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A review on proactive pomegranate one of the healthiest foods

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Abstract

Pomegranate a bioactive fruit being grown in tropical climatic conditions has various therapeutic benefits due to bioactive compounds in it. It is now being utilized in nutrition as well as medicinal industries due to its strong potential. It has potent nutritional values and immense health benefits. Pomegranate fruits, seeds and peels are intensively used in traditional medicine as a natural therapy. It contains plethora of valuable ingredients such as flavonoids, ellagitannin, punicalagin, ellagic acid, vitamins and minerals. The principal active constituents including punicalagins and ellagitannin are responsible for immeasurable health benefits due to its strong antioxidant activity. The pomegranate has been used since time immemorial in natural and holistic medicine therapies to treat sore throats, coughs, digestive disorders, urinary infections, skin disorders, arthritis, and to expel tapeworms. The health benefits reported word wide suggested that pomegranates might be useful in treating such serious conditions as different types of cancer, osteoarthritis, diabetes and Alzheimer. This is because pomegranates have the potential to thin the blood, increase blood flow to the heart, reduce blood pressure, and plaque in the arteries and ability to reduce bad cholesterol while increasing good cholesterol. Pomegranate juice can lower C-reactive proteins and reduce the inflammation of the liver. Juice of flower is used to treat nose bleeds. The fruit pulp and the seed are stomachic. Dried, pulverized flower buds are employed as a remedy for bronchitis. Research domain in this area is expanding rapidly and gaining popularity because of an understanding of the fact that naturally available phytonutrients along with polyphenols and antioxidants offer the available best protection against many diseases and disorders. Pomegranate protects our body in a cellular level. The objective of this review was to present a deep thought of the multi-functional, nutraceutical, bio-active components and medicinal effects of pomegranate in combating various human diseases, disorders and human ailments has been duly supported by various researchers in medicine, nutrition, biochemistry, physiology and horticultural sciences.

Keywords: PJ (Pomegranate juice), *Anti-oxidants, Punicalagin, Ellagic acid*

Introduction

Pomegranate (*Punica granatum* L.) is a shrub or small multi stem tree that grows approximately 16 to 26 feet tall. Pomegranate has multiple long-lived branches and its leaves are 2 cm wide and 3-7 cm long and flowers have 3-7 petals which are red in color. Fruit is berry like with a leathery rind (husk or peel) enclosing many seeds surrounded by juicy arils and seeds may vary from about 200 to 1400 in number. The husk is composed of two parts: pericarp and mesocarp (albedo). Pomegranate tree is one of the oldest domesticated tree for its countless health benefits, known even before the 21st Century. Folk medicines make use of all parts of this tree. Various researchers have identified about 153 phytochemicals including their derivatives in pomegranate. Polyphenols are the major class of phytochemicals, extracted from almost all parts of pomegranate tree, but are most abundant in fruits. Flavonoids, hydrolysable tannins and condensed tannins are the major pomegranate polyphenols. Anthocyanins, which impart red colour to the arils, are most abundant and responsible for potential health benefits. Pomegranate contain more than 18 hydrolysable tannins in leaves, bark and fruits, among which gallotannins, ellagitannins, punicalgin and punicalin have attracted most attention among researches, and which are pomegranate's most powerful antioxidants. Other phytochemicals reported in pomegranate include catechin and procyanidins, organic acids, phenolic acids, sterols, terpenoids, fatty acids, triglycerides, alkaloids and some other compounds. The prophylactic and curative potential of these bioactive compounds has been proved against cardiovascular diseases, hypertension, all types of cancers, inflammations, hyperlipidemia, diabetes, ageing, Alzheimer's disease, *etc.*, and are, in addition, antibacterial, antifungal, antiviral, anthelmintic, vermifugal tenicidal and molluscicidal agents.

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Pomegranate juice contains 3-fold more antioxidants than green tea and red wine as well as several common fruits like apples, grapes, *etc.* Researchers have used various technologies to extract, purify and analyse these phytochemicals for chemical characterization and evaluation of their antioxidant capacities.

