gangsalan
Samoan	Limoni
Brazilian	Roma, Romeira, Romazeira
Thailand	Tab tim
Malaya	Delima
German	Granatapfel
French	Grenade
Dutch	Granaatappel
Spanish	Granada (the fruit), granado (the plant)
Italian	Melogranato, Melogranogranato, Pomogranato
Roman	Carthage (Punica)

Table 2: Taxonomic Classification of *Punica granatum L.* [45]

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 5-8 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 [60-64]. 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, L-Malic acid, oxalic acid, quinic acid, caffeic acid, chlorogenic acid, cinnamic acid, o-Coumaric acid, p-Coumaric acid, cis-p-coumaric acid, coutaric 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 narigenin 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, punicacortein A-D, granatin A and B, punicafolin, corilagin, gallocatechins) 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 are 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, medioresinol, phylligenin, pinoresinol, secoisolariciresinol, syringaresinol, pomegralignan, punicatannin C as lignans. The seeds contain sex steroids like 17-Estradiol, testosterone. Other compounds like catechol, coumesterol, phenyl aliphaticglycosides (icariside D1), phenylethylrutinoside, syringaldehyde, sitosterol have also been isolated from the plant [65-72].

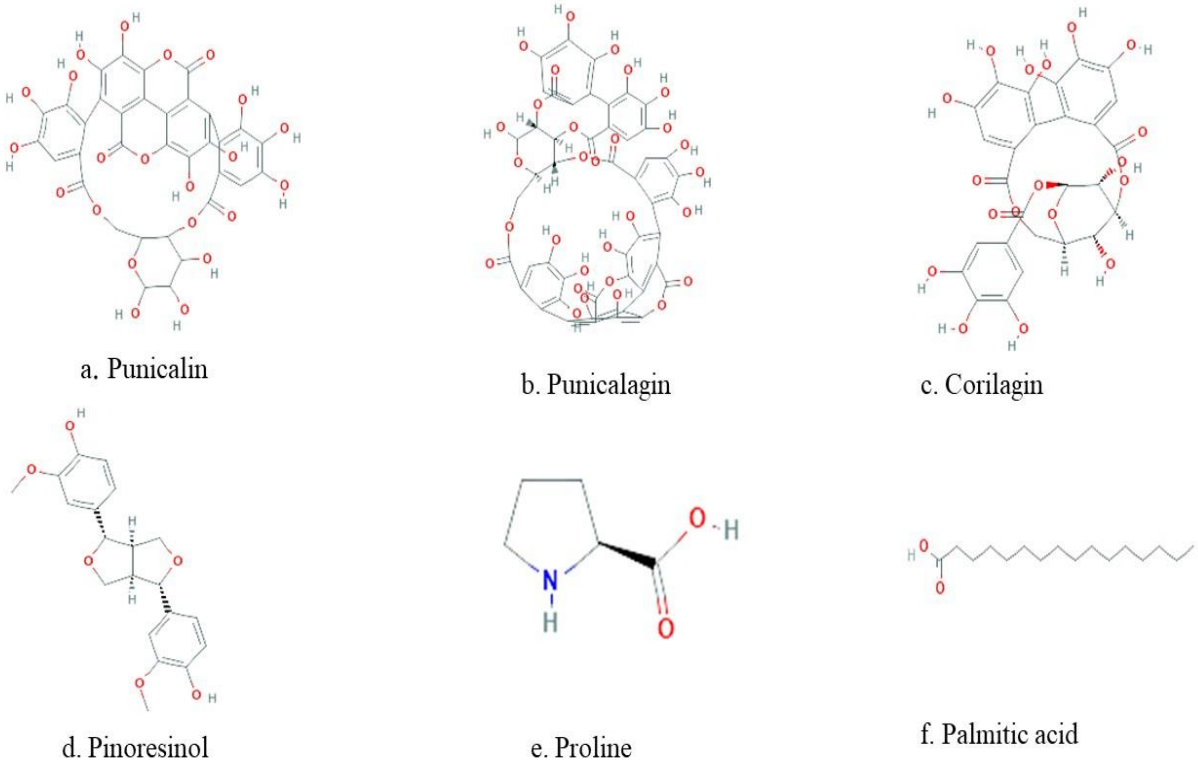

Figure 2: Chemical Structures of Some of Phytochemical Constituents of *Punica granatum L.*

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 Rasayana which consists of properties like Pathya (wholesome properties), Balya (enhances strength), Dhatuvridhikara (tissue generation and development). It is also preferred for treating conditions like cardiac and anemic [76,77]. In Ayurveda, the fruit rind is used as astringent, digestive, cardio tonic, stomachic. It is used in the treatment of chronic diarrhoea and dysentery, dyspepsia, colitis, piles and uterine related disorders [78]. Rasapanchak of *Punica granatum L.* is given in Table 3

Table 3: Rasapanchak of *Punica granatum L.* as per Ayurveda[79]

Sanskrit/English	Sanskrit/English
Virya/Potency	Shita/Cold
Vipak/Metabolic property	Madhur/Sweet, Amla/Sour
Guna/Physical property	Laghu/Light, Snigdha/Oily
Rasa/Taste	Kashaya/Astringent, Madhura/Sweet, Amla/Sour

Properties and uses *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.

