



ISSN (E): 2277- 7695

ISSN (P): 2349-8242

NAAS Rating: 5.03

TPI 2018; 7(10): 71-81

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www.thepharmajournal.com

Received: 24-08-2018

Accepted: 25-09-2018

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## Functional Properties of Pomegranate (*Punica granatum L.*)

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**Abstract**

India has the largest production of pomegranate (*Punica granatum L.*) in the world. It is an ancient fruit with excellent biological properties such as flavor, nutritional value, and pharmacological properties. It is very potential for processing and value addition, due to its attractive properties. It was traditionally used in folk medicine to eliminate various diseases such as dysentery, ulcers, haemorrhage, diarrhea, aphthae, microbial infections, acidosis, and respiratory pathologies. The edible part (arils) of pomegranate is a good source of polysaccharide, vitamins, fatty acids, minerals, organic acid, soluble solid, dietary fibers, anthocyanin's, vitamin C, phenolic and tannin biological compounds. The pomegranate and its derivatives have excellent properties for preventing various diseases such as prostate cancer, hypertension, infectious diseases, heart disease, and atherosclerosis. The ellagitannin (Polyphenol) are widely used in the pharmaceutical sector for plastic surgery, they inhibit inflammatory markers such as tumor necrosis factor-alpha (TNF- $\alpha$ ). They have potential health benefits for human due to its anti-mutagenic, antioxidative, anti-hypertension and pharmacological activities. They have functional properties such as antimicrobial, anti-inflammatory, anticancer, antioxidant, antiviral, anti-hepatotoxic and anti-diabetes. They also help to improve skin and cardiovascular health effect, sperm quality, and prevention of Alzheimer's disease. They have higher antioxidant properties as compared to grapes/cranberry, green tea, red wine, grapefruit, and orange juice. This review congregates the functional and medicinal properties of pomegranate and its derivative.

**Keywords:** Pomegranate, derivatives, therapeutic properties, antioxidants, applications

**1. Introduction**

Since, ancient time's pomegranate (*Punica granatum L.*) has been grown for its appetizing fruits, attractive flowers, and color. It is native of Iran and belongs to Punicaceae family (Meerts *et al.*, 2009; Ercisli *et al.*, 2011; Newman R.*et al.*, 2011) <sup>[101, 39, 111]</sup>. It is usually known as superfruits due to its high genetic diversification. It is also known as Chinese apple, Carthage Apple and Seeds Apple (Schubert *et al.* 1999) <sup>[139]</sup> in various regions. India is the largest producer of pomegranate (*Punica granatum L.*) in the world. The main pomegranate producer states of India are Maharashtra (pomegranate basket of India), Karnataka, Uttar Pradesh, Andhra Pradesh, Gujarat, Rajasthan, and Tamil Nadu (Saxena *et al.*, 1987; NHBMA, 2010) <sup>[113, 136]</sup>. It consists of 50% peel, 40% arils, and 10% seeds. The fruits have an irregular round shape with coriaceous skin (yellow, green, red color) (Holland *et al.*, 2009) <sup>[64]</sup>. The edible part (arils) of pomegranate is excellent source of polysaccharide, vitamins, fatty acids, and minerals, organic acid, soluble solid and dietary fibers (Ewaida *et al.*, 1987; Fadavi *et al.*, 2006) <sup>[40, 41]</sup>. The pomegranate fruit shows high antioxidant activity (Heber *et al.*, 2007) <sup>[62]</sup> due to its redox properties of phenolic compounds. There are different varieties of pomegranate and their derivatives such as aril and peel are used in processing market due to their attractive color, aroma, and taste (Rice-Evans *et al.*, 1995; Seeram *et al.*, 2005;) <sup>[129 140]</sup>. It has excellent properties such as flavor, nutritional value, and pharmacological properties. It is very potential for processing and value addition due to its functional properties. It is an ancient fruit with high biological properties (Aslam *et al.*, 2006; Durgaç *et al.*, 2008) <sup>[13, 37]</sup>. The previous research reported the modern use of pomegranate and its derivative based products to help in treatment and prevention of cancer such as lung and prostate cancer (Malik and Mukhtar, 2006; Khan *et al.*, 2007;) <sup>[157, 127]</sup>. It is consumed as a fresh juice, jelly, jam, beverage, and other products (coloring and flavoring agents) (Mousavinejad *et al.*, 2009) <sup>[107]</sup>. It is also considered as a "healing food" due to its medicinal property (Vidal *et al.*, 2003) <sup>[168]</sup>. It was generally used in folk medicine to eliminate various diseases such as ulcers, diarrhea, aphthae, dysentery, acidosis, hemorrhage, respiratory

