

REVIEW ARTICLE

The Polyphenolics and Health Effects of Pomegranate

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ABSTRAK

Buah delima (*Punica granatum L.*) merupakan buah yang banyak dikonsumsi sebagai buah segar maupun olahan oleh masyarakat. Berbagai laporan menunjukkan bahwa buah delima juga mempunyai manfaat kesehatan yang baik. Buah delima mengandung senyawa antioksidan polifenol, meliputi elagitanin (terhidrolisis), antosianin, galotanin, dan asam elagik yang terbukti dapat menjaga kebersihan mulut, kesehatan kulit, mensintesis kolesterol, membersihkan radikal bebas pembuluh darah, dan mencegah kanker prostat. Selain sebagai antioksidan, uji *in vitro* dan *in vivo* menunjukkan bahwa buah delima juga dapat berfungsi sebagai antidiabetes, hipolipidemia, antikarsinogenik, antibakteri, antiinflamasi, dan antivirus. Review berikut bertujuan untuk menyajikan gambaran tentang kandungan senyawa bioaktif, fungsi fisiologis dan kesehatan dalam buah delima.

Kata kunci: Kandungan Polifenol, Biji Delima, Kulit Delima, Senyawa Bioaktif

ABSTRACT

Pomegranate (*Punica granatum L.*) is a useful fruit which mostly consumed as fresh fruit and can also be used as a various of processed products. Reports proved pomegranate were beneficial to health. Polyphenolic compounds in pomegranate especially ellagitannin (hydrolyzed), anthocyanins, gallotannin, and ellagic acid can maintain oral hygiene, healthy skin from the effects of free radicals caused by UV radiation, has the ability to synthesize cholesterol, destroying free radicals in the human vascular system and can prevent prostate cancer. *In vitro* and *in vivo* test has shown the fruit is acting as anti diabetic drug, and hypolipidemic, anticarcinogenic, antibacterial, anti inflammation, and antiviral. This review presenting an overview about the bioactive compound contents, physiological and health function of the fruit.

Keywords: Polyphenol content, Pomegranate seed, Pomegranate peel, Bioactive compound.

INTRODUCTION

Pomegranate (*Punica granatum*; *Punicaceae*) is a fruit originated from the Middle East. Pomegranate's popularity is known for a long time by the Iranian efforts. Currently, pomegranate is spread all over the world especially in Mediterania, China, South East Asia and other tropical areas (Levin, 1994). In Rome, this species is known as "*Malum punicum*" (*punican apple*) and then it is known as "*Punicum granatum*". C. von Linneaus gave "*Punica granatum*" which was after city of Granada in Spain.

Pomegranate has 2 variants which are *Punica granatum* and *Punica protopunica*. *P. protopunica* is pink, and large, while *P. granatum* is red, smaller and less sweeter. *P. granatum* has more than 1000 cultivars (Mars, 2000). Pomegranate is considered as a well grown tree in dry zone with height of 5-8 metres. Pomegranate is one of the shrubs, bloom all year long, bunion shaped fruit, round with diameter of 5-12 cm, lots of seeds,

long round, flat shapes, hard consistency, not structured, red, pink, and white in colours (Ganes, 2010).

Pomegranate can be consumed fresh or extracted as refreshment as juice, canned beverages, jello, jams, paste, flavor enhancer and also can be used as beverages colouring agents. (Fadavi *et al.*, 2005; Mousavinejad *et al.*, 2009). Edible part of pomegranate (around 50% from weight) consists of coated seeds 80% dan 20% seeds (Aviram *et al.*, 2000). Wang (2011), has proven that the making of pomegranate juice by mixing seeds and skin together was given a better effect considering the polifenol substances has a lot of potential to increase antioxidants effects from fenolat, proantosianidin and flavonoid contains within its skin.

The potentation of antioxidant in pomegranate is very high, which is around 92% (Gil *et al.*, 2000). This is because the pomegranate skin contains a lot of punikalagin substance, while the seed and fruit contains a lot of elagic acid and galatic acid (Loren *et*

al., 2005; Zheng, 2011), which is a very good source of antioxidant (Seeram *et al.*, 2005; Singh *et al.*, 2000). Evidence showed that pomegranate can keep facial skin young because the polyphenol substance can protect the body from free radicals and even stronger if compared to orange or apple (Tyagi, 2012). Based on the facts, consuming pomegranate juice as part of the routine can protect and also fixing broken liver, protect kidney and prevent heart attack. Apart from that, pomegranate also have the ability in assisting cholesterol synthesis, destroying free radicals in human blood vessel and prevent prostatic cancer (Malik *et al.*, 2005).

