



Nutritional and therapeutic potentials of *Punica granatum*: A review

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Abstract

Pomegranate, a Mediterranean fruit, has grown in prominence as a prospective source of nutraceutical. Its juices and extracts were examined for their possible health benefits in a number of conditions. The experimental findings of antioxidant, anti-inflammatory, antimicrobial activities of the pomegranate juice are because of its important phyto-chemical constituents like phenolic acids, flavonoids, tannins. Pomegranate seed oil is a rich source of bioactive lipids due to the presence of polyunsaturated fatty acids with potential physiological benefits, promoting their use in human nutrition. Its activity in chronic disorders such as cancer, diabetes, and obesity has been described in recent clinical study. Pomegranate may be utilized to deliver potential medicinal effects for specific illness conditions, as well as advantages to human health, according to the existing data. The purpose of this review is to highlight some nutritional potentials of pomegranate that causes its use in many health promoting Properties.

Keywords: pomegranate, polyphenols, flavonoids, anticarcinogenic, antidiabetic

Introduction

Pomegranate is the well-known fruit of a plant (*Punica granatum* L.), widely grown throughout West Asia, the Mediterranean region, and other regions of the world, particularly where the climate is favorable for its growth. Except for dwarf varieties that can reach a height of 12 meters, the shrub generally grows to a height of 5 m, but in certain circumstances, it can attain the morphology of a tree that grows to a height of 10 m. This ancient fruit has been widely used in folk medicine. Its flowers are red and can occur either as single blossoms or clusters of several blossoms. Pomegranate is a berrylike fruit with a leathery rind coating sweet juicy arils^[1, 2]. Pomegranate is a part of Punicaceae family having genus *Punica*. It has both cultivated (*Punica granatum*) and wild (*Punica sativa*) species (*Punica protopunica*). The cultivated varieties are native to Central Asia, Africa, and Europe's Mediterranean regions. The Socotra islands are home to the wild pomegranate (*Punica protopunica*). It is distinguished by its pink (rather than red) blossoms and smaller, less delicious fruit. The pomegranate belongs to the Lythraceae family of flowering plants. *Punica* was previously classified in its own family, Punicaceae, but new phylogenetic analyses have revealed that it belongs in the Lythraceae, and the Angiosperm Phylogeny Group has classified it in that family. Pomegranate can tolerate a hard and dangerous environment. It's designed to survive heat, drought, and a lack of moisture. The plant's adaptability, hardiness, low maintenance cost, consistent but high yields, higher keeping quality, great table and therapeutic properties, and the ability to put the plant into a rest period when irrigation potential is normally low, all point to opportunities for expanding the pomegranate region^[3, 4].

Pomegranates have a spherical fruit with a leathery peel or rind that is generally yellow with a light or dark pink, or a deep crimson overlay. Arils, which are the fruit's edible section, can be stored as syrup or used to make fruit leather, jam, wine, vinegar, jelly as well as a flavoring and coloring alternative in beverages^[5, 6]. Pomegranates are high in bioactive chemicals.

The arils, pith, leaves, flower, bark, and root of the pomegranate can be split in to the different morphological compartments, each with unique pharmacological and toxicological properties. Various chemical compounds extracted from various portions of the plant have been documented to have diverse pharmacological activity, resulting in the treatment of a wide range of illnesses and ailments. Pomegranate has been used to treat diarrhea, parasite diseases, and diabetes mellitus since ancient times. Pomegranate was used in Greco-Arab and Islamic medicine to cure sore throats, inflammation, and rheumatism. Pomegranate's anti-inflammatory, antioxidant, and anticancer properties have prompted an increasing number of researches to use it to treat a variety of medical issues.

Studies have demonstrated that pomegranates may use as natural remedy to chemical treatment because of their ability to fight a wide variety of infections^[7, 8, 9].

The purpose of this review is to highlight some nutritional opportunities of pomegranate that causes its use in many health promoting properties. Additionally, pomegranate's anti-diabetic effects are being promoted.

