

Review Article

Medicinal Properties of Pomegranate

Esfandiar Hassani Moghaddam^{1*}, Mahdi Shaaban² Asghar Sepahvand³

¹Seed and Plant Certification and Registration Research Institute, (Lorestan branch), AREEO, Karaj, Iran

²Young researchers and Elite Club, Boroujerd Branch, Islamic Azad University, Boroujerd, Iran

³Razi Herbal Medicines Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran

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Abstract

As an ancient fruit tree, pomegranate (*Punica granatum* L.) is one of the unique fruit trees cultivated in the Mediterranean region, particularly in Iran and in the Middle East. This tree is cultivated in majority of Iranian provinces. The mineral content and medicinal properties of pomegranate have been indicated in many previous research reports. The present review focuses on the medicinal properties of pomegranate fruit. Based on previous researches, we concluded that pomegranate has several medicinal uses in human diet. All parts of pomegranate tree have medicinal uses. Anti-cancer property is the main medicinal characteristic of this fruit tree. Pomegranate fruit has high amounts of phenolic compounds with a remarkable antioxidant activity. Moreover, one of the principal phenolic ingredients of pomegranate is ellagic acid which is characterized by high antioxidant activity. This review focuses on the recent researches on the medicinal properties of pomegranate fruit. The antioxidant activities and medicinal properties of pomegranate that are effective in the treatment of certain diseases were identified. However, we collected the best results of previous studies in carried out on this subject.

Keywords: Pomegranate, Medicinal properties, Ellagic acid, Antioxidant

***Corresponding Author:** Esfandiar Hassani Moghaddam, Research Assistance Professor, Seed and Plant Certification and Registration Research Institute, (Lorestan branch), AREEO, Karaj, Iran. Email: es_hassani@yahoo.com.

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Introduction

Pomegranate (*Punica granatum* L.) is an ancient fruit tree and has been consumed in various countries for thousands of years. Pomegranate has been considered as a manifestation of life, longevity, health, magnificence, fruitfulness, awareness, morality and spirituality (1). In ancient Egyptian culture, pomegranate fruit was known as an epitome of success. In traditional medicine, various components of this tree have several therapeutic effects. Pomegranate belongs to the family *Punicaceae* as the

smallest plant family (2). Pomegranate has several anatomical parts such as seed, juice, peel, leaf, flower, bark, and roots (3). It has a genus (*Ponita*) and two species called *Punica granatum* L. (common Pomegranate) and *Punica protopunica* (non-edible pomegranate) (4). *Punica protopunica* is endemic to Scootera Island, Yemen, and is the only similar species associated with the *Punica granatum* which is cultivated (5). This tree (Anar in Persian) grows both as a fruit-bearing deciduous shrub and a small tree growing between 5 to 8 meters in height (6).



Figure 1. Pomegranate tree, flower and fruit in different growth stages.

In traditional Indian medicine, pomegranate is "a drug for the withdrawal of the worms. The fruit peel is a powerful astringent which is used to treat diarrhea. Moreover, its fruit juice is anti-fever (7).

Pomegranate juice contains minerals such as iron, which is relatively more abundant than others, and elements such as calcium, selenium, chlorine, cobalt, chromium, cesium, copper, potassium, magnesium, manganese, molybdenum, sodium, rubidium, scandium, serum, tien strontium and zinc (8).

Punica granatum L. has been used in traditional medicine for centuries in the Middle East, India, and China. It has been consumed for several therapeutic reasons. More exactly, *Punica granatum* L. has been used in the treatment of various ailments, including inflammation, rheumatism and the pain of a simple sore throat. Distinct parts of a tree such as the bark, leaves, immature fruits, and fruit rind have certain medicinal significance. As Satomi *et al.* note, the pericarps of *Punica granatum* L. encompasses seven highly active inhibitors of carbonic anhydrase (CA),

namely punicalin, punicalagin, granatin B, gallagylidilactone, punicalagin, pedunculagin and tellimagrandin (9).

Botanical Property

Pomegranate is a shrub that inherently tends to create several trunks, and in some cases it has a crawling state. In cultural condition, as a small tree pomegranate grows up to 5 meters, and under natural conditions its height could reach 7 meters (10). Furthermore, there are also semi-dwarf cultivars that do not grow taller than 1.5 meters (11). Pomegranate leaves are rectangular, linear, shiny and transparent (12). The young leaves are red, but they are green at older stages. Mature leaves are green, full, smooth, and crack-free. They have short petioles (13).

The fruit is the result of an ovarian development. The fruit is attached to a tree by a short axis (13). The pomegranate fruit is of a special type called balausta, which contains plenty of seeds (figure 1). The edible part of pomegranate seed is an external epidermis of the seed cover which is called aril and is meaty and juicy (7). Pomegranate has a shorter juvenile period

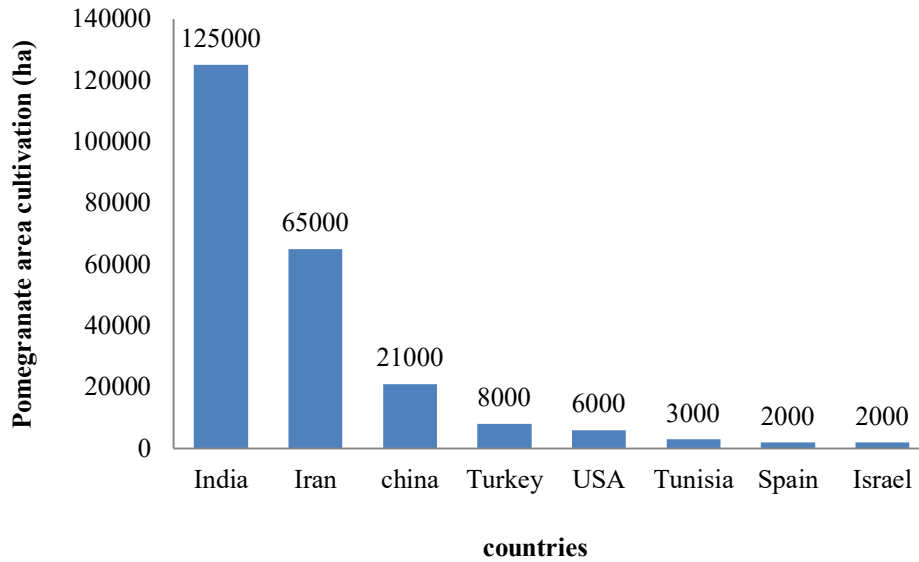


Figure 2. Pomegranate production area in the major producer countries in 2017.