Currently, pomegranate is used in cosmetic manufacture, cure for diarrhea, respiration (Lansky *et al.*, 2007), even for food (Finkel & Holbrook, 2000). For this review, we will elaborate the contents of pomegranate, bioactive substance which have the ability as antimicrobes, antioxidants, anticancer, antidiabetic, anti-inflammatory and health benefits.

Polyphenol's Content in Pomegranate

Polyphenol is secondary metabolic contents in plants with more than 8.000 phenolic substances (Gropper *et al.*, 2009). Polyphenol has a specific

marker which is a lot of phenolic groups within its molecules and usually in polar glycosides and easily soluble in polar solvents. Pomegranate has polyphenolic substances all over its fruit such as skin, seed, and coated seed which are commonly consumed. Coated seed contain 85% water, 10% sugar especially fructose and glucose, 1,5% pectine, organic acid such as ascorbat acid, citric acid, malate acid, and other bioactive substances such as phenolate and flavonoid especially antosianin (Aviram *et al.*, 2000; Tezcan *et al.*, 2009). The chemical composition for each pomegranate differs according to the cultivants, area, climate and storage conditions (Barzegar *et al.*, 2004; Fadavi *et al.*, 2005). The pomegranate skin has some substances consisting of: 1) Hidroxybenzoat acid such as elagic acid, galatic acid (Amakura *et al.*, 2000); 2) Tannin acid group such as: elagitanin, galotanin, punikalinalin, punikalagin, pedunkulagin, korilagin, kasuarinin, telimagrandin, granatin a, granatin b, antosianin, kuersetin, dan katekin; 3) Hydroxy cynamate acid which are kafeat acid, chlorogenic acid, and kumarat acid; 4) Carboxylic acid such as kuinat acid; 5) Flavanoid: katekin, epikatekin, epigalokatekin-3-galat, kaempferol, kaempferol-3-o-glycoside, kaempferol-3-o-ramnoglikosida, and