Chemical composition of Pomegranate

Pomegranates are a well-known source of beneficial nutrients. There include hydrolysable tannins, condensed tannins, flavonols (luteolin, quercetin, and kampferol), anthocyanins (pelargonidin-3-glucoside, cyanidin-3-glucoside, delphinidin-3-glucoside, pelargonidin 3, 5-diglucoside, cyanidin 3, 5-diglucoside, and delphinidin 3, 5-diglucoside), phenol gallotannins (hydrolyzed to gallic acid) and glucose, as well as ellagitannins (hydrolyzed to ellagic acid) are found in the peel and pith^[10, 11].

The edible section of the pomegranate is not less than 50% which include arils (40%) and seeds (10%), with the inedible peel making up the rest. Peels contain phenolics, flavonoids, ellagitannins, and proanthocyanidine chemicals, as well as minerals and complex polysaccharides. Sugars, phenolic compounds, minerals, water soluble vitamins and organic acids in *Punica granatum* L. have been found to differ significantly in various investigations^[11, 12].

Water (85%), sugars (glucose, sucrose, and fructose), pectin (1.5), organic acids such as citric, malic, tartaric, succinic, fumaric, and ascorbic acid, phenolics, and flavonoids (mostly anthocyanins) make up the arils^[12, 13]. Seeds contain proteins, crude fibres, vitamins, minerals, pectin, sugars, polyphenols, and isoflavones. Oil derived from seeds is high in polyunsaturated fatty acids such as linolenic and linoleic acids. Seeds also contain lipids such as punicic acid, oleic acid, stearic acid, and palmitic acid^[14, 15]. Table 1 summarizes the compounds found in the fruit of the pomegranate.

Table 1: Phytochemicals present in pomegranate fruit

Pomegranate Plant part	Constituents
Juice	gallate (EGCG), quercetin, and rutin; mineral elements; amino acids ^[16, 17, 18] .
Seed oil	ellagic acid; fatty acids; sterols; conjugated linolenic acid, linoleic acid, oleic acid, stearic acid, Punicic acid; ellagic acid ^[19, 20, 21]
Pericarp (peel, rind)	Punicalagins, gallic acid, catechin, EGCG, quercetin, rutin, anthocyanidins, and other flavonoids, luteolin, kaempferol ^[22, 23]
Leaves	Flavonols like luteolin, apgenin; ellagitannins (punicalin and punicafolin) ^[12, 24]
Flower	Triterpenoids like ursolic, maslinic, and asiatic acid, as well as gallic acid ^[24, 25]
Roots and bark	Ellagitannins; piperidine alkaloids ^[25, 26]

The bioactive chemicals found in fruits and vegetables are responsible for their good health effects in the prevention and treatment of illnesses. The presence of phytochemical constituents such as phenolic acids, flavonoids, and tannins enhances the nutritional value of pomegranates^[27].

Phenolic compounds

These are the most important components of the pomegranate, and they are responsible for the majority of the fruit's functional qualities. Flavonoids are the most frequent and extensively dispersed subgroup of natural polyphenols, which vary from basic component such as phenolic acids, phenylpropanoids, and flavonoids to highly polymerized compounds like lignins, melanins, tannins^[28].

Flavonoids have 15 carbon atoms organized in a C6-C3-C6 pattern and are low-molecular-weight compounds. A three-carbon bridge connects two benzene rings, which is usually in the form of a heterocyclic ring^[29].

The biggest and most important categories of flavonoids found in the arils of pomegranate, which are utilized to extract the juice, are anthocyanins. These pigments are responsible for the reddish color of the fruit and juice. Many different anthocyanins can be found in juice, including cyanidin-3-O-glucoside, cyanidin-3, 5-di-O-glucoside, delphinidin-3-O-glucoside, delphinidin-3, 5-di-O-glucoside, pelargonidin-3-O-glucoside, pelargonidin-3, and 5-di-O-glucoside.