Nutritional value of pomegranate

Pomegranate is a rich source of these bioactive compounds. Nutrients content in a fruit may change during the development of the tree, during fruit maturation, under different environmental and cultivation conditions and between pomegranate cultivars. It is a diet full of nourishment for growing children, ageing/elderly or sick persons and pregnant women. It has the power to cure hunger, quench thirst and refresh the drunkard. The pomegranate fruits are consumed fresh or used for the preparation of fresh juice, jelly, jam, and paste and also for flavoring and coloring the culinary preparations. The fruit has been regarded as a "healing food" with numerous beneficial effects in several diseases. Pomegranate peel comprises about 50% of the total fruit weight and is an important source of minerals especially potassium, calcium, phosphorus, magnesium, and sodium; complex polysaccharides and high levels of diverse range of bioactive compounds such as phenolics, flavonoids, proanthocyanidin compounds and ellagitannin (ETs), as well as punicalagins and its isomers, as well as lesser amounts of punicalin, gallagic acid, ellagic acid, and ellagic acid glycosides. Pomegranate seed oil (PSO) contains an exceptional conjugated fatty acid called punicic acid (trienoic acid) that makes up approximately 65% to 80% of the oil from pomegranate seeds. Punicic acid is also referred as a super conjugated linolenic acid whose effect is even more potent than that of an ordinary conjugated linolenic acid. Seeds also contain protein, crude fibers, vitamins, minerals, pectin, sugars, polyphenols, isoflavones, the phytoestrogens, coumestrol and the sex steroid, estrone. The edible part of the pomegranate fruit (50%) consists of 40% arils and 10% seeds. The fresh juice contains 85% water, 10% total sugars, 1.5% pectin, ascorbic acid and polyphenolic flavonoids (El-Nemr *et al.* 1990) [6]. The major sugars as reported by Ozgen (2008) were fructose (6.4 g/100 ml) and glucose (6.8 g/100 ml); the major acids were citric (1.78 g/100 ml) and malic (0.12 g/100 ml). They further reported that pomegranate is a rich source of Vitamin C, Vitamin K, Vitamin B₆ and pantothenic acid (Vitamin B₅). It also consists of Vitamin A, Vitamin E, thiamin and riboflavin in small amounts. In addition to these, niacin and folate are present in traces. Pomegranate is a rich source of minerals like potassium and copper and is very low in sodium, hence useful in the control of hypertension. Iron is present in small quantity, while traces of magnesium, phosphorus, zinc and selenium are also there. Ascorbic acid (vitamin C) content varies with varieties. The quality studies reported ascorbic acid content to vary between 52.8 to 72.0 mg/100 g fresh weight (fw) for arils and 76.8 to 118.4 mg/100 g fw for peels and it was found significantly higher in peels than the arils, with differences ranging from 24.4 to 97.0% depending on variety (Opara *et al.* 2009) [14]. PJ is considered beneficial for diabetics, despite the juice containing significant sugar concentrations. The explanation given in support of this is that, "In most juices, sugars are present in free and harmful forms but in PJ, however, the sugars are attached to unique antioxidants – the polyphenols forming a complex, which actually make these sugars protective against atherosclerosis" (Rock *et al.* 2008) [16]. Rozenbers *et al.*

(2006) [17] concluded from their study that PJ consumption by diabetic patients does not worsen their diabetic parameters but contributes to serum paraoxonase-1 stabilization, increased association with HDL cholesterol, and enhanced catalytic activities, leading to retardation of atherosclerosis development in diabetic patients. The fruit is low in fats (< 0.12 g/100 g arils) and sweet varieties have almost half the fat content than that of bitter/ sour varieties (Hernandez *et al.* 2001) [7].

Health benefits

Although many phytochemicals have positive effect on health, very many can be toxic and harmful, however, plants containing the most harmful phytochemicals are usually not treated as foods. The major health benefits of pomegranate are because of its anthocyanin contents, which are present in appreciably large quantities and have antioxidant properties. Andreu *et al.* (2008) [3] recently reviewed composition of pomegranate fruit juice, beneficial health effects, including association with anti carcinogenicity and anti-inflammatory properties.