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And infections (Aslam *et al.*, 2006; Longtin, 2003; Larrosa *et al.*, 2010; Lee *et al.*, 2010) [13, 17, 96, 90, 92]. The pomegranate is a rich source of bioactive compounds, water-soluble vitamins and minerals, organic acids and carbohydrates (Aviram *et al.*, 2000; Mirdehghan and Rahemi 2007; Cam *et al.*, 2009; Davidson *et al.*, 2009; Tezcan *et al.*, 2009) [14, 23, 29, 105, 160]. Several researchers have reported that pomegranate fruit is a rich source of anthocyanin's, vitamin C, tannins and phenolic contents (Artes *et al.*, 2000; Opara *et al.*, 2009; Al-Said *et al.*, 2009; Zarei *et al.*, 2010; D' Aquino *et al.*, 2010) [9, 12, 27, 116, 173]. All parts of pomegranate fruit have valuable compounds. The pomegranate and its derivative has higher antioxidant activity as compared to grapes/cranberry, green tea and orange juice (Gil *et al.*, 2000; Rosenblat and Aviram, 2006) [51, 131].

## 2. Parts of Pomegranate and their Functional Properties

### 2.1 Pomegranate Peel

Pomegranate peel is a highly nutritive by-product of pomegranate fruits. It has medicinal properties such as antibacterial, anti-oxidants, anti-cancer activity, anti-atherosclerotic and wound healing properties (Navarro *et al.*, 1996; Chidambara *et al.*, 2004; Adhami *et al.*, 2006; Rajan *et al.*, 2011) [25, 108, 132]. It is a great source of bioactive compounds such as flavonoids, polyphenols, ellagitannins compounds (gallic acid, ellagic acid, punicalagin, punicalin, luteolin, quercetin, kaempferol, glycosides, pedunculagin), minerals (calcium, phosphorus, nitrogen, potassium, magnesium, sodium) and composite of polysaccharide (Amakura *et al.* 2000; Jahfar *et al.* 2003; Van Elswijk *et al.* 2004; Seeram *et al.*, 2005; Li *et al.* 2006; Mirdehghan & Rahemi 2007) [11, 69, 93, 105, 166, 140]. The pomegranate peel has the highest antioxidant activity as compared to other parts of pomegranate fruit. (Kulkarni *et al.*, 2007; Zahin *et al.*, 2010) [83, 172].

### 2.2 Pomegranate Seeds

The edible portion of pomegranate contains seeds. They are very important parts of pomegranate fruit ranging 40-100 g/Kg (Fadavi *et al.*, 2006) [41]. They contain oil, lipid, and protein. The pomegranate oil is an excellent source of unsaturated fatty acid. The physicochemical compounds play important role in the treatment of the various disorder and diseases (Melgarejo *et al.*, 1995; Lansky and Newman, 2007; Abbasi *et al.*, 2008; Kyralan *et al.*, 2009) [2, 84, 103, 112]. Seeds are the good source of juice and oil, they contain 12-20 percent oil of the total seed weight of the pomegranate. The extracted oil of pomegranate seed is an excellent source of fatty acid (polyunsaturated) and lipids such as linoleic, oleic acid, linolenic, punicic acid, palmitic acid and stearic acid (Ozgul, 2005; Fadavi *et al.*, 2006) [41, 117]. It also contains pectin, crude fibers, minerals, vitamins, sugars, protein, sex steroid, polyphenols and isoflavones (El-Nemr *et al.*, 2006; Syed *et al.*, 2007) [38, 156].

