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Punica granatum (Pomegranate) fruit and its relevance in Oral Hygiene.

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Abstract: *Herbal mouthwashes have been considered to be a more advantageous option to their chemical counterparts, for a long time. Neem, Honey bee extract and Cranberry extract, among others, have had scientists actively researching their properties. However, having demonstrated significant medicinal uses from treating cancers to lowering heart disease, pomegranate extract is the newest talk of the dental community. This is mainly because of its active component, polyphenolic flavonoid that is believed to prevent gingivitis and basic plaque formation through its anti-inflammatory, anti-bacterial and anti-oxidant properties. Besides being able to exert considerable control over the levels of different enzymes in the oral cavity, the polyphenols are significantly active against notable oral bacteria like A. actinomycetemcomitans, S. aureus, P. intermedia and P. gingivalis. Through a series of laboratory tests and animal trials, the pomegranate extract has been shown to reduce the clinical signs associated with chronic, inflammatory periodontitis, among other indications such as treatment of oral ulcers.*

The aim of this systematic review is to propose pomegranate extract as an effective active ingredient in a mouthwash by describing the properties, significant trials and studies and past literature reviews that have marked it suitable for such a use.

Key-words: *Pomegranate, oral hygiene, Punica granatum, fruit, polyphenols*

I. Introduction

A multitude of mouthwash products have arisen, since the early days, containing different active chemical ingredients. However, increasing awareness about the disadvantages of chemicals amongst the public has created an interest in pursuing herbal options.[1]

Various herbal products such as Propolis[2], Azadirachta indica[3], Citrus paradisi[4] and Vaccinium oxycoccos[5] have shown significant advantages in reducing signs of gingival and periodontal inflammation. Punica granatum, too, being one of those, has shown to combat plaque by its anti-bacterial, anti-inflammatory and anti-oxidant properties. The following review will discuss its ability to act as an effective agent in reducing plaque and its possible use in a mouthwash.

II. Properties of the Pomegranate fruit

Punica granatum is grown as a fruit crop or as an ornamental tree. The tree is mostly, drought-tolerant, and can be grown in dry areas.[6] It can tolerate moderate frost[7] and can grow up to sixteen ft. high. Its trunk is surrounded by a red-brown coloured bark which, with time, attains a grayish hue. Its branches are stiff and spiny[8] and its flowers are over an inch across, having five to eight petals bearing a fleshy calyx.[9]

This fruit of nature has glossy leaves that are narrow and oblong in appearance. The peel contains bioactive compounds that include phenolics, flavonoids, proanthocyanidin compounds,[10] minerals such as potassium, nitrogen and sodium and complex polysaccharides.[11] Moreover, the edible part of the fruit consists of mostly arils and few seeds, in comparison. Each seed, which may range from 200-1000 in number, is surrounded by a pulp that may be white, purple or pink.[12]

The seeds are a rich source of lipids. Its oil is characterized by a high content of polyunsaturated fatty acids such as linolenic and linoleic acids and other lipids.[13] The seeds also constitute protein, fibres, vitamins, minerals, pectin and estrone, among others.[14] Arils, on the other hand, contain mostly water and a small amount of sugars, pectin, organic acid and bioactive compounds.[15]

Several characteristics between the different pomegranate genotypes vary. The most important of these are its fruit size, exocarp colour (ranging from yellow to purple), aril colour, seed hardness, ripeness and juice components.[16]

The ripening of this fruit is an integral process. This is because it is now understood that its antioxidant and sensory properties depend on factors that include the cultivar and climatic conditions during its maturation and ripening stage.[17]

III. Phenolic Compounds and their Mechanism of Action

The main components responsible for most of the purposeful properties of this fruit are the phenolic compounds.[18] Chemically, phenolic acids are defined as substances that possess an aromatic ring bound to one or more hydrogenated substituents.[19] Flavonoids, the most widely distributed subgroup of all phenolic compounds, are low-molecular-weight substances consisting of fifteen carbon atoms. Their structure primarily consists of two aromatic rings joined by a 3-carbon bridge.[20] Furthermore, the largest of all flavonoids that are present in the pomegranate arils are the Anthocyanins. Their pigments are what gives the fruit and juice its characteristic red colour.[21]