The amount of hydroxylated groups in the molecule, the kind and quantity of attached sugars to their structures, the aromatic or aliphatic carboxylate molecules connected to the sugar in the compound, and the locations of these bonds are all different^[30]. There are two types of phenolic acids found in pomegranate juice: To begin with, hydroxybenzoic acids (gallic acids and ellagic acids), on the other hand hydroxycinnamic acids (caffeic acid, chlogenic acid)^[31].

Tannins

Tannins are plant polyphenols that are grouped into three chemical and biological definite groups: condensed tannins or proanthocyanidines; hydrolysable tannins or ellagitannins and gallotannins. Pomegranate peel is high in tannins, particularly punicalin, pedunculagin, and punicalagin^[23]. Ellagitannins are hexahydroxydiphenic acid esters with a polyol, most commonly glucose or quinic acid^[32]. As demonstrated in "Figure 2," Gallagic, ellagic, and ellagic acid glycosides are among the hydroxybenzoic acids found in pomegranate peel. The principal anthocyanidins found are cyanidin, pelargonidin, and delphinidin^[33], with flavonoids such kaempferol, luteolin, and quercetin also present^[22].

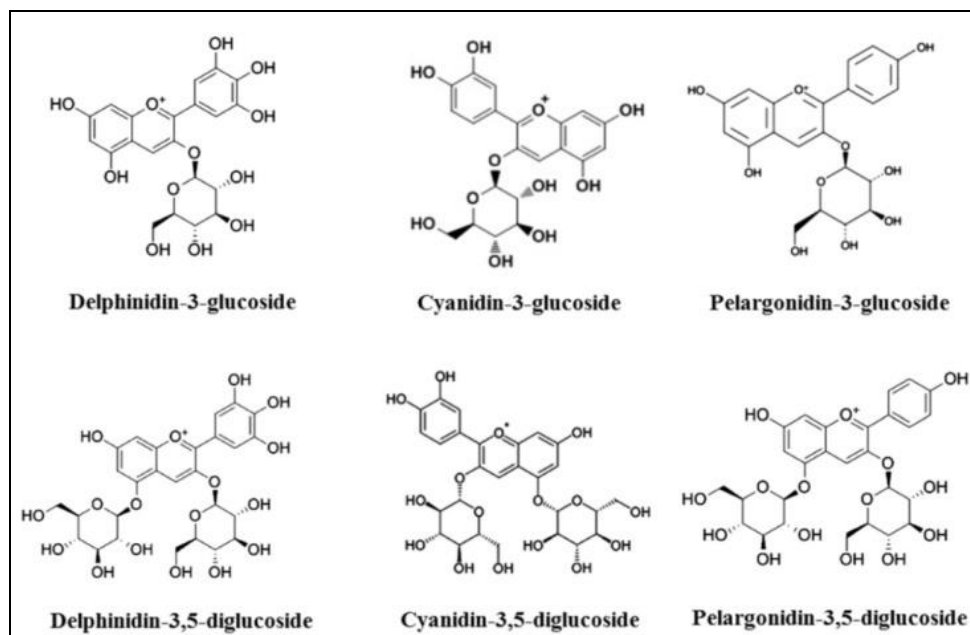


Fig 1: Principal anthocyanins present in pomegranate juice

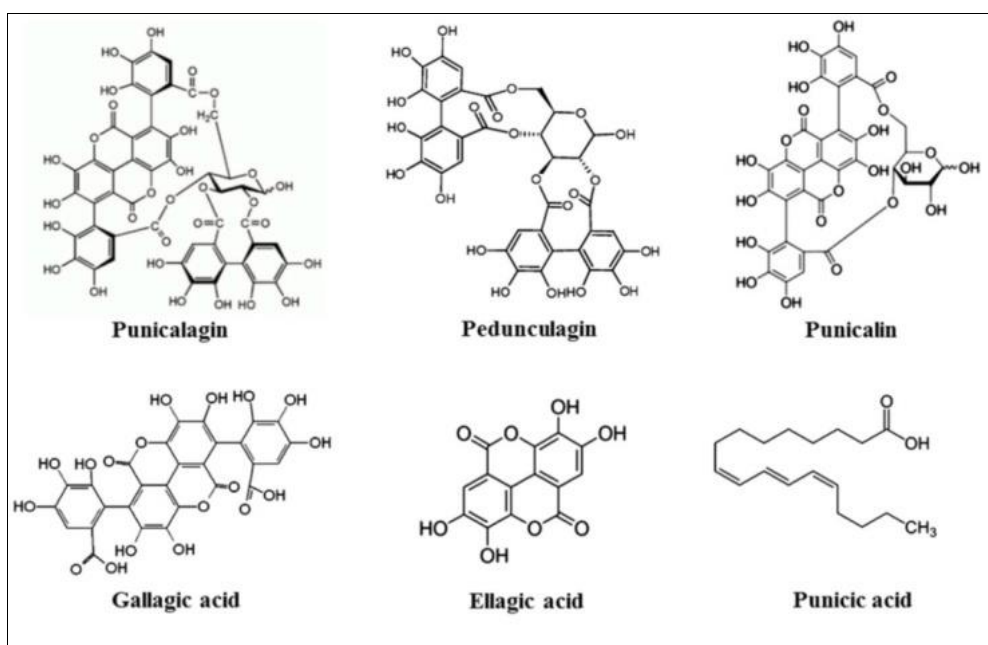


Fig 2: Principle tannins and phenolic acids found in pomegranate

The extensive range of phytochemicals found in pomegranates is thought to be responsible for its positive health effects. Phytophenols, primarily hydrolysable ellagitannins and anthocyanins, are the most prevalent phytochemical in pomegranates, as previously stated, and are responsible for improving its nutritional value.

Health beneficial properties of pomegranate

Fruits are essential for a healthy diet. Fibers, polyphenolic compounds, flavonoids, isoflavones, tocoferols, and ascorbic acid are only a few examples of natural antimutagens or anticarcinogens found in the human diet. Mutagens and carcinogens may work by causing reactive oxygen species to form. Reactive oxygen species may potentially play a key role as endogenous