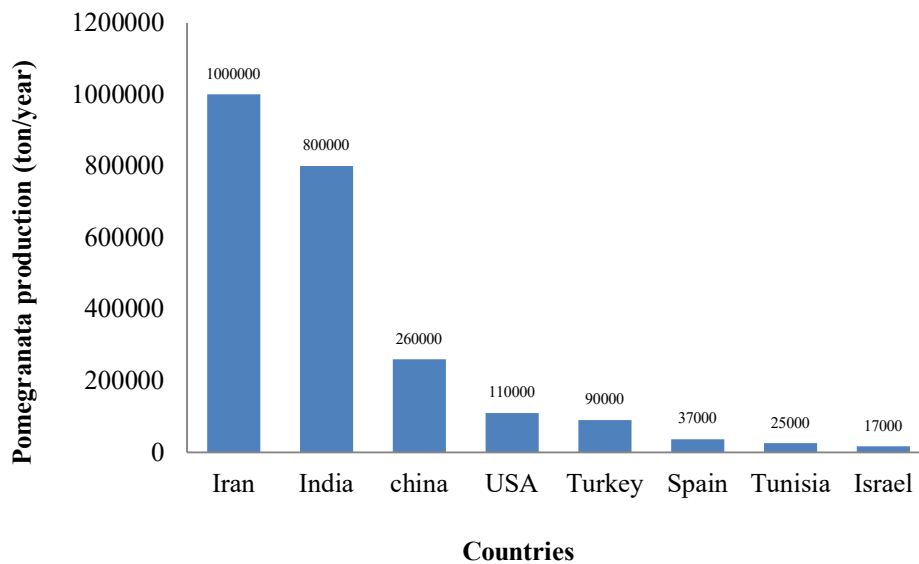


Figure 3. Pomegranate production per year in the major producer countries in 2017.

compared to other fruit trees. Normally, pomegranate propagation is conducted by cutting inter to the flowering stage in the first year and in its fruits set at the second year of planting. The fruit color of the first trees will be similar to the fruit color of the mature trees of the same variety, but the size of the fruit of the first-year crop is smaller (14). The pomegranate fruit includes three parts: the seeds,

about 3% of the weight of the fruit, and themselves contain 20% oil; the juice, about 30% of the fruit weight; and the peels which also include the interior network membranes. Pomegranate fruit is consumed throughout the world in various ways like freshly prepared or processed juice, sauce, oil, vinegar, etc.

Origin

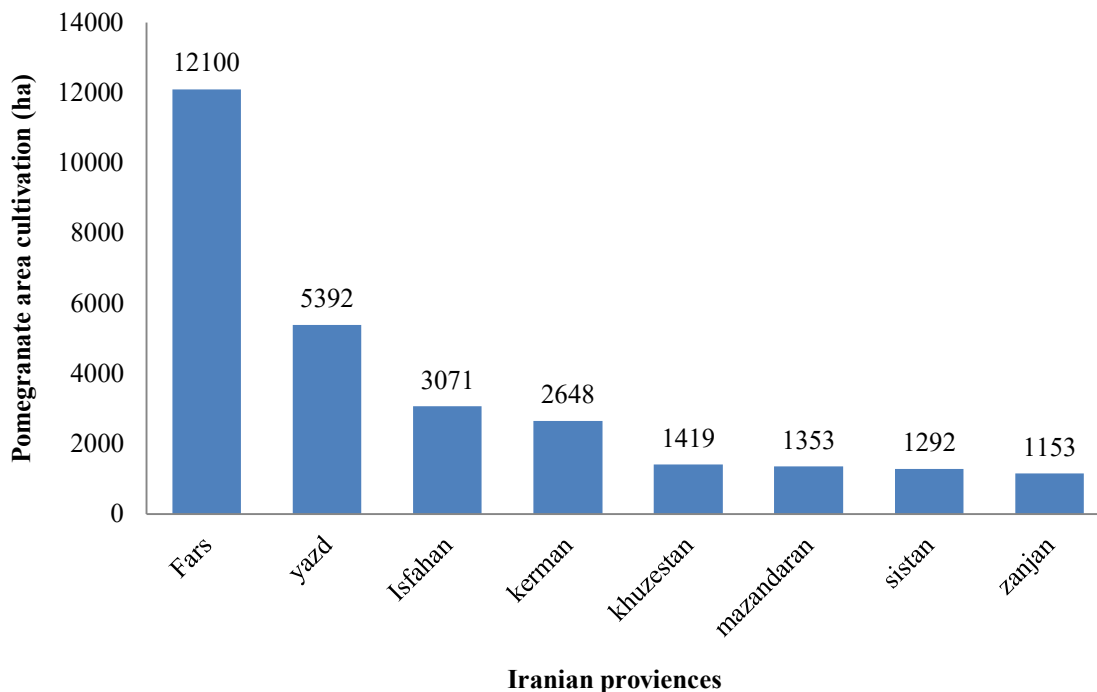


Figure 4. Pomegranate production area in the major provinces of Iran in 2017.

Pomegranate belongs to the family *Punicaceae*. Nowadays, commercial orchards of pomegranate trees are abundantly found in many regions throughout the world, especially in the Mediterranean region in which high quality fruits are grown (14). Pomegranate is one of the seven ancient edible fruits that have been mentioned in the Bible (15). It is a native of Iran, and is widely grown in both arid and semi-arid areas worldwide (16). Pomegranate has irregular branches, and spiny branches which are found in cold and semi-arid regions and in tropical regions (17).

Pomegranate is able to grow in the drier climates of California and Arizona. Moreover, it has been cultivated in Iran, Iraq, Azerbaijan, Armenia, Afghanistan, Pakistan, India, Russia, Bangladesh and the Mediterranean region for several millennia (18). Pomegranate is highly valued in human medicine, and its components have a wide range of clinical uses (3). The *P. granatum*, which is the predominant species, is cultivated worldwide whereas *P. protopunica* is only restricted to the Island of Socotra (Republic of Yemen) (6). Pomegranate is extensively cultivated in Iran, India, Afghanistan and the Mediterranean countries, and to some extent in the USA, China, Japan and Russia (10). It is considered

as one of the most significant fruits and is cultivated on a commercial scale in Iran.

Centers of Pomegranate Distribution and Cultivation in the World

Pomegranate is a native of Iran and neighboring countries. The origin and habitats of pomegranate are not yet known, but most botanists believe that the primary distribution locations of pomegranate are the Caucasus, Mazandaran beaches and the Zagros ranges, but it was gradually extended to Central Asia, Himalaya, the Middle East, Asia Minor and Mediterranean countries (8). Nowadays, pomegranate is grown in Central Asia from Iran and Turkmenistan to the north of India, and is a native of these areas. Vavilov maintained that pomegranate origin could be attributed to the Middle East (14).