It has been suggested that the antioxidant activity of pomegranate components may be related to their phenolic constituents. These compounds are known for their properties to scavenge free radicals and to prevent lipid oxidation from taking place.[22] However, there exist some differences in opinion regarding which compounds play the bigger role in performing this activity. Tzulker et al concluded in their study that punicalagin is the cause for the antioxidant activity whilst anthocyanins play only a small role.[23] On the other hand, Madrigal-Carballo et al suggested that the polyphenolic molecules' performance of redox reactions forms the basis behind their anti-oxidant activity.[24] As such, reducing properties are associated with the presence of reductones[25] that function by breaking the free radical chain by donating an atom of hydrogen. Further, these reductones also prevent peroxide formation by reacting with certain specific precursors.[26] Contradictory to the aforementioned, Amarowicz et al suggested that it is the ability to chelate metal cations, that provides the fruit with excellent antioxidant effects.[27] Consequently there has been no specific ultimatum reached as to what component contributes most.

IV. Proposed Benefits in the maintenance of Oral Hygiene

It was realised a long time ago, that eating or drinking the juice of pomegranate could place antibacterial and antioxidant agents directly into the mouth. It was pointed out by Di Silvestro et al that chronic exposure of its active agents, like in the form of a mouthwash, would, however, give better results.[28] This is thought to occur due to the fact that the oral tissue would directly be exposed to polyphenols, which would subsequently get activated by enzymes, thereby participating actively in reducing the oxidative stresses present.[29]

The total anti-oxidant strength of this super fruit is measured in terms of its oxygen radical absorbance capacity (ORAC), which is 2341 micromol TE/100 g.[30] The arils, juice and peel extracts are said to have moderate anti-oxidant activity, whereas the pulp and the seeds exhibit high levels.[31] If used regularly in combination with dentifrices that contain bioactive botanical extracts, a mouthwash consisting of pomegranate will be able to fight dental plaque and tartar formation very effectively. This will occur due to the ability of the extract to prevent microorganisms from attaching to the tooth surface and from thwarting Streptococcus species from producing chemicals that produce dental caries.

Polyphenolic flavonoids are understood to be the ones that prevent gingivitis by reducing the oxidative stress in the oral cavity, providing direct antioxidant activity[32], anti-inflammatory[33] and anti-bacterial effects and complete removal of plaque from the surface of the tooth. They have been able to bring about significant reduction in the activity of the enzymes aspartate aminotransferase and alpha glucosidase[34] and increased activity of the antioxidant enzyme ceruloplasmin.

Pomegranate extract has been discovered to be effective in reducing inflammatory signs in cases of established chronic periodontitis.[35] Further, it has also been able to demonstrate a notable inhibition of the three main periodontopathogens, P. intermedia, P. gingivalis & A. Actinomycetemcomitans[36] and an improvement in the level of anti-oxidant concentration.

Additionally, pomegranate extract has also been able to inhibit the growth of S. aureus at higher concentrations and produce delays in its growth at lower concentrations.[37] This was further researched by Prashanth and others who reported that even the methanolic extracts of Punica granatum fruit rind were active against S. Aureus.[38] Additionally, in a study conducted in Brazil, the ethyl acetate extract of Punica granatum demonstrated considerable resistance to Methicillin Resistant Staphylococcus Aureus (MRSA) strains.[39] The aforementioned studies demonstrate considerable evidence in the effectiveness of the extract against microbial growth.

Other properties of Punica granatum extract are attacking the basic causes of tooth decay at the smallest biochemical level, with excellent vigour and aggression[40] and of possessing anti-inflammatory properties that can help soothe irritated tissues or ulcers.[41] Additionally, Vasconcelos et al reported that a gel containing pomegranate extract to be effective for patients having denture stomatitis associated with

candidiasis.[42] Theses aforementioned properties indicate possibility of usage in a dentifrice, an oral ulcer ointment and an anti-fungal cream, in addition to a mouthwash.