### 2.3 Pomegranate Juice

Pomegranate juice is the rich source of water, organic acid (ascorbic acid, citric acid, and malic acid), sugar (glucose and fructose), pectin and other phenolic activity. The juice is produced after processing of pomegranate arils. It is a prominent source of phenolic compounds, flavonoids compounds such as anthocyanin, glucose, organic acid, caffeic acid, ascorbic acid ellagic acid, ETs, gallic acid, Rutin, Quercetin, Catechin, and minerals (Aviram *et al.*, 2000;

Poyrazoglu *et al.*, 2002; Lansky and Newman 2007; Heber *et al.*, 2007; Mousavinejad *et al.*, 2009; Tezcan *et al.*, 2009; Jaiswal *et al.*, 2010) [14, 62, 70, 112, 107, 160]. It has an excellent property such as antioxidant and anti-inflammatory activity (Newman *et al.*, 2007) [112].

## 3. Functional Properties of Pomegranate Fruit

The pomegranate fruit is consumed as a fresh fruit, juice, extracted arils, grenadine, wine, oilseed, tea, and other products by the consumers. Pomegranate fruits are also used in the cosmetic industry to produce beauty products. All parts of pomegranate have excellent properties to eliminate various diseases such as hypertension, prostate cancer, infectious diseases, heart disease and atherosclerosis (Seeram *et al.*, 2006a; Lansky and Newman, 2007; Holland *et al.*, 2009) [64, 112, 141]. The phenolic compounds of pomegranate fruits such as ellagitannins are widely used in the pharmaceutical sector for plastic surgery. They protect the skin flaps death due to their antioxidant activity. Punicalagin and Punicalin are the major polyphenols which are found in peel, seed, and juice of pomegranate fruit. The pomegranate fruits have the ability to inhibit inflammatory markers (tumor necrosis factor-alpha) and show antioxidant activity due to the presence of phenolic and flavonoids contents (Newman *et al.*, 2007) [112]. Pomegranate fruits and their constituent parts have high medicinal and preventive properties (Hertog *et al.*, 1997) [63], and these properties have great importance for several therapeutic treatments such as dysentery, paralysis, leucorrhea, colic and headache (Schubert *et al.*, 1999; Sadeghi *et al.*, 2009) [133, 139]. They have potential benefits for health due to the antioxidant, anti-hypertension and anti-mutagenic activities (Tsuda *et al.*, 1994; Gil *et al.*, 1996; Lansky *et al.*, 1998) [50, 85, 163]. They have potentially used in the pharmaceutical industry due to their preservative and antioxidant activity (Newman *et al.* 2007) [112]. The pomegranate fruits also show activity against heart disease, HIV-I, prostate cancer and osteoarthritis (Malik *et al.*, 2005; Sumner *et al.*, 2005) [98, 154]. Dhinesh (2016) [33] reported on the pomegranate fruits activity for boosting enzymes, which help in reducing the cardiovascular risk factors. Pomegranate juice is the rich source of anthocyanin, gallic acid, ascorbic acid, minerals, glucose, caffeic acid, catechin, amino acids, rutin, punicalagin, quercetin and ellagic acid derivatives such as pelargonidin 3-glucosides, cyaniding, 3,5 diglucosides, and delphinidin. These compounds have free radical scavenging properties and minimize the lipid oxidation. The pomegranate seed oil contains 95% ellagic acid, punicic acid, and sterols. The pomegranate peel is a great source of phenolic compounds such as gallic acid, tannins, catechin, punicalagin, flavones, flavones, and anthocyanidins. In-vitro studies have shown that the pomegranate fruit juice has potent antioxidant and anti-atherogenic activity in atherosclerotic human and mouse model (Gil *et al.*, 2000; Aviram *et al.*, 2000; Kaplan *et al.*, 2001) [14, 51, 174]. The further studies confirm that pomegranate peel has higher antioxidant activity as compared to seed by using DPPH and  $\beta$  carotene- linoleate model system (Singh *et al.*, 2002) [150].

All parts of pomegranate are regarded as functional foods due to their medicinal and pharmacological properties. They have valuable biological compounds. There are various studies reported about the pomegranate and their derivatives and their properties (functional and therapeutics) such as antimicrobial, anti-inflammatory, anticancer, antioxidant, antiviral, anti-hepatotoxic and anti-diabetes properties. They also help to

improve skin and cardiovascular health effect, sperm quality and prevention of Alzheimer's disease (Aslam *et al.*, 2006; Forest *et al.*, 2007; Singh *et al.*, 2008; Turk a *et al.*, 2008; Cam *et al.*, 2009; Hamad and Al-Momene 2009; Davidson *et al.*, 2009; Duman *et al.*, 2009; Lee *et al.*, 2010) [13, 17, 23, 29, 36, 57, 149]. *In vitro*, a study has indicated that the pomegranate fruit (peel and juice) extract can be used as an anti-plaque agent and inhibit the growth of *S. mutans* ATCC 25175 and *R. dento cariosa* Rd1. It also has the ability to inactivate the foodborne pathogens due to its anti-viral and anti-bacterial properties (Gianmaria *et al.*, 2017) [49].