initiators of degenerative processes including DNA damage and mutation, which have been linked to cancer, heart disease, and ageing [34]. Many studies have shown the significance of fruit consumption in the reduction of nutrition hazards and also revealing the possible health advantages of pomegranate beneficial in its nourishment value. Pomegranate fruit has already been used as a medicinal herb by the people from various cultures for generations to treat ulcer, snakebite, hepatic damage, dysentery, diarrhea, helminthiasis, acidosis, haemorrhage and respiratory problems. Recently its clinical efficacy is reported in case of infant brain ischemia, Alzheimer's diseases, breast cancer, prostate cancer, male infertility, arthritis and obesity. Pomegranate appears to have a putative anti-cancer impact in prostate cancer and can be administered safely in high doses [35]. In Table 2, several of pomegranate's health-promoting processes are listed.

Table 2: Health benefiting mechanisms of pomegranate

Properties	Mechanism of action	Plant part used
Hepato-protective activity	Restraint stress has protective benefits on oxidative stress in mice, which is because of its scavenging of free radicals and lipid peroxidation inhibitory impact.	Peel
Anti-hyperglycemic activity	Blood glucose levels were dramatically reduced, and the number of β cells was significantly increased.	peel
Anti-hyperlipidemic activity	Serum and hepatic lipids are decreased. Decrease in LDL; LDL/HDL and total/HDL ratios have improved.	peel
Anti-cancer effect	Prevent the growth of prostate, breast, colon and lung cancer cells	Juice, seed oil
Anti-atherosclerosis, heart diseases	effective in the atherosclerosis inhibition along with inhibition of the cardio-toxic activity	Juice
Anti-alzheimer	In a mouse model and in people, there is less deposition of amyloid by 50% and soluble A beta 42 buildup, indicating better efficacy in Alzheimer's disease.	Juice
Anti-osteoarthritis effect	Inhibits the activation of MKK-3, p38MAPK, as well as the transcription factor Interleukin-1 causes RUNX-2 to be activated in human osteoarthritis chondrocytes.	Juice, peel