The major areas of the natural regeneration of pomegranate with regard to climate are the four regions of Caspian, Mediterranean, Iran and Turan, and finally the Persian Gulf and Oman. Currently, in addition to Iran, which has the most pomegranate orchard in the world, pomegranate is found in the countries of Turkey, Afghanistan, Pakistan, India, Armenia, Uzbekistan, Tajikistan, Azerbaijan, Georgia, Libya, Lebanon, Sudan, Burma, Bangladesh, Cyprus, Greece, Morocco, Spain, France, China, Japan,

Occupied Palestine, the United States and Australia (19).

India has the most extended regions of pomegranate cultivation in the world (Figure 2). However, Iran is the main pomegranate producer in the world with 1 million ton pomegranate production per year (Figure3).

The Rate of Cultivation and Production of Pomegranate

In Iran, Fars province has the greatest pomegranate production area (Figure 4) and also the highest fruit production per year (Figure 5). Having 760 varieties, Iran has the richest pomegranate germplasm in the world. The highest levels of the cultivation and production of pomegranate after Iran are in India, Turkey and Spain, but in recent years, China and the United States have also begun to build gardens at a

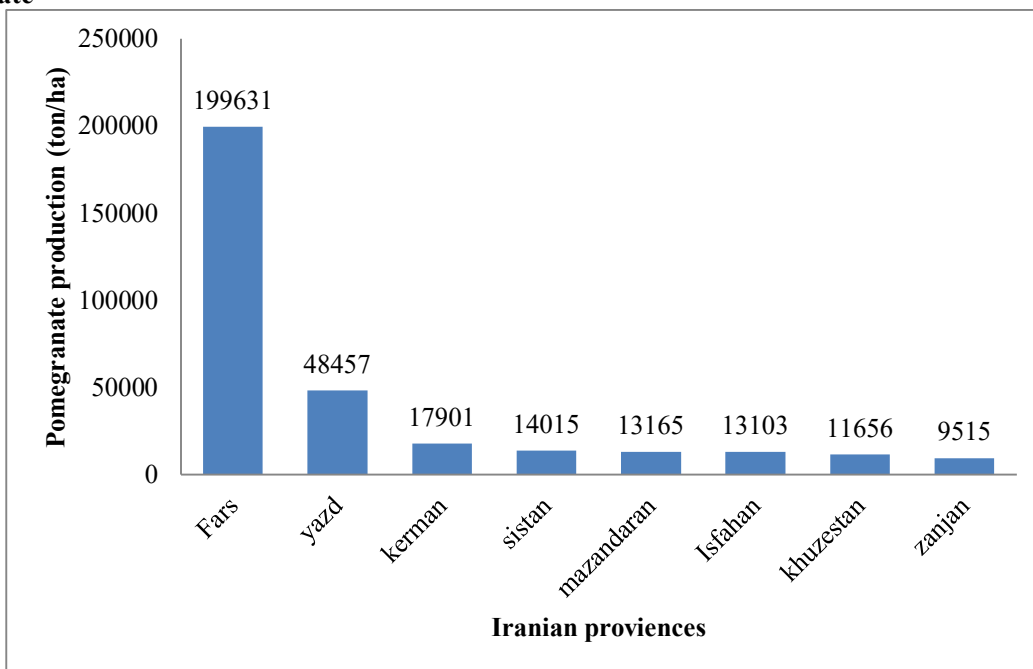


Figure 5. Pomegranate production per year in the major provinces of Iran in 2017.

Table 1: The chemical composition of pomegranate fruit.

Constituent (%)	Edible fruits	
	Fresh fruit	Dry weight basis
Moisture	78	19
Protein	1.6	7.27
Total sugars	14.6	66.36
Ascorbic acid	16	72.73
Ash	0.7	3.18
Acidity	0.58	2.64

Source: Chavan *et al.* (1993)

widespread level (9). The average yield of Iranian pomegranate was 1490kg / ha. The highest level of the cultivation of pomegranate in Iran is related to Fars province with 11613 hectares, which constitutes about 21% of the country's cultivated regions. After Fars, Isfahan, Markazi, Khorasan Razavi and Yazd provinces have rank the second to fifth with regard to the country's pomegranate cultivation area respectively. According to the available data, Fars province ranks first in the production of pomegranate in Iran with the production of 199631 tons. Markazi, Isfahan, Khorasan Razavi and Yazd, provinces have the highest production rate in Iran after Fars respectively. Moreover, the highest level of production per unit area or, in other words, the highest yield was related to Fars province with the production of 166.43 kg / ha. Pomegranate cultivation is currently taking place in 27 provinces of the Iran and is constantly

expanding (10).

Table 2: The mineral composition of pomegranate fruit.

Mineral (mg/100g)	Edible fruits	
	Fresh fruit	Dry weight basis
Ca	10	45
P	70	318
Mn	44	200
K	133	604
Na	0.9	4.09
Fe	1.79	8.14
Zn	0.82	3.73
Mg	0.77	3.5
Cu	0.34	1.55

Source: Chavan *et al.* (1995)

Climatic Conditions of Pomegranate's Growth

Today, different kinds of pomegranates are cultivated in tropical and semi-tropical regions around the world in different micro-climatic regions. The commercial areas of pomegranate production are now in the regions of North Africa, Egypt, Occupied Palestine, Syria, Lebanon, Turkey, Greece, Cyprus, Italy, France, Spain, Portugal, Iran, Iraq, India, China, Afghanistan, Bangladesh, Myanmar, Vietnam, Thailand, Kazakhstan, Turkmenistan, Tajikistan, Kyrgyzstan, Armenia and Georgia. Various cultivars of pomegranate are also cultivated in the New World (USA and Chile), and new gardens are being created in South Africa, Australia, Argentina and Brazil (14). Therefore, climatic conditions are balanced for the culture of pomegranate in Mediterranean-like climates that have high sunlight, mild and hot summers, and are dry and without summer rainfall during the final stages of fruit development. In such a situation, the fruit reaches to the maximum size, high color and the accumulation of balanced sugar without the risk of bursting (4).

Pomegranate is resistant to drought, and is suitable for warm and temperate conditions. The range of pomegranate cultivation is up to 41 degrees north and south, and its growing height is 100-1700 meters above the sea level. Its maximum cultivating height is 2600 meters above the sea level. Winter is the most important climatic factor affecting the growth and cultivation of pomegranate. In pomegranate

trees, temperatures below -15°C cause cold damage. For optimal fruits, more summer heat is needed (20). Pomegranate is resistant against drought and hard climatic conditions of winter. It can grow well under desert conditions, and is frequently affected by high salinity. To be regarded as proline means being a possible indicator of drought stress in pomegranate fruits (21).