Antioxidant properties

Pomegranate possesses punicalagins which are extremely potent antioxidants found in pomegranate juice and peel. They are of so high potency that pomegranate juice has been found to be three times the antioxidant activity of red wine and green tea and eight times higher levels than those dictated in grapes, grapefruit, and orange juices, respectively. The pomegranate extract and powder is typically made from peel due to its high antioxidant and punicalagin content. The antioxidant agents reduce oxidative damage (damage due to oxygen) such as that caused by free radicals, which are highly reactive chemicals and attack molecules by capturing electrons and thus modifying chemical structures. Oxidative damage (oxidation) to the cells is partly responsible for the effects of ageing and certain diseases. Cells produce free radicals that are deficient in electron. In order to stabilize these free radicals react by taking electrons from certain key components in the cell and in the process, they damage these cells. Antioxidants divert this damage by donating electrons to the free radicals and stabilize them, thus, saving cell components from the scavenging effect of free radicals. The environment is also a source of free radicals caused by ultraviolet radiation or airborne pollutants, such as cigarette smoke. It is a well known fact that most free radical damage is repaired naturally; a fraction may however, remain unrepaired. This free radical damage may reduce or takeover the body's natural defense. Punicalagin as a core element supports human health by protecting cells from being damaged by UV radiations by keeping more cells out of harm's way. Increase in cell damage with lapse of time leads to ageing and diseases like cancers, cardiovascular problems and some other problems. Polyphenols and vitamins, which have antioxidant properties, in one's diet help in countering some of the damage. Polyphenols especially anthocyanins and vitamins, present in appreciably large quantities in pomegranate can play an important role in benefiting human health.

Cancer cells

Cancer is caused as a result of disfunctioning of immense system due to multi-factors and numerous diseases involved in this process. In this vista, pomegranates fruits, seed and peels illustrate cancer preventive role and mechanism which

seems to be due to rich source of antioxidants. Pomegranate juice can hinder the proliferation of cancerous cells in human body. It can block the flow of blood towards the tumors resulting in reducing its size and ultimately its destruction. Breast and prostate cancer cells have significant evidence of slowing down the activities of malignant cells. Inhibition of cancerous cells causing prostate cancer in adults has been well recognized. Pomegranate extract also stops the proliferation of these dangerous cells to other parts of the body. Many phytochemicals have an anti-carcinogenic (anti-cancer) action as they slow cell proliferation (division) by interfering with the cell cycle, induce apoptosis (cell suicide) inhibit phase 1 enzymes – that convert harmless substances into carcinogens and induce phase 2 enzymes – enzymes that can attach carcinogens to molecules that facilitate speedy excretion (Best 2006)^[4]. The pomegranate extract has shown to induce programmed cell death and to inhibit tumor invasion, proliferation and angiogenesis. The fruit juice, peel and oil possess anticancer activities, including interference with tumor cell proliferation, cell cycle, invasion and angiogenesis (Lansky and Newman 2007)^[11]. A wide variety of plants produce phytoestrogen that are secondary metabolites. Controversies on use of pharmacological hormone replacement therapy (HRT) for the treatment of menopausal symptoms necessitates further studies and identification of natural sources of estrogen (Jordan 2003)^[8]. Pomegranate was identified the best known source for curing it. In fact, pomegranate tree is one of the only plants in nature known to contain estrone (Van Elswijk *et al.* 2004)^[21]. Because of its unique composition, seed-oil is a powerful health-benefiting agent, due to its antioxidative, anticancer, and antilipidemic properties. The extrogenic compounds luteolin, quercetin and kaempferol have been identified in pomegranate (Van Elswijk *et al.* 2004)^[21]. Other major components ellagic acid, caffeic acid and punicalic acid found in pomegranate fruit are having known anticancer activities.