Abhyantra naadi sansthan: It works as brain tonic.

Pachansansthan: It works as an appetizer. It relieves thirst and have stool binding properties. It is used in diarrhoea, dysentery and hyper acidity. It has anthelminthic property which is specifically effective against tapeworms.

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

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

Mootarwah sansthan; Due to its diuretic property it is used in oliguria.

Prajannan sansthan: 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 ethnobotany [83]. One of the plants with rich ethnobotany 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 Altiplane region of Mexico, people use plant pericarp syrup to get relief from gum diseases, apthous 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, diarrhea 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 onycomycosis [98]. In Sulawesi (Makassarese, 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, diarrhea, 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 Satpuda 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" [107]. 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 formation of the end product so that authenticity and quality are ensured [108].

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, Fe++ ion chelating ability and total phenolic content. The findings revealed that IC_{50} values of crude ethanolic extract in each test were significant different from the IC_{50} values of reference standards. This study supports the use of *Punica granatum* as an anti-oxidant agent [109]. *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 [110]. 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 [111].

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 *Kluvyeromyces marxianus* A230, *Rhodotorula rubra* MC12, *Candida albicans* ATCC 1023. It was observed that the aril extracts showed potent inhibitory actions against the all microbial strains which confirms its anti-microbial property [112]. 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 [113]. Antifungal property of *Punica granatum L.* has also been explored by Shjafighi et al. They conducted an *in-vitro* study on *Candida albicans* NCPF 3153 to evaluate the antifungal behavior of peel, flower, leaf and stem of the plant. It was observed that the methanolic extract of the flower showed maximum inhibitory actions in the concentration of 200 µl suggesting its antifungal potential [114]. Pradeep et al., carried out an *in-vitro* study to evaluate the anti-bacterial potential of *Punica granatum* against ten bacterial strains causing 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 [115]. 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 [116].

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 [117].

Hepatoprotective

An *in-vivo* study was conducted by Kumar et al., in rat models where hepatotoxicity was induced artificially by administering carbon tetra chloride (CCl_4). Results revealed that aqueous leaf extract is associated with hepatoprotective activity. The extract increased the level of total proteins and significantly lowered down the levels of enzymes like bilirubin, aspartate aminotransferase (AST), alanine transaminase (ALT) and alanine phosphatase (ALP) which are most reliable liver functioning markers [118].

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 [119].

Anti-peroxidative

Sudheesh et al., conducted an experimental study to evaluate the a**nti-peroxidative potential of** *Punica granatum.* Oral administration of flavonoid fractions (B and C) to the rats showed effective decrease in malondialdehyde,

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 dysfunctioning 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 at el., 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

Houstan 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 topically 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., to 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 immunonodulatory 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

References

1. Choudhary S, Kaurav H, Chaudhary G. Kasani beej (*Cichorium intybus*): Ayurvedic View, Folk View, Phytochemistry and Modern Therapeutic Uses. International Journal for Research in Applied Sciences and Biotechnology. 2021 Mar 25; 8(2):114-25.
2. Simmler C, Graham JG, Chen SN, Pauli GF. Integrated analytical assets aid botanical authenticity and adulteration management. Fitoterapia. 2018 Sep 1; 129:401-14.
3. Ayyanar M, Ignacimuthu S. Ethnobotanical survey of medicinal plants commonly used by Kani tribals in Tirunelveli hills of Western Ghats, India. Journal of ethnopharmacology. 2011 Apr 12; 134(3):851-64.
4. Kumari I, Sudan M, Walia B, Chaudhary G. *Zingiber officinale* (Ginger): A Review Based Upon Its Ayurvedic and Modern Therapeutic Properties. 2021; 13(3):16583-16587.
5. Chauhan SA, Kaur AM, Vyas MA, Khatik GL. Comparison of antidiabetic and antioxidant activity of wild and cultivated variety of Rauwolfia serpentina. Asian J Pharm Clin Res. 2017; 10(12):404-6.
6. Chukwuma EC, Soladoye MO, Feyisola RT. Traditional medicine and the future of medicinal Plants in Nigeria. Journal of Medicinal Plants Studies. 2015; 3(4):23-9.
7. Lifongo LL, Simoben CV, Ntie-Kang F, Babiaka SB, Judson PN. A bioactivity versus ethnobotanical survey of medicinal plants from Nigeria, West Africa. Natural products and bioprospecting. 2014 Feb 1; 4(1):1-9.
8. Ateş DA, Turgay Ö. Antimicrobial activities of various medicinal and commercial plant extracts. Turkish Journal of Biology. 2003 Sep 4; 27(3):157-62.
9. Hamburger M, Hostettmann K. 7. Bioactivity in plants: the link between phytochemistry and medicine. Phytochemistry. 1991 Jan 1; 30(12):3864-74.
10. Rai LK, Prasad P, Sharma E. Conservation threats to some important medicinal plants of the Sikkim Himalaya. Biological