Pomegranate cultivars exhibited similar reactions to certain environmental stress such as drought, but the severity of these reactions varied in distinct cultivars (22). It has also been indicated that all the investigated cultivars exhibited similar reactions to drought stress treatments, but the severity of these reactions varied in distinct cultivars. It was also argued that different cultivars had different responses to drought conditions, so that Rabab of Nyriz and Malase Yazd cultivars were more tolerant to drought compared to the other tolerant cultivars that were examined. However, among the cultivars that were studied, Nadery Badroud was suggested as a sensitive cultivar to drought stress (23).

Commercial Pomegranate Cultivars in Iran

The diversity and number of pomegranate cultivars in Iran are significant. Cultivars of more than 760 pomegranates cultivars are obtained from different provinces, every one of which has its own traits in terms of likeness, size, premature aging, refreshment, and storage, resistance to diseases, pests, aging, sunburn and taste (12).

The most important pomegranate cultivars of the country have large fruits with a weight of 250-350g a fairly thick skin with good transport and a clear red color, large grains of red to black, sugar 14 to 20 percent, and flavors (24).

The most important cultivars of Iran are in Fars province (Rabab Niriz, Atabaki, Makhvosh and Khodro), Isfahan province (Naderi Badood, Molasah Reza, Makhmali Shahr Reza, Black Seed of Shahr Reza), Markazi province (Meles Saveh, Aghamandali, Yousef Khani and Alec), Yazd province (Malas Yazd, Mehkosh, Shirin Shahvar, Zaggh and Goltafati) and Khorasan province (Shirestan, Ferdos, Kheszbarsakan, Molasses and sugar Kashmar) (24).

Pomegranate in the Holy Quran and Hadiths

Pomegranate has been mentioned as "ar-romman" in the Holy Quran, in sura Al-An'am (verses 99 and 141)

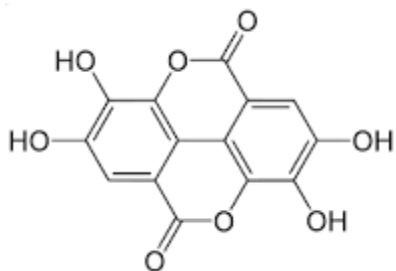


Figure 6. The chemical structure of ellagic acid.

and sura Al-Rahman (verse 68). The fact that pomegranate, date, grapes, and olive have been mentioned in these verses deems reflection. Moreover, it might be possible to examine the scientific correlation and structural links between “rain water, stars, plants, and the creation of humans” which have been mentioned in these verses as a research project. The noted verses have emphasized the diversity of fruits growing in the same soil and water, looking at and reflecting upon fruits, how they ripen, not eating unripe fruits, and eating fresh and ripe ones (25). In verses adjacent to verse 99 of Al-Anam discussing the same topic (verses 95-98), the existence of dense seeds of plants as well as rupturing the seeds and cores by God have been mentioned as signs of God for reflection. According to Islamic hadiths, pomegranate is the best fruit. It is effective in blood purification, strengthens the stomach, resolves skin tumors, treats joint inflammations, strengthens the heart, induces happiness, and resolves migraine, among other things (26). For Prophet Muhammad (Sallallah alaihi wasallam), there was no fruit on Earth more favorable than pomegranate (27).

Examples of hadiths related to pomegranate are mentioned below. Numerous hadiths introduce pomegranate as a factor illuminating and giving life to the heart, resolving obsession, adjusting humors, resolving hunger, making food more favorable after becoming full, purifying the blood, reducing blood pressure, eradicating diseases, maintaining health during sleep, increasing mental activity, purifying the stomach, and even escaping sins and disobedience to God. The Prophet says: “Pomegranate is the most important fruit” (28).

Imam Reza (Alaihi sallam) refers to pomegranate as a fruit that could beautify children. He holds that sucking sour and sweet pomegranate gives strength

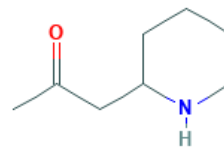


Figure 7. The chemical structure of pelletierine.

and freshness to the blood (28). Moreover, smelling pomegranate before eating this fruit illuminates the heart, and pomegranate firewood repels insects. He also forbids using pomegranate wood as toothpick (29). According to Imam Ali (Alaihi sallam), eating pomegranate albedo “purifies the stomach, repels temptations, and resolves yellowing of the tooth as well as bad breath” (28).

According to Imam Sadegh (Alaihi sallam), eating pomegranate accelerates growth in children, gives freshness to the face, strengthens the mind, strengthens the liver, the spleen, and the heart, helps resolve acute coughing, and treats digestive worms. He also remarks that pomegranate is a laxative (29). The marvelous and everlasting presence of pomegranate continues from worldly gardens to heavenly ones, as if it comes back to life on doomsday together with the heavenly human being.

Pomegranate’s Uses

Pomegranate is a delicious and nutritious fruit. Its flowers, peel, roots and stems have long been used for medicinal purposes. Pomegranate peel was consumed in the Middle Ages in the Middle East because of its high levels of tannin and phenol that enable it to be used as a dye. Furthermore, pomegranate is grown as an ornamental plant in some regions in Iran due to having highly beautiful and coarse flowers (30). Its fruit skin pigments are used to obtain the natural color of brown, yellow, and red with specific methods. Pomegranate also has medical uses. The food portion of the pomegranate fruit could be used for fresh consumption or for fresh fruit juices, jams, syrups and syrups (31).

Pomegranate seeds, or dried pomegranate seeds, have distinct sour tastes, and are commercially available in many countries in Eastern and Western Asia. They are consumed at high levels. It is also used in pharmaceutical systems for the preparation of appetizer and gastrointestinal drugs (32). Since

pomegranate wood has a lot of fibrous and has a homogeneous and elastic texture, it could be used in the production of ornamental objects and woody handicrafts (17).

Chemical Compounds of Pomegranate

There are several metabolites in distinct parts of the fruit of pomegranate including sugars, organic acids, alkaloids, polyphenols, flavonoids, anthocyanins, fatty acids and vitamins (15). As four poorly active inhibitors, gallic acid, granatin A, corilagin and ellagic acid, have antimicrobial, antifungal, and antimutagenic activities, (*Punicaceae*). They are considered as ellagitannins. Punicalin and punicalagin noncompetitively inhibit pntrophenyl acetate (33). Gallic acid and catechin are indeed the principal components of *Punica granatum* that are responsible for its healing activity. Tables 1 and 2 show that the edible portion of pomegranate contains a significant proportion of organic acids, soluble solids, polysaccharides, vitamins, fatty acids and mineral elements of nutritional significance that are excellent dietary sources for human health (4).

It seems that ellagic acid ellagitannins including punicalagins, punicic acid, flavonoids, anthocyanidins, anthocyanins, and estrogenic flavonols and flavones are the most therapeutically efficient pomegranate constituents. Figure 6 indicates the ellagic acid structure.