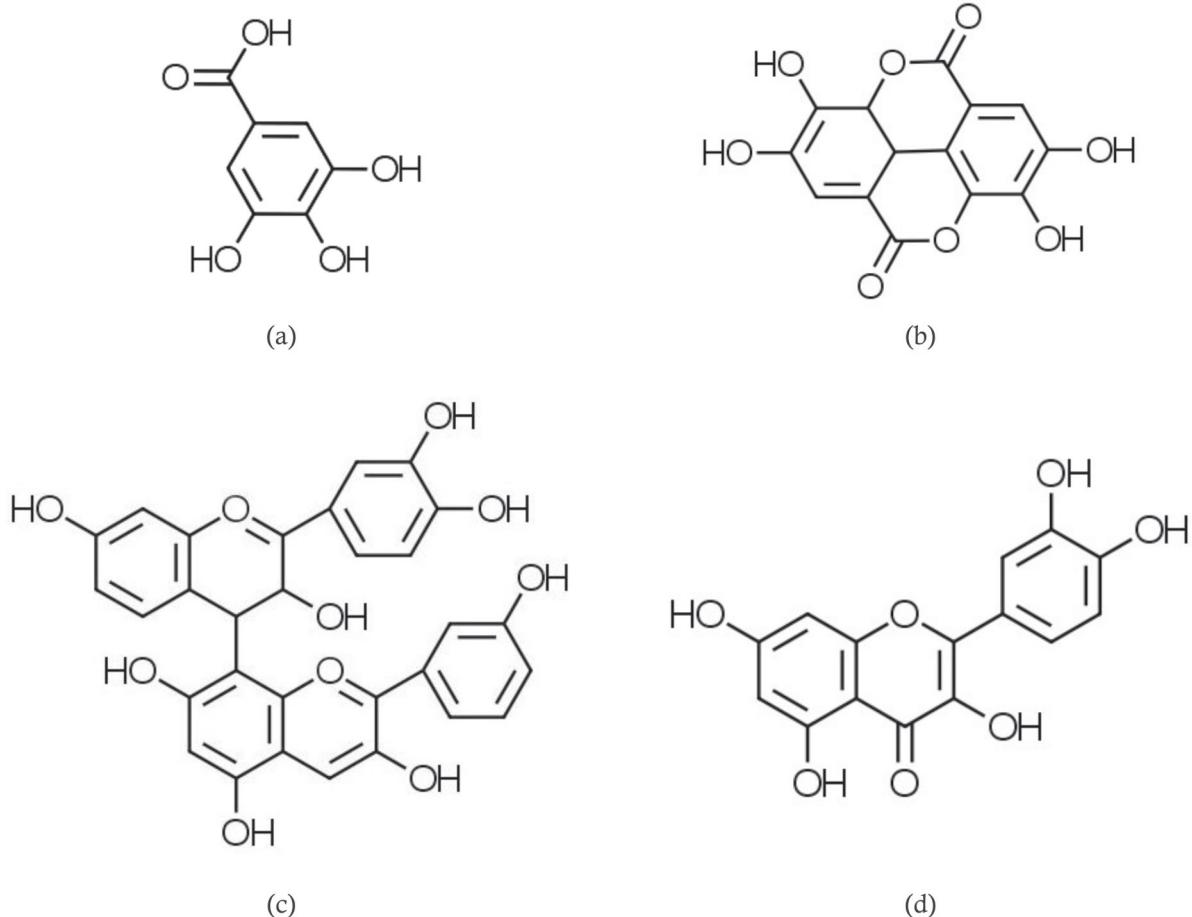


Figure 1. (a) Gallic acid's structure, (b) Ellagic acid's structure, (c) tannin's structure, (d) flavonoid's structure