conservation. 2000 Apr 1; 93(1):27-33.
11. Edeoga HO, Okwu DE, Mbaebie BO. Phytochemical constituents of some Nigerian medicinal plants. African journal of biotechnology. 2005 Aug 19; 4(7):685-8.
12. Mann, J.1978. Secondary Metabolism. Oxford University press, London, pp. 154.
13. Shanmugam MK, Lee JH, Chai EZ, Kanchi MM, Kar S, Arfuso F, Dharmarajan A, Kumar AP, Ramar PS, Looi CY, Mustafa MR. Cancer prevention and therapy through the modulation of transcription factors by bioactive natural compounds. InSeminars in cancer biology 2016 Oct 1 (Vol. 40, pp. 35-47). Academic Press.
14. Cragg GM, Newman DJ. Natural product drug discovery in the next millennium. Pharmaceutical biology. 2001 Jan 1;39(sup1):8-17.
15. Kumari I, Kaurav H, Chaudhary G. *Myristica fragrans* (Jaiphal): A Significant Medicinal Herbal Plant. International Journal for Research in Applied Sciences and Biotechnology. 2021; 8(2):213-224.
16. Sarkhosh A, Zamani Z, Fatahi R, Ebadi A. RAPD markers reveal polymorphism among some Iranian pomegranate (*Punica granatum* L.) genotypes. Scientia Horticulturae. 2006 Dec 4; 111(1):24-9.
17. Amruthesh S. Dentistry & Ayurveda V-An evidence based approach. International Journal of Clinical Dental Science. 2011; 2(1).
18. Gong XM, Zhang SM, Song FS, Zhu LW. Economic characteristics of fruits in pomegranate cultivars in China. Plant Genetic Resources. 2004; 5:17-21.
19. Khwairakpam AD, Bordoloi D, Thakur KK, Monisha J, Arfuso F, Sethi G, Mishra S, Kumar AP, Kunnumakkara AB. Possible use of *Punica granatum* (Pomegranate) in cancer therapy. Pharmacological research. 2018 Jul 1; 133:53-64.
20. Puneeth HR, Chandra SS. A review on potential therapeutic properties of Pomegranate (*Punica granatum* L.). Plant Science Today. 2020 Jan 1;7(1):9-16.
21. Guerrero-Solano JA, Jaramillo-Morales OA, Jiménez-Cabrera T, Urrutia-Hernández TA, Chehue-Romero A, Olvera-Hernández EG, Bautista M. Punica protopunica Balf., the Forgotten Sister of the Common Pomegranate (Punica granatum L.): Features and Medicinal Properties—A Review. Plants. 2020 Sep; 9(9):1214.
22. Davis PH. Flora of Turkey and the East Aegean Islands. Vol. 3. Flora of Turkey and the East Aegean Islands. Edinburgh: University Press. Vol. 3. 1970.
23. Prasad D, Kunnaiah R. *Punica granatum*: A review on its potential role in treating periodontal disease. Journal of Indian Society of Periodontology. 2014 Jul; 18(4):428.
24. Thangavelu A, Elavarasu S, Sundaram R, Kumar T, Rajendran D, Prem F. Ancient seed for modern cure–pomegranate review of therapeutic applications in periodontics. Journal of pharmacy & bioallied sciences. 2017 Nov; 9(Suppl 1):S11.
25. Jurenka J. Therapeutic applications of pomegranate (*Punica granatum* L.): a review. Alternative medicine review. 2008.1; 13(2): 128-144.
26. Sánchez-Lamar A, Fonseca G, Fuentes JL, Cozzi R, Cundari E, Fiore M, Ricordy R, Perticone P, Degrassi F, De Salvia R. Assessment of the genotoxic risk of *Punica granatum* L.(Punicaceae) whole fruit extracts. Journal of Ethnopharmacology. 2008 Feb 12; 115(3):416-22.
27. Ward C. Pomegranates in eastern Mediterranean contexts during the Late Bronze Age. World Archaeology. 2003 Jan 1; 34(3):529-41.
28. Heber D, Schulman RN, Seeram NP, editors. Pomegranates: ancient roots to modern medicine. CRC press; 2006 Jul 7.
29. Boroushaki MT, Mollazadeh H, Afshari AR. Pomegranate seed oil: A comprehensive review on its therapeutic effects. Int J Pharm Sci Res. 2016 Feb 1; 7(2):430.
30. Lansky EP, Newman RA. *Punica granatum* (pomegranate) and its potential for prevention and treatment of inflammation and cancer. Journal of ethnopharmacology. 2007 Jan 19; 109(2):177-206.
31. Naz S, Rezgui M, Rehman R, Nadeem F. Pomegranate an Ancient Seed for Modern Cure–A Review of Potential Applications. International Journal of Chemical and Biochemical Sciences. 2015; 8:78-84.
32. Bhandari PR. Pomegranate (*Punica granatum* L). Ancient seeds for modern cure? Review of potential therapeutic applications. International Journal of Nutrition, Pharmacology, Neurological Diseases. 2012 Sep 1; 2(3):171.