### 3.1 Antioxidant Activity

Oxidation is the major problem which leads to a significant loss of nutritive value of foods. It reduces the organoleptic properties and appearance of food products (Fernandez *et al.*, 2007) [45]. The pomegranate fruits and their derivatives show high antioxidant activity, they are an excellent alternative to synthetic antioxidant in the agro-food industry. The polyphenol and flavonoid activities of pomegranate have health benefits for the prevention of inflammatory, cardiovascular and other diseases (Noda *et al.*, 2002; Miguel *et al.*, 2004) [104, 114]. The pomegranate fruits and their derivative parts such as oil, peel, and juice contain a higher level of flavonoids, polyphenol, and anthocyanins such as cyanidine, pelargonidin, and delphinidin. There are various reports presence on antioxidant in pomegranate juice (Noda *et al.*, 2002; Seeram *et al.*, 2006b) [114, 142]. The pomegranate fruits extract has free radical scavenging activity against anions (superoxide) and radicals (hydroxyl) (Guo *et al.*, 2007) [54]. Research also indicates that the pomegranate peel has highest antioxidant activity in the methanolic extract which was performed by FRAP, DPPH, and Cupric Reducing antioxidant Capacity (CUPRAC) assays (Kulkarni *et al.*, 2007; Zahin *et al.*, 2010) [83, 172]. Antioxidant activities of pomegranate and its part are beneficial to prevent disease both in-vivo and in-vitro. The consumption of pomegranate juice has the ability to protect against ultraviolet-A&B-induced cell damage, inactivate pro-carcinogen by the help of CYP (CYP1A2 and CYP3A) expression and reduce hepatic oxidative stress (Faria *et al.*, 2007a; Faria *et al.*, 2007b; Pacheco *et al.*, 2008; Sun *et al.* 2016) [43, 44, 118].

### 3.2 Anti-inflammatory

Inflammation is the first defense system (physiological) in the body. It protects against various injuries and diseases such as physical wounds, poisons, and others. It helps to maintain physiological function in the human body (Lee *et al.*, 2010) [17]. Several types of research have reported anti-inflammatory properties of pomegranate fruit and their derivative parts (Lansky and Newman 2007; Shukla *et al.*, 2008; Larrosa *et al.*, 2010; Lee *et al.*, 2010) [17, 90, 112]. The various studies have been reported that the pomegranate has observed to inhibit inflammation in a colitis rat model by a different mechanism (Balkwill *et al.*, 2005; Simmons *et al.*, 2005; Larrosa *et al.*, 2010) [90]. It inhibits-38 mitogen and activates protein kinase pathway (p38-MAPK) and NF-KB) due to anti-inflammatory activity. The nuclear factor (p38-MAPK and NF-kB) kappa light chain helps to activate B cells and is associated with increased gene expression of MCP1, COX-2, IL-1 $\beta$ , TNF- $\alpha$ , and iNOS (Hayden *et al.*, 2004) [60]. The pomegranate fruit extract decreases TNF- $\alpha$ , IL-1 $\beta$ , malondialdehyde (MDA) levels in-vitro with liver fibrosis (Toklu *et al.*, 2007) [164]. The seed oil of pomegranate is a good source of conjugated fatty

acid (punicic acid) has *in vivo* anti-inflammatory effect by limiting neutrophil activation and lipid peroxidation consequences (Boussetta *et al.*, 2009; Lee *et al.*, 2010) [17, 22]. Pomegranate fruits extract in methanol inhibited the production and expression of TNF $\alpha$  in microglial cells, in a dosed manner (Ahmed *et al.*, 2005; Jung *et al.*, 2006) [7, 72]. The pomegranate fruit extract has an anti-inflammatory effect *in vitro* against various disease models and inhibits the activation of kinase and NF- $\kappa$ B in human chondrocytes (De Nigris *et al.*, 2007) [30]. Pomegranate fruits and their parts significantly reduce and inhibit the expression of vascular inflammation markers, thrombospondin (TSP) and growth of cytokine-transforming factor- $\beta$ 1 (TGF- $\beta$ 1) arterial endothelial-nitric oxide synthase (eNOS), cytokine IL-8, prostaglandin PGE2 and secretion of nitric oxide (Romier-Crouzet *et al.*, 2009; Larrosa *et al.*, 2010) [90, 130].