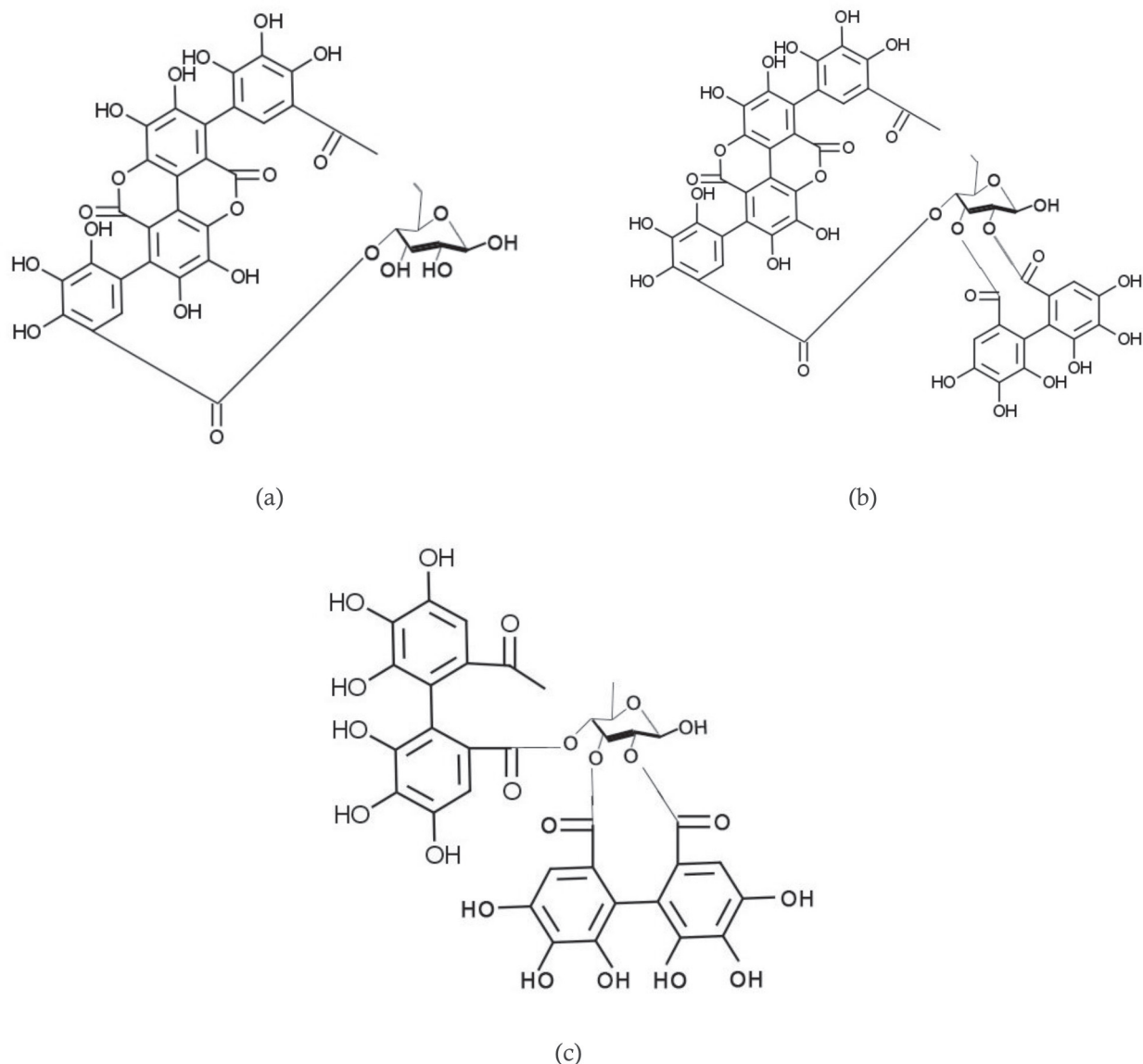


Figure 2. (a) Punikalin's structure, (b) Punikalagin's structure, (c) Pedunkulagin's structure. (Martos *et al.*, 2010)

naringin; 6) antosianin substance which are cyanidin, pelarginidin, dan delphinidin; 7) Alkaloid: peletierin (Prakash, 2011). Those substances are well known for preventing and inhibiting the formation of free radicals within the body, repair damaged body cells so it can give protection for the skin (Mousavinejad, 2009).

Pomegranate's seed is rich in fat which contains 12 - 20% from the seed's total weight. This oil contains non conjugated fatty acid such as linoleic acid, oleic acid, palmitic acid and stearic acid (Ozgul-Yucel 2005; Fadavi *et al.*, 2006). Apart from that, pomegranate's seed also contain elagic acid, punisatic acid (Hornung *et al.*, 2002), sterol, isoflavon, and lignin (Wang *et al.*, 2004). Those substances have roles as antioxidants and clinically proven to have anticancer activities (Lansky *et al.*, 2006), can be used as cosmetics, wound treatment and anti-allergy (Al-sabahi *et al.*, 2014).

Polyphenol is the main substance responsible in functionality of food (Viuda-Martos *et al.*, 2010). Polyphenol components are 80-90% elagitannin and galotannin, 8 -15% antosianin, dan 2 - 5% elagic acid (Allison *et al.*, 2008). Phenolic acid has 3 aromatic rings tied together which are punikalin, pedunkulagin, dan punikalagin (Seeram *et al.*, 2005). Punikalagin is converted during metabolism to become elagic acid also known as elagitanin (Pedriali *et al.*, 2008). Punikalagin has isomeric structure of 2,3-(s)-heksahidroksidifenoil-4,6-(s,s)-galagil-D-glukosa.

Biosynthesis of Elagic Acid in Pomegranate

Elagic acid's biosynthesis in pomegranate follow the generic pattern of substance as follows: ellagic acid synthesized from hexahydroxy-dyphenil dycarboxylic through lactonization between carboxylic and hydroxylic