Anti-carcinogenic activity

Prostate, breast, colon, skin, lung, cervical cancers, and leukaemia have all been studied using pomegranate extracts. The well-studied of them has been prostate cancer, with favorable results in a cell model of prostate cancer [36] and renal cell carcinoma experimentally [37] when blocking nuclear factor kappa B (NF-B) activity. As a result, fruit extracts could be used as nutritional supplements to treat people who have unintentionally discovered small, localized kidney cancers, potentially avoiding nephrectomy. Punicalagin kills papillary thyroid cancer cells in vitro [38] and it suppresses cell growth in a non-small lung carcinoma cell line and has ability to prevent or retard the spreading of cells in human breast, lung, cervical cancer cell lines, according to research [39]. Also in experimental animal tests, oral administration of pomegranate extract suppressed the formation of lung, skin, colon, and prostate cancers [40].

Hepato-protective activity

Pomegranate has been shown to have preventive benefits against liver injury and to have hepato-protective properties in recent investigations. The pomegranate peel extract was found to have a significant protective ability against oxidative stress, which is likely due to its anti-free radical and anti-lipid peroxidation properties. Pomegranate flowers also have considerable hepato-protective and antioxidant property against Ferric Nitrotriacetate [41].

The findings of a molecular and histological analysis revealed that pomegranate has hepato-protective properties against CCl₄-induced oxidative stress in liver tissue [42].

Antioxidant activity

Pomegranate peel extract and juice contain strong antioxidant activity. It may be due to its major polyphenolics content. Pomegranate peel extract has considerably more antioxidant power than pomegranate pulp extract (10 times higher). Pomegranate peel extract also has a strong ability to neutralise hydroxyl and superoxide anion radicals. Pomegranates are supposed to produce two active ingredients that inhibit aldose reductase while also acting as antioxidants [43]. Because pomegranate juice, peel extract, and seed oil are high in polyphenolic chemicals, they have a high antioxidant capability. The enzymes cyclooxygenases and lipoxygenases found in pomegranate peel extracts can suppress pro-inflammatory enzymes [42].

In rats, pomegranate extracts diminish oxidative stress and lipid peroxidation in macrophages by scavenging free radicals. According to the study, pomegranate peel methanolic extract increased or sustained the free radical scavenging activity of liver enzymes like catalase, peroxidase, and superoxide dismutase [44].

Anti-inflammatory activity

Increased synthesis of pro-inflammatory mediators including tumor necrosis factor, interleukin-1 (IL-1), interleukin-6, interleukin-8, as well as the activity of inflammatory cells like neutrophils, lymphocytes and the generation of reactive oxygen species, cause inflammatory diseases. Chemical components extracted from pomegranate arils and peel were shown to hold the following effects: (i) reduction of Cyclooxygenase-2 expression and, as a result, eicosanoid production; (ii) inflammatory cytokine expression is suppressed in a synergistic manner [45]. Given the anticarcinogenic, antioxidant and anti-inflammatory capabilities of pomegranate fruit and its derivatives, it's reasonable to assume that pomegranate and its metabolites have a significant inflammatory impact. The study found that pomegranate fruit extract suppressed the activation of kinases and nuclear factor (NF) in human chondrocytes experimentally, protecting them from expression of matrix metalloproteinases when induced with IL-1. Due to the activity of ellagic acid found in the extract,

dietary supplementation of pomegranate products lowered the prostaglandin E2 levels in colon mucosa by downregulating the over-expressed cyclooxygenase-2 and prostaglandin E synthase levels [25, 46].