### 3.3 Carcinogenesis/Anticancer

Pomegranate fruits have the ability to prevent against various types of cancer such as lung, colon, breast and prostate (Khan *et al.*, 2007a; Rettig *et al.*, 2008; Khan *et al.*, 2009; Koyama *et al.*, 2010; Sturgeon *et al.*, 2010; Kasimsetty *et al.*, 2010;). It inhibits NF-k Band cell viability (Hong *et al.*, 2008) [65, 75, 77, 82, 128, 153] and gene expression of AKR1C3 (aldo-keto reductase family 1 member C3), HSD3B2 (3-beta-hydroxysteroid dehydrogenase type 2), SRD5A1 (steroid 5 alpha-reductase type 1) due to anti-cancer properties of pomegranate fruits. During a study, it was observed fruit extract of pomegranate after 72 hours have significant inhibition of cancer (lung) (Khan *et al.*, 2007b) [78]. Pomegranate fruits have potential activity as chemo protective against cancer. These compounds inhibit and blockage carcinogen formation in phase I, detoxification of enzymes, scavenging of DNA-reactive agents, homeostatic hormones modulation, suppression of hyper-cell proliferation induced by carcinogens, apoptosis, angiogenesis, inhibition of phenotypic expressions of preneoplastic and neoplastic cells (Tanaka and Sugie 2008). Several studies have been reported that the anticancer properties of pomegranate and its derivative showed due to the higher antioxidant properties, which help to protest cancer (Afaq *et al.*, 2005; Lansky *et al.*, 2005a; Lansky *et al.*, 2005b; Lansky and Newman 2007; Syed *et al.*, 2007; Hong *et al.*, 2008; Hamad and Al-Momene 2009) [57, 65, 98, 112, 156]. All parts of the pomegranate have the ability to inhibit cancer cell proliferation and invasion. They are a potential inhibitor of cell growth (Hong *et al.*, 2008) [65]. Pomegranate oil and juice has activity on prostate human against cancer proliferation and invasion *in vitro* due to its antiproliferative activity (Seeram *et al.*, 2005; Pantuck *et al.*, 2006; Kohno *et al.*, 2004) [129, 140]. Pomegranate and its derivative have the ability for inhibited type 1 17-beta-hydroxysteroid dehydrogenase (Adams *et al.*, 2006) [3]. Its constituents may be a promising therapy for prostate cancer and inhibit breast cancer cell proliferation and invasion (Malik *et al.*, 2005; Koyama *et al.*, 2010) [82, 98]. Joseph *et al.* (2013) [71] observed during his study both in-vivo and *in-vitro*, the galactomannan polysaccharide (PSP001) of pomegranate has a directly effect on cancer cell lines and ascites tumor.

#### 3.3.1 Prostate Cancer

Prostate cancer is the 2nd largest disease in male cause high cancer death in the world. The previous researchers have been reported that the pomegranate fruit has the ability to inhibit the growth of cells and induced cell death programme. The

phenolic activity of fermented juice and oil can inhibit the proliferation of the PC-3 and DU145 human prostate cancer cell lines and LNCaP. Pomegranate fruits extract significantly decrease specific antigen level in serum and inhibit the growth of tumor cell (Albrecht *et al.*, 2004; Malik *et al.*, 2005; Rettig *et al.*, 2008) [8, 98, 128].

### 3.3.2 Breast Cancer

The pomegranate fermented juice has an antiproliferative effect on breast cancer cell line MCF-7 and MB-MDA-231. The seed oils of pomegranate prevent 90% proliferation of MCF-7 cells (Mehta *et al.*, 2004; Khan *et al.*, 2007a) [77, 102].