V. Review of Clinical in- Vivo Trials and in- Vitro Experiments:

Clinical Studies regarding the in-Vitro Antibacterial Activity

In a study comparing the growth of bacteria in three different concentrations of a methanolic pomegranate peel extract it was found that all concentrations had significant antibacterial activity against S. aureus and S. epidermidis and that the higher concentrations were effective against L. acidophilus, S. mutans, and S. salivarius.[43]

In another study, ethanol and water extracts of pomegranate demonstrated inhibitory effects against S. mutans and P. gingivalis.[44] Further, the results of a Brazilian study suggested that the application of a pomegranate gel may prevent attachment of bacteria in the oral cavity. In other in-vitro studies, pomegranate extract also inhibited strains of the periodontal bacteria, A. actinomycetemcomitans, P. gingivalis, P. Intermedia[45], Klebsiella, E. coli, and Proteus sp.. [46]

Clinical Study on combating Dental Plaque

A study was conducted to observe the difference in plaque build up, after the usage of a mouthwash containing pomegranate extract, chlorhexidine and a placebo rinse. After ensuring that all the healthy volunteers had refrained from basic oral hygiene measures for four days, the results were observed on the fifth day. It was concluded that the volunteers using pomegranate extract had significantly less plaque build-up than those using the placebo rinse. Furthermore, the pomegranate extract results had been comparable to that of the chlorhexidine rinse.[47]

Clinical Studies on preventing Gingivitis

A clinical study that enlisted volunteers with chronic gingivitis to use a pomegranate extract gel along with daily scaling for a week, showed significant improvement of the experimental group over the control group that only underwent scaling.[48]Another study was conducted wherein some volunteers were made to use a pomegranate extract mouth rinse and others were given a placebo, for a period of 4 weeks. The trial reported the former volunteers to show reduced total protein associated with presence of plaque-forming bacteria, reduced cell injury, reduced levels of enzyme alpha-glucosidase and increased activity of the enzyme ceruloplasmin.[49]

Clinical Study on fighting Periodontitis

A biodegradable chip impregnated with pomegranate peel extract, meant for sub-gingival use as an adjunct to scaling in patients with periodontitis, demonstrated decreased plaque build-up, pocket depth size and bacterial attachment in patients compared to the those with the placebo chip after a period of six months.[50]

Projected method of preparation of a mouthwash containing Pomegranate Extract

The mouthwash currently available in the market, containing pomegranate extract, has the following ingredients: water, glycerin, Aloe barbadensis leaf juice, Xylitol, Punica granatum extract, Camellia sinensis leaf extract, Chamomilla recutita (matricaria) flower extract, polysorbate 20, Mentha piperita (peppermint) oil, citric acid, menthol, poloxamer 331, colloidal silver and potassium sorbate.[51] A similar combination of components with slight modifications to adjust flavour, has been suggested in future products.

The following method was employed to extract the pomegranate in a research which isolated antimicrobial ellagitinnin from Punica gratum: The fresh fruit pericarp was exhaustively extracted with EtoH (ethanol), first. Then the dried ethanolic extract was suspended in water and successively divided with hexane, chloroform, ethyl acetate and butanol. The most active fraction on bioassay (ethyl acetate) was chromatographed on a XAD-16 column using water-methanol gradient. The active fraction was then eluded from the column with (Water) H2O:MeoH (methanol)(1:1), which was then submitted to chromatography on a sephadex LH-20 column using a gradient H2O:MeoH.[52] Subsequently, the active fraction was purified on a preparative column to afford the active compound punicalagin and the passive ones, ellagic acid and punicalin.[53]

A similar method, with more adjustments, as dictated by further research, can be employed while extracting the active components of this fruit while preparing a mouthwash.

Scope of use in Dentistry

The health risks caused by long-term use of chemical and pharmaceutical preparations are known to all. Hence there exists a natural need to investigate more plant-based options. This coupled with the worry of finding a suitable choice that would be practical for use in rural areas and lesser developed countries, gives mouthwashes containing pomegranate extract the much needed boost.[54] Besides, such products could be made

available at lower costs since they would be made using natural components and would be free from artificial colours, flavours and other chemicals.[55] Moreover, it would be easier to convince children to use it because of its agreeable smell.[56] Mouthwashes of this nature may also find use in children and adults that are mentally challenged as the product would have a pleasant smell which they would find more comfortable in using.