33. Endo EH, Cortez DA, Ueda-Nakamura T, Nakamura CV, Dias Filho BP. Potent antifungal activity of extracts and pure compound isolated from pomegranate peels and synergism with fluconazole against Candida albicans. Research in Microbiology. 2010 Sep 1; 161(7):534-40.
34. Aviram M, Dornfeld L. Pomegranate juice consumption inhibits serum angiotensin converting enzyme activity and reduces systolic blood pressure. Atherosclerosis. 2001 Sep 1; 158(1):195-8.
35. Batra A, Mehta BK, Bokadia MM. Fatty Acid Composition of *P. granatum* Seed Oil. Acta Pharm. Jugosl. 1968; 3(1):63-6.
36. Batta AK, Rangaswami S. Crystalline Chemical Components of Some Vegetable Drugs. Phytochemistry.1973; 12:214-216.
37. Berköz M, Allahverdiyev O. Punicalagin isolated from *Punica granatum* husk can decrease the inflammatory response in RAW 264.7 macrophages. Eastern Journal Of Medicine. 2017 Apr 1; 22(2):57.
38. Zhang X, Yuan W, Zhao Y, Ren Y, Zhao X, Yuan Z. Genome-Wide Identification and Evolutionary Analysis of AOMT Gene Family in Pomegranate (*Punica granatum*). Agronomy. 2021 Feb; 11(2):318.
39. Ganguly S. Medicinal utility of pomegranate fruit in regular human diet: A brief review. International Journal of Forestry and Horticulture. 2017; 3(1):7-18.
40. Anesini C, Perez C. Screening of plants used in Argentine folk medicine for antimicrobial activity. Journal of ethnopharmacology. 1993 Jun 1; 39(2):119-28.
41. Andrade MA, Lima V, Silva AS, Vilarinho F, Castilho MC, Khwaldia K, Ramos F. Pomegranate and grape by-products and their active compounds: Are they a valuable source for food applications?. Trends in Food Science & Technology. 2019 Apr 1; 86:68-84.
42. Mavlyanov S, Islambekov S, Karimdzhanov A, Ismailov A. Polyphenols of pomegranate peels show marked anti tumor and anti-viral action.1997:124-126.
43. Baradaran Rahimi V, Ghadiri M, Ramezani M, Askari VR. Antiinflammatory and anti-cancer activities of pomegranate and its constituent, ellagic acid: Evidence from cellular, animal, and clinical studies. Phytotherapy Research. 2020 Apr; 34(4):685-720.
44. Middha SK, Usha T, Pande V. A review on antihyperglycemic and antihepatoprotective activity of eco-friendly *Punica granatum* peel waste. Evidence-Based Complementary and Alternative Medicine. 2013 Jan 1; 2013.
45. Panth N, Manandhar B, Paudel KR. Anticancer activity of Punica granatum (pomegranate): a review. Phytotherapy research. 2017 Apr; 31(4):568-78.
46. Stover ED, Mercure EW. The pomegranate: a new look at the fruit of paradise. HortScience. 2007 Aug 1; 42(5):1088-92.
47. Rana TS, Narzary D, Ranade SA. Systematics and taxonomic disposition of the genus Punica L. Pomegranate. Fruit Veg. Cereal Sci. Biotechnol. 2010; 4(2):19-25.
48. Shaygannia E, Bahmani M, Zamanzad B, Rafieian-Kopaei M. A review study on *Punica granatum* L. Journal of evidence-based complementary & alternative medicine. 2016 Jul; 21(3):221-7.
49. Purseglove JW. Tropical crops. Dicotyledons 2. Tropical crops. Dicotyledons 2.1968.
50. Watson L, Dallwitz MJ. onwards. The families of flowering plants: descriptions, illustrations, identification, and information retrieval.1992; 25.
51. Lawrence GH. Taxonomy of vascular plants. Macmillan and Co. New York .1951:628-629.
52. Holland D, Hatib K, Bar-Ya'akov I. 2 Pomegranate: botany, Horticulture, Breeding. Horticultural reviews. 2009 Jan 8; 35(2):127-91.
53. Yan M, Zhao X, Zhou J, Huo Y, Ding Y, Yuan Z. The complete chloroplast genomes of *Punica granatum* and a comparison with other species in Lythraceae. International journal of molecular sciences. 2019 Jan; 20(12):2886.
54. LaRue JH. Growing pomegranates in California. Division of Agricultural Sciences, University of California; 1977.
55. Mars M. La culture du grenadier (*Punica granaturn* L.) et du figuier (Ficus carica L.) en Tunisie. Cahiers Options Méditerranéennes. 1995(13):85-95.
56. Levin GM. Pomegranate (*Punica granatum*) plant genetic resources in Turkmenistan. Bulletin des Ressources Phytogenetiques (IPGRI/FAO); Noticiario de Recursos