### 3.3.3 Lung Cancer

The pomegranate fruit inhibits many signaling pathways such as Mitogen-activated protein kinases (MAPK) PI3K/Akt and NF $\kappa$ B. It is used for the treatment of lung cancer. The several studies have been reported that, the chemo preventive effects of pomegranate fruits (Khan *et al.*, 2007a; Newman *et al.*, 2007) [77, 112].

### 3.3.4 Colon Cancer

The pomegranate juice has an anti-inflammatory effect on human colon cancer. It reduces the phosphorylation of the p65 subunit of NF $\kappa$ B response and 79% inhibition in TNF- $\alpha$  protein expression (Adams *et al.*, 2006) [3].

### 3.3.5 Skin Cancer

The pomegranate and its derivative reduce (7%) tumor incidence, reduction in ornithine decarboxylase (ODC) activity (17%), decrease the numbers of tumors. The pomegranate is effective against ultraviolet A and B. It damages fibroblast cells of a human (SKU-1064) and reducing transcription of NF $\kappa$ B (Hora *et al.*, 2003; Syed *et al.*, 2006; Pacheco *et al.*, 2008) [66, 118, 157].

### 3.4 Anti-angiogenesis

It is a most important process for the development of new blood vessels. It is imperative for the supply of the nutrition and oxygen for tumor. It has the ability for a target of prevention of cancer (Pfeffer *et al.*, 2003; Scappaticci *et al.*, 2003) [121, 138]. Fibrocyte is the most angiogenesis and secretes extracellular matrix-degrading enzymes (MMP-9). It stimulates endothelial cell invasion and secretes pro-angiogenic factors such as vascular endothelial growth factor (VEGF), basic fibrocyte growth factor (bFGF) and interleukins (IL) (Hartlapp *et al.*, 2001) [58]. The anti-angiogenesis activity of pomegranate measured vascular growth factor (VEGF), estrogen resistant (MDA-MB-231) human breast cancer cells and immortalized normal human breast epithelial cells (MCF-10A), IL-4, and migration inhibitory factor (MIF) in the conditioned media of estrogen-sensitive (Toi *et al.*, 2003) [161].

### 3.5 Cell-apoptosis

It is a programme of cell death and useful for the anti-cancer treatments. Pomegranate has the ability of the cell death programme with the help of various mechanisms. It was observed *in vitro*, ellagitannin of pomegranate increase activity of caspase-3 in cancer cell line (WA4) (Dai *et al.*, 2010) [28]. The Punic acid of pomegranate has been showed apoptosis in both estrogen-sensitive cell line developed from MDA-MB-231 cells (MDA-ERalpha7) and estrogen insensitive breast cancer cell line (MDA-MB-231) by the help

of lipid peroxidation and the PKC (Protein kinase C) signaling pathway (Grossmann *et al.*, 2010) [53]. The major phenolic content such as ellagitannin, tannin and Ellagic acid of pomegranate has the ability to apoptosis in human colon cancer caco cell-2 through down regulations of block S phase cycle of cell and down-regulation of cyclins A and B1 (Larrosa *et al.*, 2006) [91].

### 3.6 Cardiovascular

It is a major risk factor to develop coronary heart disease known as dyslipidemia. It elevated low-density lipoprotein cholesterol (LDL-C) levels and help to reduce high-density lipoprotein cholesterol (HDL-C) (Esmailzadeh and Azadbakht, 2008) [1]. It was investigated through several types of research, the pomegranate help to attenuation of atherosclerosis and LDL oxidation (Aviram *et al.*, 2000; Fuhrman *et al.* 2005; Ignarro *et al.*, 2006; Sezer *et al.*, 2007; Basu and Penugonda 2009; Davidson *et al.*, 2009; Fuhrman *et al.*, 2010) [14, 20, 29, 47, 48, 68, 144]. It showed antihypertensive, anti-atherogenic and anti-inflammatory effects in-vitro (Gil *et al.*, 2000) [51].

Pomegranate juice reduces blood pressure and prevents serum angiotensin-converting enzyme activity. The consumptions of pomegranate juice decrease 30% intima-media thickness after 1 year (Aviram *et al.*, 2004; Stowe *et al.*, 2011) [15, 152]. Punic acid (polyphenols) of pomegranate seed oil showed anti-atherogenic effect. It decreases triglycerides (TG) and TG: High-density lipoprotein (HDL) cholesterol ratio (Mirmiran *et al.*, 2010) [106].