Alkaloids

Alkaloids are organic compounds of complex herbs that have plant origins with significant biological activities. Today, identified more than 10 types of alkaloids in pomegranate trees have been identified the most important of which are pelletierine (Figure 7) and its derivatives that include isopelletierine, methylpelletierine and pseudopelletierine (9).

Tannins

Tannins are a class of secondary metabolites with biological significance that are found in plants. The most important property of tannins is their astringency. Tannins, by inactivating microbial and fungal enzymes, inhibit the invasion of these microorganisms to plants, and play a protective role in plants. Regardless of the biological significance of tannins in plant life, these compounds have long been used by humans. They were initially used in leather manufacturing. Moreover, tannins are very important

in industries, animal husbandry and medicine, and they have remarkable effects in ecosystems. Three types of yellow tannins, including ellagitannin, granatan and punicalin, are found in pomegranate. Altogether, ten types of tannins have been found in different parts of the pomegranate tree, most of which are found in fruit peel and leaves and are now used for pharmaceutical and industrial purposes (11).

Phenolic Compounds

Phenolic compounds are secondary plant-derived metabolites that include a large group of compounds, and have a significant contribution to human and animal diets. These compounds are highly significant because they are able to protect plants against biological and environmental pressures. They are created in reaction to fungal and bacterial pathogens and / or lengthy exposure to ultraviolet radiation (34). Most of phenolic compounds are produced in a common biosynthetic pathway, which is the result of the incorporation of the materials into paths known as shikimate and acetate-malonate. Phenylalanine is a substrate for phenylalanine ammonia lyase that catalyzes the first reaction of the phenylpropanoid pathway and leads to the formation of more phenolic compounds (35).

Polyphenols

Plants produce a large group of secondary products that have a phenolic group. Each phenolic group has a hydroxyl group located on an aromatic chain. Plant phenols are chemically a heterogeneous group consisting of approximately 10,000 separate compounds. Some of them are soluble only in organic solvents, and others are soluble carboxylic acids and glycosides in water, and the rest are large molecular-weight insoluble polymers. Due to their chemical diversity, phenols play different roles in plants (36). Tannins, especially punicalagin, and also anthocyanins and ellagic acid, are members of the polyphenols group (37). Polyphenols are powerful compounds that can neutralize free radicals and toxic effects of these invasive agents and play an important role in human health.

Medicinal Compositions

Some chemical compositions in all parts of pomegranate such as fruit, juice and related parts have medicinal and antioxidant properties. Pomegranate has several anatomical organs such as peel, seeds, and arils

that have medicinal property. Pomegranate chemical composition varies based on the cultivar, growing region, climate, maturity, cultivation practice, and storage conditions (13). Some compositions such as organic acids, phenolic compounds, sugars, water-soluble vitamins, and minerals of pomegranates have been already investigated in former studies (35, 38). Roughly 50% of the total fruit weight pertains to the peel, which is a significant source of bioactive compounds, including phenolics, flavonoids, ellagitannins, and proanthocyanidin compounds. However, major chemical compositions such as ellagic acid, ellagitannins, punic acid, flavonoids, anthocyanins, estrogenic flavonoids and flavones have medicinal properties (5).

The peel and arils, which are the main reservoir of flavonoids and include flavonols (luteolin, quercetin, and kaempferol), flavanols, and anthocyanins (pelargonidin-3-glucoside, cyanidin-3-glucoside, delphinidin 3-glucoside, pelargonidin 3,5-diglucoside, cyaniding 3,5-diglucoside and delphinidin 3,5-diglucoside). Moreover, the juice of pomegranate contains the organic acids such as gallic acid, chlorogenic acid and citric acid along with gallotannins and ellagitannins (24).

The pomegranate juice contains 85.4% water, 10.6% total sugar, 1.4% pectin and 0.2-1% polyphenols. The other compositions in pomegranate juice are alpha-tocopherols, organic acids, indole acids etc. (36). However, pomegranate seeds contain 12-20 % oil in weight that had 7% linoleic acid. The chemical composition of pomegranate parts is used for the treatment of inflammation and cancer. Phenols, some of which are unique ones, could be detected in pomegranate pericarp, leaf and flower. Moreover, the peel contains complex polysaccharides. Triacylglycerols that are found in the seeds constitute the oil. They contain high levels of punicic acid. Furthermore, this oil contained sterols, steroids and cerebroside in very small levels. Apart from the seed oil, noticeable antioxidant activities have been found in lignin and their derivatives (3).

Satomi *et al.* (33) noted that the pericarps of *pomegranate* contains seven inhibitors of carbonic anhydrase that are highly active. These inhibitors include punicalin, punicalagin, granatin B, gallagylidilactone, punicalagin, pedunculagin and

tellimagrandin. They also remarked that there are four weakly active inhibitors, i.e. gallic acid, granatin A, corilagin and ellagic acid, that exhibit antimicrobial, antifungal, antimutagenic activities and are considered as ellagitannins.

Punicalin and punicalagin noncompetitively inhibit pnitrophenyl acetate as a substrate (33).

Pomegranate is a natural source of phenolic compounds containing antioxidants such as tannin, polyphenols, flavonoids and vitamins. Other pomegranate antioxidants such as tocopherols, and anthocyanins represent their preventive and therapeutic properties. Biochemical properties of these chemicals are often due to their reduction properties as reducing agents, hydrogen vectors, extinguishers of single oxygen and even molecules with chelating power metal ions (39).

Medicinal Products

Pomegranate could be used as a fresh fruit, juice, fermented juice, dried seeds, frozen seeds, tinned grains, pomegranate sauce, jelly, vinegar, and dough, and also as flavoring products. Pomegranate juice, which is the most common pomegranate product, is prepared by a rotating device with pressure so that the kernel would not be crushed. The juices is obtained with pasteurized heat at the temperature of 79-82°C, and then it is cooled. Subsequently, the juice sediments for 24 hours, and finally straightens. The clear juice which is obtained could be protected with preservative chemicals (40). According to previous findings, there are high amounts of total phenol and flavonoid in pomegranate leaves that have high antioxidant capacity, and could possibly be used in pharmaceutical industry to produce drugs (41).