Fitogeneticos (IPGRI/FAO). 1994.
57. Ismail T, Sestili P, Akhtar S. Pomegranate peel and fruit extracts: a review of potential anti-inflammatory and anti-infective effects. Journal of ethnopharmacology. 2012 Sep 28; 143(2):397-405.
58. Ozgen M, Durgaç C, Serçe S, Kaya C. Chemical and antioxidant properties of pomegranate cultivars grown in the Mediterranean region of Turkey. Food chemistry. 2008 Dec 1; 111(3):703-6.
59. Soriano JM, Zuriaga E, Rubio P, Llácer G, Infante R, Badenes ML. Development and characterization of microsatellite markers in pomegranate (Punica granatum L.). Molecular Breeding. 2011 Jan; 27(1):119-28.
60. Lansky EP, Harrison G, Froom P, Jiang WG. Pomegranate (*Punica granatum*) pure chemicals show possible synergistic inhibition of human PC-3 prostate cancer cell invasion across Matrigel™. Investigational new drugs. 2005 Jan; 23(2):121-2.
61. Basuny AM. Utilization from leaves of olive and pomegranate as a source of bioactive components. Journal of Advances in Biological and Basic Research. 2015; 1:01.
62. Jayaprakash A, Sangeetha R. Phytochemical screening of *Punica granatum* Linn. peel extracts. Journal of academia and industrial research. 2015 Oct; 4(5):160-2.
63. Ali Redha A, Hasan A, Mandeel Q. Phytochemical determinations of Pomegranate (*Punica granatum*) Rind and Aril extracts and their antioxidant, antidiabetic and antibacterial activity. Nat Prod Chem Res. 2018; 6(4):1-9.
64. Belkacem N, Djaziri R, Lahfa F, El-Haci IA, Boucherit Z. Phytochemical screening and in vitro antioxidant activity of various *Punica granatum* l. Peel extracts from Algeria: A comparative study. Phytothérapie. 2014 Dec 1; 12(6):372-9.
65. Satomi H, Umemura K, Ueno A, Hatano T, Okuda T, Noro T. Carbonic anhydrase inhibitors from the pericarps of Punica granatum L. Biological and Pharmaceutical Bulletin. 1993 Aug 15; 16(8):787-90.
66. Noda Y, Kaneyuki T, Mori A, Packer L. Antioxidant activities of pomegranate fruit extract and its anthocyanidins: delphinidin, cyanidin, and pelargonidin. Journal of agricultural and food chemistry. 2002 Jan 2; 50(1):166-71.
67. Mohammad SM, Kashani HH. Chemical composition of the plant Punica granatum L.(Pomegranate) and its effect on heart and cancer. Journal of Medicinal Plants Research. 2012 Oct 17; 6(40):5306-10.
68. Arun N, Singh DP. Punica granatum: a review on pharmacological and therapeutic properties. International journal of pharmaceutical sciences and research. 2012 May 1; 3(5):1240.
69. Jacob J, Rajiv P, Gopalan R, Lakshmanaperumalsamy P. An Overview of Phytochemical and Pharmacological Potentials of *Punica granatum* L. Pharmacognosy Journal. 2019; 11(5).
70. Jain V, Murugananthan G, Deepak M, Viswanatha GL, Manohar D. Isolation and standardization of various phytochemical constituents from methanolic extracts of fruit rinds of *Punica granatum.* Chinese Journal of Natural Medicines. 2011 Nov 1; 9(6):414-20.
71. Wu S, Tian L. Diverse phytochemicals and bioactivities in the ancient fruit and modern functional food pomegranate (*Punica granatum*). Molecules. 2017 Oct; 22(10):1606.
72. Jasuja ND, Saxena R, Chandra S, Sharma R. Pharmacological characterization and beneficial uses of *Punica granatum*. Asian Journal of Plant Sciences. 2012 Aug 20; 11(6):251.
73. Torwane NA, Hongal S, Goel P, Chandrashekar BR. Role of Ayurveda in management of oral health. Pharmacognosy reviews. 2014 Jan; 8(15):16.
74. Hankey A. CAM modalities can stimulate advances in theoretical biology. Evidence-Based Complementary and Alternative Medicine. 2005 Feb; 2(1):5-12.
75. Lad V. The human constitution. Ayurveda: The Science of Self-Healing. Lotus Press, Wilmot. 1985:26-36.
76. Balasubramani SP, Mohan J, Chatterjee A, Patnaik E, Kukkupuni SK, Nongthomba U, Venkatasubramanian P. Pomegranate juice enhances healthy lifespan in Drosophila melanogaster: an exploratory study. Frontiers in public health. 2014 Dec 16; 2:245.
77. Balasubramani SP, Padmagiri G, Venkatasubramanian P, Vidyashankar R, Godbole A. Pomegranate juice improves iron status and ameliorates iron deficiency induced cellular changes in Saccharomyces cerevisiae. Journal of Nutritional Therapeutics. 2015 Oct 28; 4(3):104-12.