The pomegranate and its derivative help in the reduction of oxidation-sensitive responsive genes such as p-CREB and ELK-1 and risk of heart disease (Esmailzadeh *et al.*, 2008) [1].

### 3.7 Antidiabetic

Diabetes is the 3rd most prevalent disease in the world (WHO). According to the international diabetes federation, approx. 194 million people were suffering from diabetes in 2003 and it will be expected 333 million people by 2025 (Sicree *et al.*, 2003) [147]. The pomegranate and their part such as peel, seed arils have excellent properties against preventing diabetes (Huang *et al.*, 2005; Li *et al.*, 2005; Katz *et al.*, 2007; Parmar and Kar 2007; Li *et al.*, 2008; Bagri *et al.*, 2009) [18, 67, 76, 95, 120]. The pomegranate phenolic contents such as oleanolic, ursolic and gallic acids are combined with anti-diabetic effects (Katz *et al.*, 2007; Li *et al.*, 2005) [76, 95]. The pomegranate peel help in increase  $\alpha$ -amylase activity and serum level of glucose and decreasing serum insulin levels (Szkudelski, 2001; Parmar and Kar, 2007) [120, 158]. The phenolic property of pomegranate peel affect glycemia with the help of different mechanism and constrain glucose absorption in the gut (Scalbert *et al.*, 2005) [137].

### 3.8 Skin Health

The ultraviolet radiation is the main cause of adverse effect on human body skin, oxidative stress, skin aging and immune suppression (Widmer *et al.*, 2006; Aslam *et al.*, 2006) [13, 171]. The several researchers reported that the pomegranate and its derivative are shown stimulate keratinocyte proliferation in monolayer culture. They are accelerated type I procollagen synthesis and inhibited matrix metalloproteinase-1 (MMP-1; interstitial collagenase) production by dermal fibroblasts, but had no growth-supporting effect on keratinocytes (Pacheco *et al.*, 2008) [118]. The phenolic activity of pomegranate protect against ultraviolet A and B induced cell apoptosis of human skin fibroblasts may be attributed to increasing intracellular

antioxidant capacity and reducing the generation of intracellular ROS. It inhibits ultraviolet rays and decreases proinflammatory cytokines IL-1  $\beta$  and IL-6 due to the phenolic activity (Syed *et al.*, 2006; Bae *et al.*, 2010) <sup>[17, 157]</sup>.

### 3.9 Oral Health

Pomegranate and its derivative are considered for good oral health and gingivitis development (Di *et al.*, 2009) <sup>[39]</sup>. They are effective against patients afflicted by candidiasis associated with denture stomatitis (Vasconcelos *et al.*, 2003) <sup>[167]</sup>. The various studies have been reported, the hydraulic extract of pomegranate is effective against plaque (dental) microorganism (Di *et al.*, 2009) <sup>[39]</sup> and effective as an adjunctive periodontal therapy (Sastravaha *et al.*, 2005). They provide antibacterial and antioxidants agents in mouth and gum areas (Di *et al.*, 2009; Badria and Zidan 2004) <sup>[16, 39]</sup>. The phenolic content of pomegranate fruits is potentially effective against oral cavity disease. They have direct contact with tissues before being absorbed and metabolized and activated into glycones by human and bacterial enzymes (Halliwell *et al.*, 2000; Walle *et al.*, 2005) <sup>[56, 170]</sup>.

### 3.10 Antimicrobial

Antimicrobial agents are the inhibitor and growth inhibitor of microorganism. The applications of antimicrobial in food industry very important, they are working as a preservative of foods (Viuda *et al.*, 2008) <sup>[169]</sup>. The pomegranate fruits and its derivative exhibit antibacterial activity against highly pathogenic and antibiotic-resistant organism (Reddy *et al.*, 2007; McCarrell *et al.*, 2008; Al-Zoreky 2009; Choi *et al.*, 2009; Gould *et al.*, 2009) <sup>[10, 26, 52, 100, 127]</sup>. They have wide applications in pharma and food sector due to their properties. The pomegranate peel extracts exhibit antimicrobial effect against MSSA, PVL, and MRSA. The highest antibacterial activity showed against E.coli in ethanol extract (Lansky *et al.*, 2004; Satish *et al.*, 2007; Jurenka, 2008; Gould *et al.*, 2009; Sharma *et al.*, 2010) <sup>[52, 112, 145]</sup>. Pomegranate derivative (juice) has anti-HIV-1 property. It inhibits CD4 and CXCR4/CCR5 cells virus binding. It helps to prevent infection by primary virus clades A, G and O groups (Neurath *et al.*, 2005) <sup>[110]</sup>.