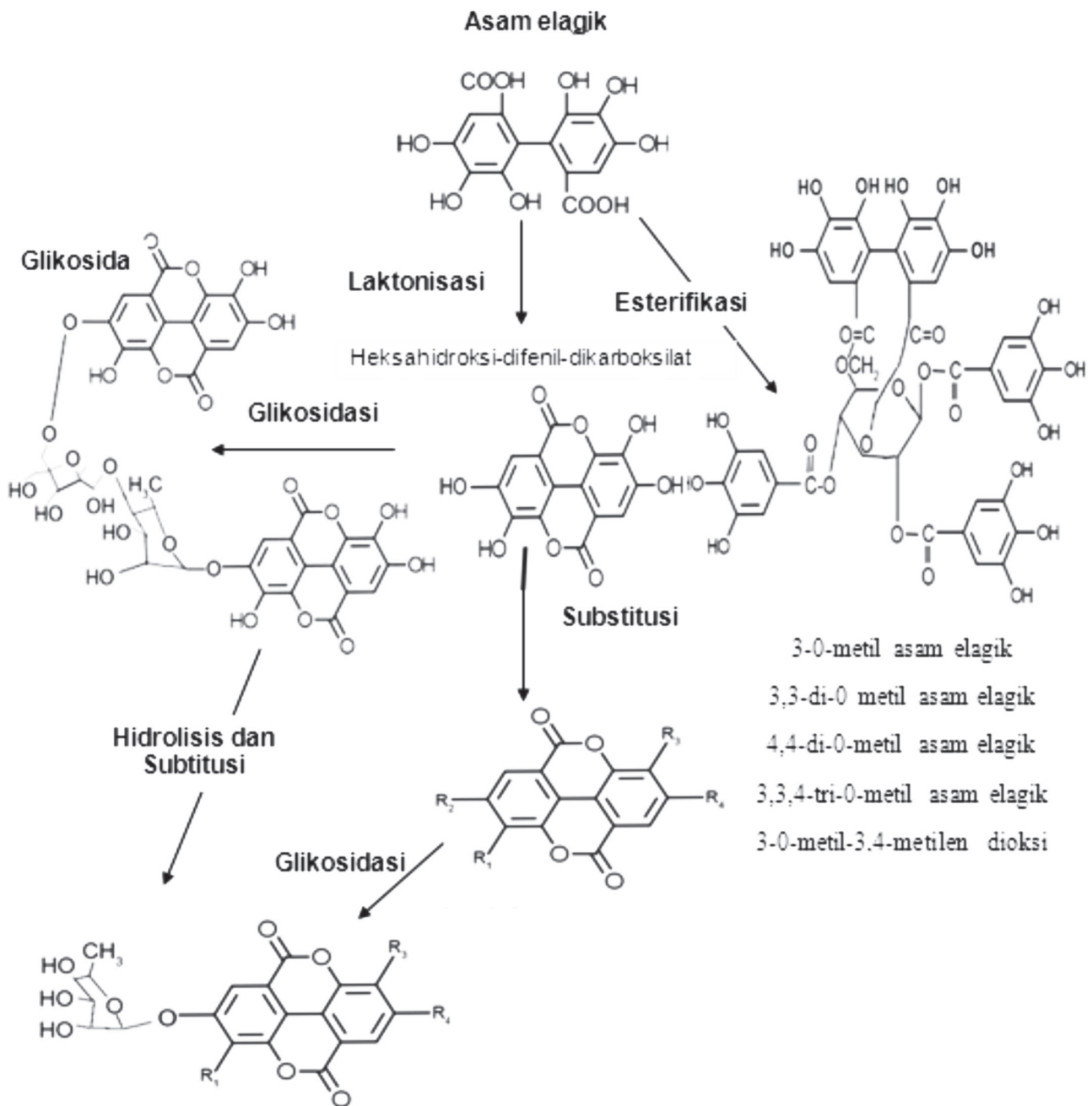


Figure 3. e Ellagic acid's biosynthesis in pomegranate (Wang *et al.*, 2010)

group considered as the main substance (figure 3). Hydroxylic group of ellagic acid is transformed to form derivatives of ellagic acid such 3-O-metil ellagic acid, 3,3-di-O metil ellagic acid, 4,4-di-O-metil ellagic acid, 3,3,4-tri-O-metil ellagic acid, dan 3-O-metil-3,4-metilen dioksi ellagic acid. Ellagic acid and its derivatives produce glycoside through glycosylation with saccharide. Some hexahydroxy diphenyl dicarboxylic acid can be polymerized through esterification between carboxyl group from one monomeric and hydroxylic group from one another (Wang *et al.*, 2006). The Galotanin, which mostly found in leaves contains groups of galoyl

which can be considered as derivatives from galatic acid (Li *et al.*, 2002). From biosynthesis perspectives, substances such as elagitanin was synthesized through esterification, lactonization, glycosidation between one group with other molecules. (Wang *et al.*, 2006).