78. Sivarajan VV, Balachandran I. Ayurvedic drugs and their plant sources. Oxford and IBH publishing; 1994. / Sivarajan VV, Balachandran I. Ayurvedic drugs and their plant sources. In: Mohan P, editor. Oxford7 IBH Publishing Co. Pvt. Ltd.; 1994.
79. Shekokar S, Thombare C. A Phytopharmacological Review of *Dadim-Punica granatum* Linn. International Journal of Ayurveda and Pharma Research. 2019 Jul 12:21-31.
80. Muddgal D. Dravyagun Vijnana. Ayurvedic hindi pustak bhandar. 2nd edition 2019.
81. Sharma PV. Dravyagun Vigyan. Chaukambha Bharti Academy, Varanasi. 2019.
82. Sawant MV. Dadim–Pomagranate (Punica granatum Linn.)–An Advantageous Fruit. International Journal of Scientific Research. 2020 Dec 21;9(11):72-73.
83. Rahman AH, Alam MS, Khan SK, Ahmed F, Islam AK, Rahman MM. Taxonomic studies on the family Asteraceae (Compositae) of the Rajshahi division. Research Journal of Agriculture and Biological Sciences. 2008; 4(2):134-40.
84. Ali K, Khan S, Khan N, Khan W, Rahman IU, Ullah F, Nisar M. Ethnobotanical and ecological study of *Punica granatum* in Dir district, Khyber Pakhtunkhwa, Pakistan. Regulatory Mechanisms in Biosystems. 2017; 4(8):656-661.
85. Qasim M, Abideen Z, Adnan MY, Ansari R, Gul B, Khan MA. Traditional ethnobotanical uses of medicinal plants from coastal areas. J coast life Med. 2014; 2(1):22-30.
86. Abbasi AM, Khan MA, Khan N, Shah MH. Ethnobotanical survey of medicinally important wild edible fruits species used by tribal communities of Lesser Himalayas-Pakistan. Journal of ethnopharmacology. 2013 Jul 9; 148(2):528-36.
87. Rosas-Piñón Y, Mejía A, Díaz-Ruiz G, Aguilar MI, Sánchez-Nieto S, Rivero-Cruz JF. Ethnobotanical survey and antibacterial activity of plants used in the Altiplane region of Mexico for the treatment of oral cavity infections. Journal of ethnopharmacology. 2012 Jun 14; 141(3):860-5.
88. Delfan B, Bahmani M, Hassanzadazar H, Saki K, Rafieian-Kopaei M, Rashidipour M, Bagheri F, Sharifi A. Ethnobotany study of effective medicinal plants on gastric problems in Lorestan province, West of Iran. Journal of Chemical and Pharmaceutical Research. 2015(2):483-92.
89. Nasab FK, Khosravi AR. Ethnobotanical study of medicinal plants of Sirjan in Kerman Province, Iran. Journal of ethnopharmacology. 2014 May 28; 154(1):190-7.
90. Dolatkhahi M, Dolatkhahi A, Nejad JB. Ethnobotanical study of medicinal plants used in Arjan–Parishan protected area in Fars Province of Iran. Avicenna journal of phytomedicine. 2014 Nov; 4(6):402.
91. Jouad H, Haloui M, Rhiouani H, El Hilaly J, Eddouks M. Ethnobotanical survey of medicinal plants used for the treatment of diabetes, cardiac and renal diseases in the North centre region of Morocco (Fez–Boulemane). Journal of Ethnopharmacology. 2001 Oct 1; 77(2-3):175-82.
92. Ouhaddou H, Boubaker H, Msanda F, El Mousadik A. An ethnobotanical study of medicinal plants of the Agadir Ida Ou Tanane province (southwest Morocco). Journal of Applied Biosciences. 2014; 84:7707-22.
93. Silva JD, Nascimento MG, Grazina LG, CASTRO KD, Mayo SJ, Andrade IM. Ethnobotanical survey of medicinal plants used by the community of Sobradinho, Luís Correia, Piauí, Brazil. Embrapa Meio-Norte-Artigo em periódico indexado (ALICE). 2015.
94. Uzun M, Kaya A. Ethnobotanical research of medicinal plants in Mihalgazi (Eskişehir, Turkey). Pharmaceutical biology. 2016 Dec 1; 54(12):2922-32.
95. Semenya S, Potgieter M, Erasmus L. Ethnobotanical survey of medicinal plants used by Bapedi healers to treat diabetes mellitus in the Limpopo Province, South Africa. Journal of Ethnopharmacology. 2012 May 7; 141(1):440-5.
96. Partha P, Hossain AE. Ethnobotanical investigation into the Mandi ethnic community in Bangladesh. Bangladesh Journal of Plant Taxonomy. 2007; 14(2):129-45.
97. Rahman AM, Sultana N, Islam AR, Zaman AT. Study of Medical Ethno-botany at the Village Genda under Savar Upazilla of District Dhaka, Bangladesh. Journal of Medicinal Plants. 2013; 1(5):72-86.
98. Rahmatullah M, Mukti IJ, Haque AK, Mollik MA, Parvin K, Jahan R, Chowdhury MH, Rahman T. An ethnobotanical survey and pharmacological evaluation of medicinal plants used by the