Phytotherapy

Phytotherapy is a complementary procedure which is used to prevent and treat certain diseases (40). In traditional medicine, different parts of pomegranate tree are used in the prevention and treatment of several diseases. Pomegranate has long been used since the ancient times has been used in diverse systems of medicine. Julie (2) notes that in the Middle East and India, pomegranate was described also as a remedy for diabetes. Schwartz *et al.*, (42) argue that the edible part of the fruits contains acids, sugars, vitamins, polysaccharides, polyphenols and minerals. Nonetheless, several determinants might be influential

in the chemical alterations such as cultivars, environmental conditions, ripening, storage and postharvest treatments, which might in turn influence fruit quality and health beneficial compounds. With regard to the therapeutic uses of pomegranate, Julie states that in Ayurvedic medicine, pomegranate is used as an antiparasitic agent, and a blood tonic (2). He also remarks that it is efficient in healing aphthae, diarrhea and ulcers. Julie also argues that pomegranate was used in Unani medicine, which was practiced in the Middle East and India, as a remedy for diabetes (2).

Medicinal Properties

Juice: Pomegranate juice is effective in lowering the risk factors of heart disease such as LDL oxidation, macrophage oxidative status, and foam cell formation (15). It has also been argued that these components reduce cancer cells' attraction to a chemical signal that might develop the metastasis of prostate cancer to the bones. Furthermore, pomegranate juice is effective against prostate cancer. Pomegranate juice could be consumed as an antibacterial and antiviral agent that contributes to the reduction of dental problems.

Peel: The amount of polyphenols, which includes catechins, gallic catechins condensed tannins and prodelphinidins, in pomegranate peel is three times more than the fruit pulp. The existence of higher phenolic content in the peel suits it to be used as a dietary supplement and food preservative (32).

Three: The rind of the fruit and the bark of the pomegranate tree are efficient traditional remedies against diarrhea, dysentery and intestinal parasites (15).

Seeds: Proteins, crude fibers, vitamins, minerals, pectin, sugars, polyphenols, isoflavones, phytoestrogen coumestrol, sex steroid, and estrone are found in pomegranate seeds (43). The seeds and juice could be consumed as tonics for the heart, throat, and eyes. Moreover, they could be consumed for several purposes, such as stopping nose bleeds and gum bleeds, toning the skin, firming-up sagging breasts and treating hemorrhoids (15). Furthermore, it has been indicated that the seed oil, lignin and their derivatives have significant antioxidant properties (3).

Ash: Ashes of *P. grantum* have a protective effect

against skin infections. The powder prepared from its rind is used as tooth powder, and also is employed in cosmetic industries (5).

Pomegranates contain high levels of antioxidants called flavonoids. These flavonoids effectively fight against certain types of cancers. The fruit juice reduces the high risk of prostate and breast cancers, and fights the existing cancer cells in the body (32). The regular consumption of the fruit contributes to the maintenance of the normal blood flow in the body. Moreover, it reduces the risks of cardiac arrests and heart attacks. Pomegranate juice is efficient in the prevention of coronary ailments in diabetic patients. Furthermore, pomegranate seed extract provides the blood with iron. Hence, it contributes to the reduction of the occurrence of anemic symptoms such as weakness, fatigue, and hearing loss.

The juice, peel, and seed oil of pomegranate are capable of exhibiting anti-cancer properties that enable them to inhibit the proliferation of cells, cell cycles, and angiogenesis. The capability of pomegranate to combat diverse types of cancers has been confirmed. Some studies have reported the evidence confirming cancer chemoprevention or treatment by pomegranate (49). However, pomegranate fruit, juice, seed and seed oil are useful against several types of cancers, i.e. colon, lung, mouth, prostate, breast, skin and leukemia cancers due to their antioxidant, antiproliferation, antiangiogenesis and anti-inflammatory mechanisms of action. As one of the major components of pomegranate juice and seed oils, ellagic acid is effective in combating against cancers of pancreas, breast, prostate, colon, skin, leukaemia, liver and neuroblastoma (31). Some researchers have indicated that punicalic acid could inhibit the proliferation of estrogen-insensitive breast cancer cells. The lipid peroxidation of cells and activation of protein kinase are considered as the two principal reasons contributing to the inhibition of proliferation (16). Toi *et al.* (46) revealed that pomegranate seed oil and fermented juice polyphenols inhibit the promotion of the apoptosis of breast cancer cells and also the proliferation of breast cancer cells.

Certain pharmaceuticals drugs and supplements that are useful for human health have been produced by international companies. Some body lotions, for instance, have been produced by Guangzhou Beauty

Natural Cosmetics Factory and Green Tech International Industrial Limited. Moreover, some drug supplements have been produced by Hill Pharmaceutical Co., Ltd, Shanghai Seebio Biotech. Inc, Swansom health products, Super-Smart, Xanthigen, Piping Rock and Granatum Plus companies in different forms such as pills, capsules, gel capsules, syrups and gray powder. Many medicinal plant extracts in powder form such as ellagic acids have been produced as antioxidant and anti-aging substances by Nanjing Zelang Medical Technology Co., Ltd. Furthermore, some plant oils extracted from pomegranate seeds have been produced by Daxinganling Lingonberry Boreal Biotech Co., Ltd for skin moisturizing.

Antioxidant Properties

The antioxidant activity of pomegranate has been examined *in vitro* in several studies. Various methods could have been used to determine this particular property. Some researches concentrate on the comparative studies of the antioxidant activities of distinct fruits and vegetables (43). Pomegranate juice had the greatest antioxidant activity, and there were remarkable linear correlations between phenolic concentration and its antioxidant capacity. All parts of pomegranate could exhibit antioxidant activity against oxidative stresses. A review that has recently been carried out focused on the chemical components of diverse parts of *P. granatum* as well as their potential to prevent and treat inflammation and cancer. Wild pomegranate ethanolic seed extract exhibited noticeable antioxidant and anti-ulcer activities (11). Seventy-nine percent of the antioxidant activity of pomegranate seeds extract was lost during light exposure (17). Moreover, it has been revealed that extracts obtained from pomegranate seeds by the use of distinct solvents could exhibit various levels of antioxidant activity (44).

Pomegranate rind has antioxidant activity the same as other parts of this fruit. Rajan *et al.* (20) indicated in their research that the extracts of *P. granatum* fruit rind is a potential source of natural antioxidant. Qu *et al.* (12) maintained that pomegranate peel had a greater level of antioxidant activity in comparisons with its seeds. They also stated that dried peel extract could significantly increase the antioxidant activity

of the juice, proportional to the concentrations that are added.

Cambay *et al.* (34) noted that pomegranate fruit had antioxidant activity, and could be used to treat oxidative stress caused by diabetes mellitus which in turn results in damages in the brain and consequently the impairment of cognitive functions. Kishore *et al.* (37) examined the role of pomegranate (*Punica granatum* L.) fruit extract, and exhibited that its antioxidant activity was greater than the antioxidant capacity of red wine and green tea against adriamycin-induced oxidative stress in chick embryos.