Breast cancer

Extracts of pomegranate have anti estrogenic properties. Hormone levels in serum are well controlled by pomegranate extracts by inducing beneficial effects in blood plasma. The extracts from peel, seed, the seed oil and fermented/unfermented fruit juice all have suppressive effect on human breast cancer cells (Settheetham *et al.* 1995)^[19]. Bingham *et al.* (1998)^[5] had reported that diets rich in phytoestrogens protect against breast, prostate, colon cancer as well as cardiovascular disease and osteoporosis. The whole pomegranate seed oil is more chemopreventive for breast cancer and avoids the use of chemical agents to slow the development of cancer (Mehta and Lansky 2004)^[13]. The fermented PJ polyphenols in comparison to fresh juice recorded approximately twice the antiproliferative activity and inhibited cancerous lesion formation induced by a popular carcinogen (Kim *et al.* 2002)^[9]. Bioavailability and maximal oral intake of pomegranate supplements juice extracts for getting protein response in breast cancer. Tanner *et al.* (2008)^[20] in a study found that PJ may be a useful nutrient-based, non-chemotherapeutic treatment alternative for the inhibition of estrogen receptor negative breast cancer cell proliferations of feline and human breast cancer cell types. It can delay the onset of breast cancer by blocking aromatase enzymes and cancer cell differentiation.

Colon cancer

PJ, ellagic acid, punicalgin and pomegranate tannins show

apoptosis in specific colon cell and get rid of unneeded or abnormal cells. (Larrosa *et al.* 2006)^[12]. Punicalgin is freely bioavailable, body readily breaks down and as an antioxidant, it helps to neutralize free radicals. Pomegranate seed oil which is composed of 70% of conjugated linolenic acid, suppress colon carcinogenesis hence, dietary pomegranate seed oil significantly inhibits incidence of adenocarcinomas (Kohno *et al.* 2004)^[10]. In a study by Saruwatari *et al.* (2008)^[18], the results indicated that the inhibition of sulfotransferase activity by punicalgin in Caco-2 cells was responsible for the reductions seen in 1-naphthyl sulfate accumulation. They also suggested that constituents of PJ, most probably punicalgin, impair the enteric functions of sulfoconjugation and that this might have positive effects upon the bioavailability of drugs and other compounds present in food and in the environment. These effects might be due to the anticarcinogenic properties of PJ. Punicalgin is an ellagitannin, a type of phenolic compound which is responsible for more than 50% of the juice potent's antioxidant activity. The maximum levels of ellagic acid are present in pomegranate and anticarcinogenic properties of ellagic acid has been found the probable anti-inflammatory role in the treatment of lacerative colitis as to prevent the development of colon cancer.

Skin cancer

Exposure to ultraviolet (UV) radiation has been associated with several acute and chronic conditions. The UV-B component may cause sunburn, hyperpigmentation, edema, hyperplasia, immunosuppression, photo ageing, and skin cancer whereas UV-A may be responsible for tumor formation. The biochemicals delphinidin, cyaniding and pelargonidin, (anthocyanidins), Punicalin, pedunculagin, punicalagin and gallagic and ellagic acid esters of glucose (hydrolysable tannins) in pomegranate are strong antioxidants and antiinflammatory agents these compounds which account for 92% of the antioxidant of the whole fruit (Afaq *et al.* 2005)^[2], protect from ultraviolet radiation. Pomegranate fruit extract contains antioxidants and anti-inflammatory phytochemicals that can treat human epidermal keratinocytes. Fruit extracts provided protection against Ultraviolet A mediated activation of signal transducers and activators of transcription.

Cholesterol level

The phytosterols in pomegranate both lower the existing LDL cholesterol and cease the production of bad cholesterol. Pomegranate is rich in major antioxidants like anthocyanins and tannins that may help to block the buildup of cholesterol in arteries which in return protect heart damage. Juice of this fruit may help to reduce the concentration of low density lipoproteins from the body which may protect the body from stroke attack. Energy and body HDL levels decreased showing beneficial effects of leaf extract of pomegranate. Pomegranate juice decreased cholesterol absorption, increased faecal excretion of cholesterol, had a favourable effect on enzymes concerned in cholesterol metabolism, drastically reduced LDL cholesterol, and improved LDL/HDL cholesterol and total/HDL ratios (Esmailzadeh *et al.*, 2006)^[1]. Pomegranate juice consumption decreased LDL susceptibility to aggregation and retention and increased the activity of serum paraoxonase. Pomegranate juice improve cholesterol profiles and treat the atherosclerotic plaque that are responsible for many heart attacks and many strokes. All these evidences suggest the potential cardioprotective effect of pomegranate fruit.