Antidiabetic activity

Diabetes is a devastating physiological disease in the world, and its incidence is on the rise. After cardiovascular and oncological diseases, it is the third most frequent disease, as per the World Health Organization. The fruit of the pomegranate and its derivatives can help control diabetes through diet. There are many studies have described Antidiabetic activity of pomegranate fruit parts. Pomegranate extracts have been shown to reduce inflammation and low-density lipoprotein (LDL) cholesterol in high-fat diet-induced obese mice. The extract also reduces hepatic lipid peroxidation and serum glucose levels in healthy rats, as well as improves glycemic control and increases relative beta cell number in alloxan-induced diabetic rats, in several mouse intervention studies [47, 48]. Unani and Ayurvedic medicines prescribed pomegranate flowers containing abundant ellagitannins as a remedy for diabetes [16]. Increased blood glucose, total cholesterol, triglycerides, very low density lipoproteins, glutathione-S-transferase, and superoxide dismutase with decrease in high density lipoprotein (HDL)-cholesterol, glutathione peroxidase, glutathione reductase, glutathione-S-transferase, and superoxide dismutase can be reversed. The peroxisome proliferator activated receptor- α is activated by pomegranate flower extract (PFE). PPAR- α is a cardiac transcription factor that has a role in fatty acid absorption and oxidation in myocardial energy production. Because of activation of PPAR- α , cardiac uptake and circulation of lipids are decreased. Due to this there could be decrease in cardiac tissue triglyceride content. These findings show that pomegranate fruit can be used as a nutraceutical to treat and prevent chronic illnesses with hyperlipidemia and impaired glucose metabolism [49, 12].

200 mg/kg aqueous pomegranate peel extract reduced blood glucose levels and lipid peroxidation in the heart, liver, and kidneys [48]. Alloxan-induced diabetic rats were given pomegranate peel extract rich in polyphenols, causes lower fasting serum glucose and higher insulin levels, as well as an anti-lipid peroxidation effect [47]. Extended oral therapy of flower extract of pomegranate (500 mg/kg) to Zucker fatty diabetic rats reduced heart triglycerides, plasma triglycerides, total cholesterol, and fatty acids, according to a study [50]. Fresh pomegranate juice, as previously said, includes a variety of bioactive chemicals, primarily phenolic acids including gallic acid, caffeic acid, chlorogenic acid, ferulic acid, and coumaric acids and non-phenolic acids, citric acid, succinic acid, malic acid, oxalic acid, and ascorbic acid are also present. The effects of juice of pomegranate have been the focus of human investigations linking pomegranate with type 2 diabetes. Many factors are analyzed in the human research study that examined the impact of juice on factors in type 2 diabetes.

Conclusion

The present review provides more evidence on the importance and value of pomegranate fruit. Pomegranate fruit parts are important source of several high value compounds such as flavonoids, anthocyanins, punicic acid, ellagitannins, alkaloids, fructose, sucrose, glucose, simple organic acids, and other components with potential beneficial physiological properties. According to phytochemical screening, all morphological parts of the fruit were reported to retain therapeutic activity including anticancer, anti-inflammatory, antiatherogenic, Antidiabetic, hepatoprotective, and antioxidant activity.

The current study contains evidence relevant to antidiabetic property of pomegranate and its derived products. Punicic acid present in pomegranate peel extract as well as methanolic seed extract reduced fasting blood glucose levels. Punicalagin and ellagic, gallic, and oleanolic acids, which are contained in pomegranates, have been proven to have anti-diabetic properties. Furthermore, because of antioxidant content of pomegranate juice, it has an effect on type 2 diabetes factors. Despite the fact that several *in vitro* and *in vivo* studies are done to explore and confirm the therapeutic properties of pomegranate, more human trials and studies are required to fully comprehend its therapeutic potential. It is hoped that this evaluation would provide some useful information for future research into this fascinating botanical species.

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