However, significant levels of antioxidant activity was observed in arils, juice and rinds of *Punica granatum* fruits and their aqueous and ethyl acetate extracts (19). Gil *et al.* (45) investigated the antioxidant activity of pomegranate juices and extracts, and found that certain hydrolyzable tannins were present in the fruit rind. This phenomenon could explain the higher level of the antioxidant activity of commercial juices in comparison with experimental ones. Acids, sugars, vitamins, polysaccharides, polyphenols and minerals are found in the edible part of pomegranate. Nevertheless, several determinants might be effective in chemical alterations, such as cultivars, environmental conditions, ripening, storage and postharvest treatments, which might influence the fruit quality and those compounds that are beneficial for health (42). Kaur *et al.* (44) indicated that the alcoholic (ethanolic) extract of pomegranate flowers exhibited 81.6% antioxidant activity in DPPH model system.

The Nutritional Value of Pomegranate

Traditionally, pomegranate flowers, leaves, young shoots skin, and peel have been used throughout the world (17). The edible portions of pomegranate fruit are acids, sugars, vitamins, polysaccharides, polyphenols, iron, calcium, chlorine, cobalt, chromium, cesium, copper, potassium, magnesium, manganese, molybdenum, sodium, rubidium, selenium, strontium and zinc (46). There are several anthocyanins in pomegranate ariel, including delphinidin 3 and 5-diclofen acid, cyanidin 3 and 5-dicarboxylic acid, delphinidin 3-glycoside, cyanidin 3-glycoside, and polygonidine 3-glycoside (18). The peel and seeds of this fruit are good sources of anthocyanins (2). Moreover, pomegranate is rich in potassium (about 27mg per 100g). The potassium

which is found in pomegranate plays a significant role in improving muscle activity and intracellular water regulation. It is also able to improve vitamin C performance in the body. Pomegranate purifies the blood and removes its toxins. The consumption of this fruit regulates body fluids, and could be effective in the treatment of intestinal anomalies such as diarrhea (47).

Pomegranate is one of the major, unique sources of several physiological factors in the human body, which has significant effects on human health. The flavonoids in the pomegranate have an enzymatic inhibitory effect in addition to their antioxidant properties. The fruit and its juice are good supplements that might be effective in prolonging life and preventing heart disease and cancer (16).

Pomegranate is rich in various flavonoids that inhibit free radicals and also have inhibitory effects on the lipoxygenase enzyme. Hence, it could be consumed as a nutritional agent against acquired immune deficiency syndrome or AIDS (48). Moreover, pomegranate is one of the 9 herbs that are used in the formulation of Japanese drugs for the treatment of AIDS (35). The pomegranate peel and its root have alkaloids, which are nowadays used in medicine and pharmacy (7). This part of the fruit has long been used to treat common diarrhea (7). Pomegranate oil contains high amounts of unsaturated fatty acids of the omega-3 type that are highly significant in the prevention of cardiovascular diseases and atherosclerosis (31).

Conclusion

Pomegranate fruit contains a wide range of chemical components with medicinal properties. These components include polyphenols, alkaloids, and vitamins with antioxidant properties. This review article indicates that pomegranate is a valuable fruit in human diet. This fruit can play a key role in the prevention of several diseases such as certain types of cancers. Hence, the consumption of pomegranate in any form is highly recommended, particularly for patients, in order to utilize it for its medicinal properties.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. S M. Outline of the beginnings of alchemy and its antecedents. *Am J Chin Med.* 1984;12:21-32.
2. MT JJ. Therapeutic applications of pomegranate (*Punica granatum L.*): A review. *Altern Med Rev.* 2008;13(123-144).
3. Lansky EP NR. *Punica granatum* (pomegranate) and its potential for prevention and treatment of inflammation and cancer. *J Ethnopharmacol.* 2007;109:177-206.
4. Chavan AR. Physicochemical properties of pomegranate rind powder. *Beverage and Food World.* 1995;22(1):36-41.
5. Afaq ZM, Khan N, Dreher M, Mukhtar H. Protective effect of pomegranate-derived products on UVB-mediated damage in human reconstituted skin. *Exp Dermatol.* 2009;18(6):553-61.
6. JS J. Therapeutic applications of pomegranate (*Punica granatum L.*): A review. *Altern Med Rev.* 2008;13(2):128-44.
7. Naovi KM, Vohora SB. Antibacterial, anti-fungal and anthelmintic investigations on Indian medicinal plants. *Fitoterapia* 1991;62:222-5.
8. Waheed S SN, Rahman A, Zaidi JH, Ahmad S. INAA for dietary assessment of essential and other trace elements in 14 fruits harvested and consumed in Pakistan. *J Radioanal Nucl Chem.* 2004;260:523-6.
9. Jafri AM, Javed K, Singh S. Effect of *Punica granatum* Linn. (flowers) on blood glucose level in normal and alloxan induced diabetic rats. *Journal of Ethnopharmacology.* 2000;70:309-14.
10. Narzary D MK, Rana TS, Ranade SA Analysis of genetic diversity among wild pomegranates in Western Himalayas, using PCR methods. *Sci Hortic.* 2010;121:237-42.
11. Gill NS, Jain A, Arora R, Bali M. Antioxidant and anti-ulcerogenic activity of wild *Punica granatum* ethanolic seed extract. *Research Journal of Medicinal plants.* 2012;6(1):47-55.
12. Qu W ZP, Haile M. Extraction modeling and activities of antioxidants from Pomegranate marc. *Journal of Food Engineering* 2010;99:16-23.
13. Fadavi BM, Azizi MH, Bayat M. Physicochemical composition of ten pomegranate cultivars (*Punica granatum L.*) grown in Iran. *Food Sci Technol Int.* 2005;11:113-9.
14. Holland D, Hatib K, Bar-Yáakov I. Pomegranate: botany, horticulture, breeding. In: *Horticultural Reviews.* Publication W-B, editor. New Jersey; 2009.
15. Bhowmik D, Harish Gopinath B, Pragati Kumar S, Aravind G, Sampath Kumar KP. Medicinal Uses of *Punica granatum* and Its Health Benefits. *Journal of Pharmacognosy and Phytochemistry.* 2013;1(5):28-35.
16. Grossmann ME MN, Schuster T, Cleary MP Punicic acid is an -5 fatty acid capable of inhibiting breast cancer proliferation. *Int J Oncol.* 2010;36:421-6.
17. Pedriali FA, Santos P, Silva M, Severino D, Dilva M B. Antioxidant activity, cito- and phototoxicity of Pomegranate (*Punica granatum L.*) seed pulp extract". *Cienc Tecnol Aliment.* 2010;30(4):1017-21.
18. Adhami KN, Mukhtar H. Cancer chemoprevention by pomegranate: Laboratory and clinical evidence. *Nutr Cancer.* 2009;61(6):811-6.
19. Ricci DGL, Bucchini A, Fraternali D. Antioxidant activity of *Punica granatum* fruits. *Fitoterapia.* 2006;77(4):310-2.
20. Rajan S. MS, Deepa V.M., Sathya K., Shajitha S., Thirunalasundarii T Antioxidant potentials of *Punica granatum* fruit rind extracts. *International Journal of Pharmacy and Pharmaceutical Sciences.* 2011;3(3):82-8.
21. Halilova H Y. Does climate change have an effect on proline