Discussion Bioactive

There are epidemiologic studies showed that by consuming rich contents of polyphenol food and beverages can decrease some disease risk such as hypertension, coronary heart disease, atherosclerosis,

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stroke and dementia (Hemendra & Anand 2007). The most important part from pomegranate's bioactive is polyphenol which has the ability as antioxidants. As antioxidant, polyphenol also helps cancer, diabetes, heart disease and UV radiation towards skin. (Wang *et al.*, 2010). Bioactive substance within the pomegranate have the ability as follows:

1. Antioxidants

The antioxidants of pomegranate juice is widely studied. The result of the study is that the juice extract can bind free radicals and create better effect significantly compared to other fruit extract such as oranges, grapes, plums and pineapples (Halvorsen *et al.*, 2002). Pomegranate's juice can inhibit the in vitro LDL oxidation (Aviram, 2000) and also effective to decrease the level of in vivo LDL oxidation in mice (Xu *et al.*, 2005). Kawamada *et al.* 2002 and Moayadi *et al.*, 2004, suggested that polyphenolic substance in pomegranate can protect skin from free radical effects of the UV radiation. Pomegranate also have the ability to help cholesterol synthesis, break free radicals in human blood vessel and prevent prostatic cancer (Malik *et al.*, 2005). Pomegranate's antioxidant activity is mediated by phenolic hydroxyl group with double bindings including tannin, flavonoid, non fatty acid. The result is linear correlation between total antioxidant activity and phenolic contents resulting that phenolic is the most dominant antioxidant inside pomegranate (Surveswaran *et al.*, 2007).

Tanin is one of the best antioxidant found in almost part of pomegranate. Tanin such as elagic acid and punikalagin have important roles in pomegranate (Sestili *et al.*, 2007). Seeram *et al.*, 2008 compared antioxidant capacity and polyphenolic composition from 12 fruit juices in United States by using 3 methods. Those methods are: 1) test the antioxidant potential of the oxygen radical absorbance capacity (6 - hydroxy - 2,5,7,8 - tetramethylchroman - 2 -carboxylic acid (Trolox) Equivalent Antioxidant Capacity / TEAC), oxygen radical absorption capacity (Oxygen Radical Absorbance Capacity / ORAC), 2,2 - diphenyl - 1 - picrylhydrazyl (DPPH), and ferric reducing ability of plasma (ferric reducing ability of plasma - / FRAP; 2) test the antioxidant function, ie, inhibition of oxidation of low - density lipoprotein (LDL) ; and 3) evaluation of total polyphenol content. Those twelve fruit juices tested had the highest level of elagitanin and had the highest antioxidant capacity (Halvorsen *et al.*, 2002). Elagic acid reacts with free radicals because its ability to bind metallic ions, is a strong antioxidant towards lipid peroxyde in mitochondria and microsome

(Seeram *et al.*, 2005). Barrier toward lipid peroxidation makes pomegranate skin have major contribution as antioxidant. This inhibition was given by giving electron as donor so the electron can dispel the free radicals from lipid peroxidation (Anand *et al.*, 2004; Lansky *et al.*, 2007).

2. Antimicrobial

Apart from *Helicobacter pylori*, *Escherichia coli*, *Salmonella typhi*, dan *Shigella*, pomegranate's extract is also showed significant inhibition effect towards pathogenic bacteria especially gram positive bacteria. As stated by Nagaraju (1990), dried pomegranate skin boiled in water can be used for diarrhea and warts problems. Studies reported that *Staphylococcus aureus* both metilcyllin resistance (MRSA) and metycyllin sensitive are susceptible to pomegranate's skin fruit extract. This can be seen from the usage of pomegranate skin on bacterial infection (Machado *et al.*, 2003; Braga *et al.*, 2005). Apart from that, other bacteria such as *Streptococcus hemolyticus*, *Vibrio cholerae*, *Bacillus typhosus*, *Proteus bacillus*, *Proteus vulgaris*, *Bacillus subtilis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Listeria monocitogenes*, dan *Candida albicans*, are also reported to be susceptible to pomegranate extract (Navarro *et al.*, 1996). Active antibacterial from pomegranate skin are showed by substances from tannin such as elagitanin and flavonoid (Machado *et al.*, 2003; Wang *et al.*, 2008).

3. Anti Diabetic

Diabetes is the most common disease in the world and the number of the patients are today increasing. One way to control diabetes mellitus (DM) is by diet, consuming various fruits especially pomegranate. Finding suggest that pomegranate can prevent diseases and preserve health. Various researches have described the antidiabetic activities of pomegranate (Huang *et al.*, 2005; Li *et al.*, 2005; Katz *et al.*, 2007; Parmar & Kar 2007; Li *et al.*, 2008; Bagri *et al.*, 2009). Katz *et al.*, (2007) reported hypoglycaemic activities from flower, seed and skin of pomegranate. Li *et al.*, (2005) suggested that pomegranate flower extract increases hyperglycemic on type 2 diabetes postprandial and obesity, by inhibiting intestinal α -glukosidase. Huang *et al.*, (2005) showed the potential mechanism from pomegranate flower as antidiabetic which involves activation of PPAR- γ .