### 3.11 Antiviral

The Punicalagin, Ellagic acid, caffeic acid, and luteolin are the major polyphenols in pomegranate. Punicalagin is reacting as the anti-influenza phenolic content of pomegranate (Haidari *et al.*, 2009) <sup>[55]</sup>. It inhibits replication of human influenza A/Hong Kong (H3N2) and blocked replication of RNAs virus (Song *et al.*, 2005). The pomegranate fruit extract used as a viricidal agent and has a microbiocidal effect on HIV-1 (Neurath *et al.*, 2004; De *et al.*, 2006) <sup>[39, 109]</sup>.

### 3.12 Anti-Diarrheal

The pomegranate fruits and its derivative show anti-diarrheal properties in alcohol and aqueous solution. They exhibited a concentration-dependent inhibition of the spontaneous movement of the ileum and attenuated acetylcholine-induced contractions (Pillai, 1992; Olapour *et al.*, 2009) <sup>[115, 123]</sup>.

### 3.13 Gut Microbiota and Sperm Quality

The pomegranate fruits and its derivative lead to accumulation of the ellagitannins in the large intestine of the human body and joined with gut microflora complex (Seeram *et al.*, 2006a; Bialonska *et al.*, 2009) <sup>[21, 141]</sup>. The pomegranate

juice has increased concentration in epididymal sperm, the cell density of spermatogenic, motility of sperm and diameter of seminiferous tubules and germinal cell layer thickness. It helps to decrease the rate of abnormal sperm. The various studies investigated, ellagitannins of pomegranate have a protective effect against testicular and spermatozoal toxicity, sperm quality (cyclosporine A) and oxidative stress (Turk *et al.*, 2008; Turk *et al.*, 2010) <sup>[164, 165]</sup>.

### 3.14 Malaria and Alzheimer

Pomegranate and its derivative have the ability to induce a level of the MMP-9 mRNA through hemozoin and decrease the TNF, which helps to inhibition of the proinflammatory mechanisms responsible for the onset of cerebral malaria and ant parasitic activity (Dell *et al.*, 2009, Dell *et al.*, 2010) <sup>[31, 32]</sup>. The several types of research have been reported pomegranate juice has the ability to the improvement of Alzheimer disease (Hartman *et al.*, 2006) <sup>[59]</sup>.

### 3.15 Wound healing

The pomegranate and their derivatives have the ability to reduce wound area and increase bands of collagen, few inflammatory cells, and fibroblast. The hydraulic extract of pomegranate fruits shows protein synthesis, collagen, wound contraction and the period of epithelialization (Pirbalouti *et al.*, 2010a; Pirbalouti *et al.*, 2010b; Hayouni *et al.*, 2011) <sup>[61, 124, 125]</sup>.

### 3.16 Obesity

The World Health Organization reported currently there are more than 1 billion adults are overweight and approx. 300 million are obese (Cerda *et al.*, 2003; Mackay and Mensah 2004) <sup>[24, 97]</sup>. Several studies investigated the effective property of pomegranate and its derivatives against obesity.

## 4. Conclusions

This review congregates published studies on pomegranate and their derivatives. They have medicinal properties such as antimicrobial, antioxidant, anti-inflammatory, anticancer, antiviral, anti-hepatotoxic and anti-diabetic etc. Several studies in worldwide investigate that, the pomegranate fruits and its derivative are used in the prevention of chronic disease. The phenolic compounds of pomegranate and its derivative such as ellagitannins, Gallic acid, Ellagic acid, Quercetin, Punicalagin, Punicalin have been shown the pharmacological property. These properties and mechanism obstruct signaling pathways (AKT/P13K, PI3K, Bax, Bad, MPAK, ERK1/2, P38, and JNK). There are several in-vivo and in-vitro studies reported that the pomegranate and its derivative roles in the prevention of various diseases. It was concluded after the congregate literature review, more study is needs warranted to further determine the properties and applications of galactomannan polysaccharide pharma and food sector.

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