Blood pressure

Systolic blood pressure can be reduced by juice of pomegranate to a significant level. Potassium in it can prevent arteries from stiffness and atherosclerosis. It improves blood flow to the heart and reduces the incidents of heart attack. Clinical examination of improving blood pressure and endothelial functions of the body by consuming pomegranate juice have been performed. Chronic administration of pomegranate juice extract showed reduction in the mean arterial blood pressure and vascular reactivity changes to various catecholamines. The potent flavonoids such as catechus, tannic and ellagic acid, make pomegranate a stronger antioxidant than red wine and equal to or better than green tea.

Memory and mood enhancer

Flavonoids are believed to improve memory from declining and delay the onset of Alzheimer disease. These antioxidants have potential role for fighting against depression that can cause memory loss. Vinegar of pomegranate juice contains flavonoids of deep red color that helps prevent against radical formation. Pomegranate juice have natural compound Estrone that improves mood in menopausal women. It is generally believed that this compound can act as a replacement therapy for women suffering from mood disturbances.

Arthritis and Joint Pain

The foods that are rich in nutrients, minerals and antioxidants may help to neutralize rheumatoid arthritis. Pomegranate is low in fat, cholesterol and sodium but rich in nutrients, minerals and antioxidants. The studies suggested the extract of pomegranate may block production of cartilage destroying enzyme. Inflammation of joints can result in Pain and swelling in later age. Presence of Flavones in pomegranate extract has anti-inflammatory effects that may reduce collagen induced arthritis and painful swelling of joints. Cyclooxygenases and lipoxygenase enzymes inhibits by extracts present in pomegranate seed oil. These key mediators of inflammation decreases 75 percent by seed oil while pomegranate juice causes 23.8 percent reduction in these enzymes. In osteoarthritis these extracts diminishes matrix metallo-proteinases which is involved in degradation of extracellular joint matrix. It prevents collagen degradation and stops joint destruction.

Bacterial infections

Antibiotics are effective remedy in the inhibition of bacteria growth or growth of microorganism. The recent surge in multi-drug resistant bacteria and the likely chance of widespread global pandemics necessitate the need for additional therapeutic options to counteract conventional drugs. On the other side, antibiotics resistance against microorganism is one of the major problems in the use of antibiotics against microorganism. Pomegranate has millions of bioactive compounds fighting against infections like diarrhea and ulcers. Nearly every part of pomegranate plant including ingredients of seeds, flowers, stem, bark and leaves show very effective role in the inhibition of growth of pathogens. Plants are one of the good sources of secondary metabolites including tannins, terpenoids, alkaloids, flavonoids and glycosides, which confirmed antimicrobial activities. Ellagic and gallic acids as natural antimicrobial agents has been used against *Staphylococcus aureus* and *Escherichia coli* for their ability to precipitate membrane proteins and inhibit enzymes that leads to lysis of cells.

Preservation and/or enhancement of probiotic bacteria in the gut is important for maintaining gastrointestinal health.

Hypercholesterolaemia

A recent study shows that peel of pomegranate has prebiotic potential for lowering down the fat content of the body. It reduces the cholesterol of high fat diet over a period of 4 weeks and gut microbiota supports its action. Polyphenols present in pomegranate has the ability to prevent atherosclerosis and macrophage formation. This can be done by either direct combination of polyphenols with lipoproteins of the body or by indirect means through accumulation in arterial macrophages. This in return blocks the synthesis of oxygen species and lipid peroxidation and lipid rich macrophages. It also results in hydrolysis of lipids in atherosclerotic lesions.

Immune system

The benefits of pomegranate can be potentially utilized for the people of lesser development countries. Various health conditions related to throat and respiration can be resolved by pomegranates. As this fruit is rich in iron content it ensures normal platelet count of the body by which a person feels less fatigue symptoms. These fruits are often recommended for liver prevention. Pomegranate juice helps in the reduction of platelet aggregation and oxidative stress in humans. Pomegranate juice inhibits aggregation and oxidation of atherosclerotic lesion and attenuate platelet activation. Pomegranate exerts bactericidal activity against food and water borne pathogenic bacteria.