Alternate uses in Medicine

Pomegranate extract, apart from the various herbal uses that it is said to have, has been shown to reduce platelet aggregation[57], a factor that prevents both heart attacks and strokes. Apart from that, pomegranate extracts have shown overwhelming advantages in the inhibition of prostate cancer, breast cancer, colon cancer, lung cancer[58], leukaemia[59] and preventing vascular changes that promote tumour growth.[60] Also of note is that pomegranate's phytochemical compounds stimulate serotonin and oestrogen, which have shown to improve signs of depression in laboratory tested animals.[61] Other studies have revealed that this fruit might help improve erectile dysfuntion and reduce imflammation in patients suffering from arthritis.[62]

Pomegranate arils provide 12% of the DV (Daily Value) for vitamin C and 16% DV for vitamin K per 100 g, and have polyphenols, like ellagitannins and flavonoids. These are all excellent sources of dietary fibre.[63] Moreover, in preliminary laboratory research and clinical trials, the juice of the pomegranate has been considered effective in reducing heart disease risk factors, including LDL (Low Density Lipoprotein) oxidation, foam cell formation and macrophage oxidative status.[64] In a study on hypertensive patients, consumption of pomegranate juice for two weeks showed a decrease in systolic blood pressure by inhibiting serum angiotensin-converting enzymes.[65] Simple juice consumption is also said to inhibit viral infections.[66] On the other hand, punica granatum has also started to pave way for its use in preventing brain injuries.[67]

VI. Limitations

It has been reported that the ingestion of large amounts of pomegranate preparations can cause gastrointestinal problems like vomiting and nausea, for which further research is required. Additionally, allergic reactions to pomegranate have been reported on few occasions, and hence, can be cause of concern.[68] However, it should be kept in mind that the aforementioned limitations have been found on very rare occasions and should not serve to discern one from pursuing this fruit and its widespread uses in the dental profession.

VII. Conclusion

Pomegranate is slowly gathering interest as an exciting new oral hygiene product. It has been shown to improve oral hygiene considerably, by means of destroying plaque and suppressing the adherence of microorganisms to the surface of the tooth. It is additionally, a rich source of natural anti-oxidants and hence, useful in reducing the inflammatory signs in cases of established chronic periodontitis. Ongoing research in the medical field has shown it to bring improvements in cosmetic management and providing break-through treatment options in the diseases that plague mankind, especially, the elderly. In spite of having numerous benefits, no significant side effects have been reported till now. However, more research is required in checking the effectiveness of the extract on human subjects, possibility of cross reactions with concurrent medications such as warfarin[69] and reaction to over-dosing[70], among others. The aforementioned trials have limitations of their own, ranging from insufficient standardization of procedures followed to different concentrations of extracts being used each time. The authors would like to sincerely encourage further research in this field, wishing more standardized procedures and quantification methods are followed in the conduction of additional large scaled trials.

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References

[1]. Speight P. Summary of: Are alcohol containing mouthwashes safe? British Dental Journal. 2009; 207(10): 488-489.
[2]. Parolia A, Thomas M, Kundabala M., Mohan M. Propolis and its potential uses in oral health. International Journal of Medicine and Medical Sciences. 2010; 2(7): 210-215.
[3]. Almas K. The antimicrobial effects of extracts of Azadirachta indica (Neem) and Salvadora persica (Arak) chewing sticks. Indian J Dent Res. 1999; 10(1):23-26.
[4]. Kumamoto J, Scora RW, Lawton HW, Clerx WA. Mystery of the forbidden fruit: Historical epilogue on the origin of the grapefruit, Citrus paradisi (Rutaceae). Econ Bot 1987; 41(1): 97-107.