Parmar (2007) reported that by giving 200 mg/kg of pomegranate skin can normalize all changes caused by aloxan, a substance used to induce DM because it can increase glucose serum level, activity of α -amilase, level of water consumption, lipid peroxidation in the liver, heart, and kidney as well as reducing insulin serum

(Szkudelski, 2001). The main antidiabetic substance in pomegranate is polyphenol which can affect the blood level in two different mechanisms which are inhibiting the glucose absorption by the intestine or absorption through perifer tissue (Scalbert *et al.*, 2005). Hypoglycaemic effect of anthocyanin within 10 mg/kg dose, was observed on maltose as source of glucose (Matsui *et al.*, 2002), this proves that such effect is caused by glucoside inhibition in the intestinal mucosa. Some in vitro studies in cultured cell also shown that polyphenol can increase glucose by perifer tissue, which can lower the sugar level (Scalbert *et al.*, 2005). Furthermore, Shiraishi *et al.*, (2002) & Aviram *et al.*, (2002) explained that by consuming pomegranate juice on daily basis can protect as well as fixing a broken liver and also protecting kidney and prevent heart attack.

4. Anti inflammatory and Anti Cancer

Inflammation is the first physiological defense system in the human body which can protect wounds caused by physical harms, toxic, etc. The defense system is also known as short term inflammatory, breaking the infectious microorganisms, remove irritants, and preserving physiological functions. However, in long term can cause dysfunctional such as asthma and rheumatoid arthritis (Lee *et al.*, 2010). Acute inflammatory can effects joints, intestines and can cause cancer (Balkwill *et al.*, 2005). Acute inflammation can cause early changes involved in cancer development through pro inflammatory mediator such TNF- α , interleukin (ex.IL-6 and IL-8), transcription activating factor and lipid bioactive such as eicosanoid (prostaglandin E2 and derivatives products of lipoxigenase) (Lansky *et al.*, 2007). Inflammatory process was triggered by various chemical and biology factors such are pro-inflammatory enzyme, cytokine, eicosanoid, or tissues enzymatic degradations (Dao *et al.*, 2004). Some studies related to cyclooxygenase 2 (COX-2) (Cho *et al.*, 2004), isoform of cyclooxygenase (COX), responsible to catalyze arachidonate acid to become prostaglandin which related to inflammatory process. Other isoform is cyclooxygenase 1 (COX-1), which regulates the homeostasis process (Dao *et al.*, 2004). Extract from pomegranate seed oil consists of polyphenol and fatty acid showed that 31-44% persecution on sheep's cyclooxygenase and 69-81% persecution of lipoxigenase on mules, whilst the rind fermented showed that 21-30% lipoxigenase inhibition on mules (Schubert *et al.*, 1999). Polyphenol in seeds oil also reported able to weaken the inflammatory cellular signal towards various colon cancer cells (Adams *et al.*, 2006). Many studies have shown the

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anti inflammatory properties of pomegranate (Lansky & Newman 2007; Shukla *et al.*, 2008; Larrosa *et al.*, 2010; Lee *et al.*, 2010).

Other information about the benefit of pomegranate is to keep oral hygiene (Kim, 2002), as eye ointments (Bruijn *et al.*, 2003), weight loss soap (Guojian, 1995), and as additional therapy to increase bioavailability of radioactive colourings (Amorim, 2003). Currently, pomegranate as medication and nutritional products have been published by more than 300 new scientific researches related to health effects. Some scientific research have put foundation of the studies based on reliable research for the studies on the usage of traditional medicine from pomegranate (Julie, 2008).

CONCLUSION

According to the findings above, we can conclude that pomegranate as an antioxidant rich fruit, have antibacterial properties, useful for oral hygiene, dermatological disease, improving heart condition, and other medical applications. The antioxidant properties of pomegranate juice is effective to bind free radicals and have better effects compared to other fruit extract. The anti carcinogenic and anti inflammatory properties of pomegranate allows its use in therapy or adjuvant therapy in prevention to some cancer and heart disease.

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