Tooth loss

The flavonoids present in pomegranate exerts beneficial action which are conducive to oral health. Pomegranate juice is effective against dental plaque microorganisms decreasing the CFU. Additionally, there was significant reduction in the level of dental plaque microorganisms after the rinsing with pomegranate juice. Dental plaque and tooth loss can be prevented by seeds of this fruit. It possesses anti-microbial functions which can be helpful against oral bacteria. Health of gums can be improved by its seeds. It has been demonstrated by performing a study regarding the ability of peel or pulp of pomegranate richness in antioxidants. Flavonoids and phenolic compounds were also high in peel extract that were beneficial against oxidation and atherosclerosis and can be used as a natural supplement.

Anti-diabetic effect

A range of studies evidences that medicinal plants or constituents of medicinal plants show role in the management of diabetes and its complication including Diabetic retinopathy. By various studies it has been confirmed that by giving 200 mg of peel extract according to per kg of the body weight, polyphenols present in it affects glycemic index of the body by either inhibiting the uptake of glucose to peripheral tissues or by blocking its absorption by the gut. Administration of crude powder of *Punica granatum* husk decreased the concentration of glucose, triglycerides, cholesterol, LDL cholesterol and raised the level of HDL cholesterol and hemoglobin content in the blood. The well known compounds in pomegranate like punicalagin acid, ellagic, gallic, oleanolic, ursolic and uallic acids have been recognized as having antidiabetic actions.

Pregnancy outcomes

Pomegranate is rich in antioxidants so they protect placenta from oxygen reactive species. They also contain little amount of folate that helps fight against birth defects. It can help in the purification of blood and can enhance milk production. Acidity of urine reduces by the intake of pomegranate juice and improves health of urinary bladder by preventing harmful bacteria from entering into the urinary tract. This prevents inflammation and enhances immunity of the body. The intake of pomegranate juice decreases placental oxidative stress *in vivo* and *in vitro* and may limit placental injury and thus confer protection to the exposed foetus.

Effect on reproductive system

Pomegranate shows pivotal role in the elevation of hormones linked to reproductive system. Pomegranate juice showed elevation in testosterone, luteinizing hormone and follicle stimulating hormone depleted after the injection of carbon tetra chloride (CCL4). Pomegranate extract and ascorbic acid administration reduced the deleterious effect of lead acetate on daily sperm production and epididymal sperm number. PJ consumption showed increase in epididymal sperm concentration, sperm motility and spermatogenic cell density. Long-term pomegranate juice intake increased intracavernous blood flow, improved erectile response and smooth muscle relaxation in erectile dysfunction. Pomegranate increases testosterone production which is primarily responsible for men's health both inside and outside. Pomegranate augments nitric oxide; a vital ingredient for getting an erection pomegranate tends to increase it most.

Conclusion

Pomegranate is a pivotal source of all essential nutrients and rich in polyphenols particularly Ellagitannins (ET) and ellagic acid (EA) which can be digested easily and refreshes physically or mentally tired people from regular intake. All parts of this fruit have been utilized in food industry for prevention and treatment of various diseases. It has been regarded best vis a vis green tea due to its strong antioxidant potential. The biological screening of *Punica granatum* extracts and compound have shown antioxidant, antiperoxidative, antibacterial, inflammation, antitumor, hepatoprotective, antiarthrogenic and antidiarrhoeal. It shows no toxic effects to liver and other organs of pomegranate extract and can be used as natural supplement. However, it is the dire need of the time to promote its cultivation by traditional and non- traditional means in order to gain benefits of this fruit as well as to compete in global market for its export. In addition to this more conclusive studies and experiments are needed to evaluate effects of pomegranate in treating diarrheal diseases and in preventing fungal proliferation. The immense potential of this fruit in overcoming infections can bring tremendous progress in nutritional and therapeutic industries. The available research offers substantial supplementation and evidence to enrich the diet with pomegranate juice or extract to harness the benefits for protecting us from important stresses and diseases particularly diabetics, development of cancer and improvement of oral health and skin texture. The wide array of benefits can be utilized by inclusion of pomegranate in dietary schedule.

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