[5]. Toivanen M, Huttunen S, Duricová J, Soininen P, Laatikainen R, Loimaranta V et al. Screening of binding activity of Streptococcus pneumoniae, Streptococcus agalactiae and Streptococcus suis to berries and juices. Phytother. Res. 2009; (24) 1:S95-101.
[6]. Morton JF. Fruits of warm climates. Morton JF. 1987. p. 517
[7]. Sheets MD, DuBois ML, Williamson GJ. The Pomegranate. JCooperative Extension Service, Institute of Food and Agricultural Sciences, University of Florida Gainesville FL 32611. 2011; 997.
[8]. Kumari A, Dora J, Kumar A, Kumar A. Pomegranate (Punica granatum)-Overview. International Journal of Pharmaceutical and Chemical Sciences. 2012; 1(4): 1218- 1222.
[9]. Ross, Maxine S. Pomegranate: its role in cardiovascular health. Holistic nursing practice 2009; 23(3): 195-197.
[10]. Li Y, Guo C, Yang J, Wei J, Xu J, Cheng S. Evaluation of antioxidant properties of pomegranate peel extract in comparison with pomegranate pulp extract. Food Chemistry. 2006; 96(2), 254-260.
[11]. Jahfar M, Vijayan KK, Azadi P. Studies on a polysaccharide from the fruit rind of Punica granatum. Res J Chem Environ. 2003; 7:43–50.
[12]. Kader, Adel A. Postharvest biology and technology of pomegranates. Pomegranates: Ancient Roots to Modern Medicine. 2006. p 211-220.
[13]. Fadavi A, Barzegar M, Azizi HM. Determination of fatty acids and total lipid content in oilseed of 25 pomegranates varieties grown in Iran. J Food Comp Anal. 2006; 19:676–80.
[14]. Syed DN, Afaq F, Mukhtar H. Pomegranate derived products for cancer chemoprevention. Sem Cancer Biol. 2007; 17:377–85.
[15]. Tezcan F, Gültekin-Özgüven M, Diken T, Özçelik B, Erim FB. Antioxidant activity and total phenolic, organic acid and sugar content in commercial pomegranate juices. Food Chemistry. 2009; 115(3), 873-877.
[16]. Stover E, Mercure EW. The pomegranate: a new look at the fruit of paradise. HortScience. 2007; 42(5):1088-1092.
[17]. Aziz NA, Wong LM, Bhat R, Cheng LH. Evaluation of processed green and ripe mango peel and pulp flours (Mangifera indica var. Chokanan) in terms of chemical composition, antioxidant compounds and functional properties. Journal of the Science of Food and Agriculture. 2012; 92(3), 557-563.
[18]. Kelawala NS, Ananthanarayan L. Antioxidant activity of selected foodstuffs. Int J Food Sci Nutr. 2004; 55(6):511-516.
[19]. Marín FR, Martínez M, Uribesalgo T, Castillo S, Frutos MJ. Changes in nutraceutical composition of lemon juices according to different industrial extraction systems. Food Chem. 2001; 78:319–324.
[20]. Balasundram N, Sundram K, Samman S. Phenolic compounds in plants and agri-industrial by-products: antioxidant activity, occurrence, and potential uses. Food Chem. 2006; 99:191–203.
[21]. Jaiswal V, DerMarderosian A, Porter JR. Anthocyanins and polyphenol oxidase from dried arils of pomegranate (Punica granatum L.). Food Chem. 2010; 118:11–16.
[22]. Noda Y, Kaneyuka T, Mori A, Packer L. Antioxidant activities of pomegranate fruit extract and its anthocyanidins: delphinidin, cyanidin, and pelargonidin. J Agric Food Chem. 2002; 50:166–171.
[23]. Tzulker R, Glazer I, Bar-Ilan I, Holland D, Aviram M, Amir R. Antioxidant activity, polyphenol content and related compounds in different fruit juices and homogenates prepared from 29 different pomegranate accessions. J Agric Food Chem. 2007; 55:9559–9570.
[24]. Madrigal-Carballo S, Rodriguez G, Krueger CG, Dreher M, Reed JD. Pomegranate (Punica granatum L.) supplements: authenticity, antioxidant and polyphenol composition. J Funct Foods. 2009; 1:324–329.
[25]. Singh R, Murthy K, Jayaprakasha G. Studies on the antioxidant activity of pomegranate (Punica granatum) peel and seed extracts using in vitro models. Journal of agricultural and food chemistry. 2002; 50(1): 81-86.
[26]. Naveena BM, Sen AR, Kingsly RP, Singh DB, Kondaiah N. Antioxidant activity of pomegranate rind powder extract in cooked chicken patties. Int J Food Sci Technol. 2008; 43:1807–1812.