Garo tribal community living in Netrakona district, Bangladesh. Advances in Natural and Applied Sciences. 2009 Sep 1; 3(3):402-18.
99. Zumbroich TJ. The ethnobotany of teeth blackening in Southeast Asia. Ethnobotany Research and Applications. 2009 Nov 16; 7:381-98.
100. Sarri M, Boudjelal A, Hendel N, Sarri D, Benkhaled A. Flora and ethnobotany of medicinal plants in the southeast of the capital of Hodna (Algeria). Arabian Journal of Medicinal and Aromatic Plants. 2015; 1(1):24-30.
101. Kumar M, Paul Y, Anand VK. An ethnobotanical study of medicinal plants used by the locals in Kishtwar, Jammu and Kashmir, India. Ethnobotanical Leaflets. 2009; 2009(10):5.
102. Jain DL, Baheti AM, Jain SR, Khandelwal KR. Use of medicinal plants among tribes in Satpuda region of Dhule and Jalgaon districts of Maharashtra—an ethnobotanical survey. 2010; 9(1):151-157.
103. Tetali P, Waghchaure C, Daswani PG, Antia NH, Birdi TJ. Ethnobotanical survey of antidiarrhoeal plants of Parinche valley, Pune district, Maharashtra, India. Journal of ethnopharmacology. 2009 Jun 22; 123(2):229-36.
104. Ayyanar M, Ignacimuthu S. Ethnobotanical survey of medicinal plants commonly used by Kani tribals in Tirunelveli hills of Western Ghats, India. Journal of ethnopharmacology. 2011 Apr 12; 134(3):851-64.
105. Samy RP, Thwin MM, Gopalakrishnakone P, Ignacimuthu S. Ethnobotanical survey of folk plants for the treatment of snakebites in Southern part of Tamilnadu, India. Journal of Ethnopharmacology. 2008 Jan 17; 115(2):302-12.
106. Agarwal A. Critical issues in quality control of herbal products. Pharma times. 2005; 37(6):09-11.
107. Simmler C, Graham JG, Chen SN, Pauli GF. Integrated analytical assets aid botanical authenticity and adulteration management. Fitoterapia. 2018 Sep 1; 129:401-14.
108. Wallace LJ, Boilard SM, Eagle SH, Spall JL, Shokralla S, Hajibabaei M. DNA barcodes for everyday life: routine authentication of natural health products. Food Research International. 2012 Nov 1; 49(1):446-52.
109. Hossain H, Ahmed T, Howlader MS, Dey SK, Hira A, Ahmed A, Sen R. In-vitro antioxidant potential from the leaves of *Punica granatum* Linn. Grown in Bangladesh. Int J Pharm Phytopharmacol Res. 2012; 2(3):160-6.
110. Boggula N, Peddapalli H. Phytochemical analysis and evaluation of in vitro anti-oxidant activity of *Punica granatum* leaves. International Journal of Pharmacognosy and Phytochemical Research. 2017; 9(8):1110-8.
111. Singh RP, Chidambara Murthy KN, Jayaprakasha GK. Studies on the antioxidant activity of pomegranate (*Punica granatum*) peel and seed extracts using in vitro models. Journal of agricultural and food chemistry. 2002 Jan 2; 50(1):81-6.
112. Duman AD, Ozgen M, Dayisoylu KS, Erbil N, Durgac C. Antimicrobial activity of six pomegranate (*Punica granatum* L.) varieties and their relation to some of their pomological and phytonutrient characteristics. Molecules. 2009 May; 14(5):1808-17.
113. Bassiri-Jahromi S, Katiraee F, Hajimahmoodi M, Mostafavi E, Talebi M, Pourshafie MR. In vitro antifungal activity of various Persian cultivars of *Punica granatum* L. extracts against Candida species. Jundishapur Journal of Natural Pharmaceutical Products. 2015; 10(3).