- accumulation in pomegranate (*Punica granatum* L.) fruits. *Sci Res Essay*. 2009;4:1543-6.
22. Hassani Moghaddam E. Screening of six Iranian commercial pomegranate (*Punica granatum* L.) cultivars in response to drought stress based on some morphological, physiological and biochemical markers. Hamedan: BU-Ali Sina University; 2015.
 23. Hassani Moghaddam E, Esna-Ashari, M. and Rezaeijad, A. Effect of Drought Stress on Some Physiological Characteristics in Six Commercial Iranian Pomegranate (*Punica granatum* L.) Cultivars. *The Journal of Plant Production Technology*. 2016;15(1):1-11.
 24. Mena P GA, Collado-Gonzalez J, Ondono S, Garcia-Viguera C, Ferreres F. Sustained deficit irrigation affects the colour and phytochemical characteristics of pomegranate juice. *J Sci Food Agric*. 2013;93(8):1922-7.
 25. Ghara'ati M. Translation and interpretation of the Holy Quran (summary of the ten-volume Tafsir Noor) (3rd ed.). Lessons from the Quran Cultural Center; 2016. p. 146.
 26. Faghihi Rezaee M. Translation of the Holy Quran: Annotations on selected verses and a table of topics, for students Tehran: Islamic Republic of Iran Center for Publication of the Holy Quran; 2015.
 27. Rezaee Esfahani MA. Interpretation of the Holy Quran (Mehr Javan: An interpretation of Tafsir Mehr). Qom: Nasim-e Hayat 2012.
 28. Mohammadi Reyshahri M. Encyclopedia of medical hadiths Qom: Dar al-hadith 2004.
 29. Fa'ali MT. *he Razavi lifestyle: Health and nutrition*. Mashhad: Imam Reza International Cultural Institution 2015.
 30. Sadegi N, JBOMR, Photovat M. Antioxidant activity of Iranian Pomegranate (*Punica granatum* L.) seed extracts. *J Agri Sci Tech*. 2009;11:633-8.
 31. Maria G, Miguel MANaMDA. Pomegranate (*Punica granatum* L.): A medicinal plant with myriad biological properties - A short review. *Journal of Medicinal Plants Research*. 2010;4(25):2836-47.
 32. 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.
 33. Satomi H UK, Ueno A, Hatano T, Okuda T, Noro T. Carbonic anhydrase inhibitors from the pericarps of *Punica granatum* L. *Biol Pharm Bull*. 1993;16:787-90.
 34. Cambay Z BG, Tuzcu M, Bal R. Pomegranate (*Punica granatum* L.) flower improves learning and memory performances impaired by diabetes mellitus in rats. *Acta Physiol Hung*. 2011;98(4):209-20.
 35. Tezcan F G-OuM, Diken T, Elik B, Erim FB. Antioxidant activity and total phenolic, organic acid and sugar content in commercial pomegranate juices. *Food Chem*. 2009;115(3):878-7.
 36. Chaturvedula V. SPaIP. Bioactive Chemical Constituents from Pomegranate (*Punica granatum*) Juice, Seed and Peel-A Review. *International Journal of Research in Chemistry and Environment* 2011;1:1-18.
 37. Kishore R K, SD, Parthasarathy P.R. Embryo protective effect of Pomegranate (*Punica granatum* L.) fruit extract in adriamycin-induced oxidative stress. *Indian Journal of Biochemistry & Biophysics*. 2009;43:106-11.
 38. Davidson MH MK, Dicklin MR, Feinstein SB, Witchger MS, Bell M, McGuire DK, Provos JC, Liker H, Aviram M. Effects of consumption of pomegranate juice on carotid intima-media thickness in men and women at moderate risk for coronary heart disease. *Ame J Cardiol*. 2009;104(7):936-42.
 39. Seeram N SRN, Heber D. Pomegranates: Ancient roots to modern medicine. CRC Press/Taylor & Francis, editor. Boca Raton 2006.
 40. Akpınar-Bayızit A. TOaLY-E. The Therapeutic Potential of Pomegranate and Its Products for Prevention of Cancer, Cancer Prevention - From Mechanisms to Translational Benefits. Georgakilas DAG, editor; 2012.
 41. Hassani Moghaddam E, Esna-Ashari, M. and Shaaban M. An Investigation of the Secondary Metabolites and Antioxidant Capacity of Some Commercial Iranian Pomegranate (*Punica granatum* L.) Cultivars under Drought Stress. *Med J*. 2018;3(1):14-25.
 42. Schwartz E TR, Glazer I, Bar-Ya'Akov I, Wiesman Z, Tripler E, Bar-Ilan I, Fromm H, Borochoy-Neori H, Holland D, Amir R. Environmental conditions affect the color, taste, and antioxidant capacity of 11 pomegranate accessions' fruits. *J Agric Food Chem*. 2009;57(9179-9209).
 43. Stangeland T RS, Lye KA. Total antioxidant in 35 Ugandan fruits and vegetables. *Food Chem*. 2009;113:85-91.
 44. Kaur G JZ, Athar M, Alam S. *Punica granatum* (pomegranate) flower extract possesses potent antioxidant activity and abrogates Fe-NTA induced hepatotoxicity in mice. *Food and Chemical Toxicology*. 2006;44:982-93.
 45. Gil M I, FA, Hess-Pierce B, Deirdre M, Adel A. K. Antioxidant activity of Pomegranate juice and its relationship with phenolic composition and processing. *J Agric Food Chem*. 2000;48:4581-9.
 46. Toi M BH, Ramachandran C, Melnik SJ, Imai A, Fife RS, Carr RE, Oikawa T, and Lansky EP. Preliminary studies on the anti-angiogenic potential of pomegranate fractions in vitro and in vivo. *Angiogenesis*. 2003;6(2):121-8.
 47. Cravatto G BL, Genzini L, Garella D. Phytotherapeutics: An evaluation of the potential of 1000 plants. *J Clin Pharm Ther*. 2010;35:11-48.
 48. Syed DN AF, Mukhtar H. Pomegranate derived products for cancer chemoprevention. *Sem Cancer Biol*. 2007;17:377-85.
 49. Amin ARMR KO, Khuri FR, Shin DM. Perspectives for cancer prevention with natural compounds. *J Clin Oncol*. 2009;27:2712-25.

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