114. Shafighi M, Amjad L, Madani M. In vitro antifungal activity of methanolic extract of various parts of *Punica granatum* L. Int J Sci Eng Res. 2012; 3(12):2229-5518.
115. Pradeep BV, Manojbabu MK, Palaniswamy M. Antibacterial activity of *Punica granatum* L. against gastro intestinal tract infection causing organisms. Ethnobotanical leaflets. 2008; 2008(1):143.
116. Choi JG, Kang OH, Lee YS, Chae HS, Oh YC, Brice OO, Kim MS, Sohn DH, Kim HS, Park H, Shin DW. In vitro and in vivo antibacterial activity of Punica granatum peel ethanol extract against Salmonella. Evidence-Based Complementary and Alternative Medicine. 2011 Jan 1; 2011:1-8.
117. Wang Y, Huang M, Yang X, Yang Z, Li L, Mei J. Supplementing punicalagin reduces oxidative stress markers and restores angiogenic balance in a rat model of pregnancy-induced hypertension. The Korean journal of physiology & pharmacology.2018; 22(4):409-417.
118. Kumar M, Dandapat S, Sinha MP. Hepatoprotective activity of *Punica granatum* leaf extract against Carbon Tetrachloride induced Hepatotoxicity in Rats. Balneo Research Journal. 2018 Feb 1; 9(1):24-7.
119. Gharib E, Kouhsari SM. Study of the antidiabetic activity of *Punica granatum* L. fruits aqueous extract on the alloxan-diabetic wistar rats. Iranian journal of pharmaceutical research: IJPR. 2019; 18(1):358.
120. Sudheesh S, Vijayalakshmi NR. Flavonoids from *Punica granatum*—potential antiperoxidative agents. Fitoterapia. 2005 Mar 1; 76(2):181-6.
121. Nasiri E, Hosseinimehr SJ, Akbari J, Azadbakht M, Azizi S. The effects of Punica granatum flower extract on skin injuries induced by burn in rats. Advances in pharmacological sciences. 2017 Jan 19; 2017.
122. Sumner MD, Elliott-Eller M, Weidner G, Daubenmier JJ, Chew MH, Marlin R, Raisin CJ, Ornish D. Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease. The American journal of cardiology. 2005 Sep 15; 96(6):810-4.
123. Türk G, Sönmez M, Aydin M, Yüce A, Gür S, Yüksel M, Aksu EH, Aksoy H. Effects of pomegranate juice consumption on sperm quality, spermatogenic cell density, antioxidant activity and testosterone level in male rats. Clinical nutrition. 2008 Apr 1; 27(2):289-96.
124. Forest CP, Padma-Nathan H, Liker HR. Efficacy and safety of pomegranate juice on improvement of erectile dysfunction in male patients with mild to moderate erectile dysfunction: a randomized, placebo-controlled, double-blind, crossover study. International journal of impotence research. 2007 Nov; 19(6):564-7.
125. Joseph MM, Aravind SR, George SK, Varghese S, Sreelekha TT. A galactomannan polysaccharide from Punica granatum imparts in vitro and in vivo anticancer activity. Carbohydrate polymers. 2013 Nov 6; 98(2):1466-75.
126. Houston DM, Bugert J, Denyer SP, Heard CM. Anti-inflammatory activity of Punica granatum L.(Pomegranate) rind extracts applied topically to ex vivo skin. European Journal of Pharmaceutics and Biopharmaceutics. 2017 Mar 1; 112:30-7.
127. Ross RG, Selvasubramanian S, Jayasundar S. Immunomodulatory activity of *Punica granatum* in rabbits—a preliminary study. Journal of ethnopharmacology. 2001 Nov 1; 78(1):85-7.
128. Riaz A, Khan RA. Anticoagulant, antiplatelet and antianemic effects of *Punica granatum* (pomegranate) juice in rabbits. Blood Coagulation & Fibrinolysis. 2016 Apr 1; 27(3):287-93.