[27]. Amarowicz R, Pegg RB, Rahimi-Moghaddam P, Barl B, Weil JA. Free-radical scavenging capacity and antioxidant activity of selected plant species from the Canadian prairies. Food Chem. 2004; 84:551–562.
[28]. Di Silvestro RA, Di Silvestro DJ, Di Silvestro DJ. Pomegranate extract mouth rinsing effects on saliva measures relevant to gingivitis risk. Phytother Res. 2009; 23:1123–1127.
[29]. Johnson IT. New approaches to the role of diet in the prevention of cancers of the alimentary tract. Mut Res. 2004; 551:9–28.
[30]. Lansky, Ephraim P, Robert A. Newman. Punica granatum (pomegranate) and its potential for prevention and treatment of inflammation and cancer. Journal of ethnopharmacology. 2007; 109(2): 177-206.
[31]. Li Y, Guo C, Yang J, Wei J, Xu J, Cheng S. Evaluation of antioxidant properties of pomegranate peel extract in comparison with pomegranate pulp extract. Food Chemistry. 2006; 96(2), 254-260.
[32]. Battino M, Bullon P, Wilson M. Oxidative injury and inflammatory periodontal diseases: the challenge of antioxidants to free radicals and reactive oxygen species. 2008; 12(3): 79–83.
[33]. Madianos PN, Bobetsis YA, Kinane DF. Generation of inflammatory stimuli: how bacteria set up inflammatory responses in the gingiva. J Clin Periodontol. 2005; 32 (s6): 57–71.
[34]. Beighton D, Radford JR, Naylor MN. Glycosidase activities in gingival crevicular fluid in subjects with adult periodontitis or gingivitis. Arch Oral Biol. 1992; 37(5):343-8.
[35]. Menezes SM, Cordeiro LN, Viana GS. Punica granatum (pomegranate) extract is active against dental plaque. J Herb Pharmacother. 2006; 6(2):79-92.
[36]. Bhadbhade SJ, Acharya AB, Rodrigues SV, Thakur SL. The antiplaque efficacy of pomegranate mouthrinse. Quintessence international (Berlin, Germany: 1985). 2011; 42(1), 29.
[37]. Braga LC. Synergic interaction between pomegranate extract and antibiotics against Staphylococcus aureus. Canadian journal of microbiology. 2005; 51(7): 541-547.
[38]. Prashanth, D., M. K. Asha, and A. Amit. Antibacterial activity of Punica granatum. Fitoterapia. 2001; 72(2): 171-173.
[39]. Thelma de B, Machadoa, Ivana C.R. Leala, Antimicrobial ellagitannin of Punica granatum. Fruits J. Braz. Chem. Soc. 2002;13(5)
[40]. Astravaha G, Gassmann G, Sangtherapitikul P, Grimm WD. Adjunctive periodontal treatment with Centella asiatica and Punica granatum extracts in supportive periodontal therapy. J Int Acad Periodontol. 2003; 5(4):106-115.
[41]. Lansky EP, Newman RA. Punica granatum (pomegranate) and its potential for prevention and treatment of inflammation and cancer. J Ethnopharmacol. 2007; 109(2):177-206.
[42]. Vasconcelos LC, Sampaio MC, Sampaio FC, Higino JC. Use of Punica granatum as an antifungal agent against candidosis associated with denture stomatitis. Mycoses. 2003; 46(5–6):192–196.
[43]. Abdollahzadeh S, Mashouf RY, Mortazavi H, Moghaddam MH, Roozbahani N, Vahedi M. Antibacterial and antifungal activities of Punica granatum peel extracts against oral pathogens. Journal of Dentistry, 2011; 8(1): 1-6.

[44]. Vasconcelos LC, Sampaio FC, Sampaio MCC, Pereira MDSV, Higino JS, Peixoto MHP. Minimum inhibitory concentration of adherence of Punica granatum Linn (pomegranate) gel against S. mutans, S. mitis and C. albicans. Braz Dent J. 2006; 17:3
[45]. Bhadbhade SJ, Acharya AB, Rodrigues SV, Thakur SL. The antiplaque efficacy of pomegranate mouthrinse. Quintessence International. 2011; 42(1): 29–36.
[46]. Menezes SMS, Cordeiro LN, Viana GSB. Punica granatum (pomegranate) extract is active against dental plaque. Journal of Herbal Pharmacotherapy. 2006; 6(2): 79–92.
[47]. Somu A, Ravindra A, Ajith S, Ahmed MG. Efficacy of a herbal extract gel in the treatment of gingivitis: a clinical study. Journal of Ayurveda and Integrative Medicine. 2012; 3(2): 85-90.
[48]. DiSilvestro RA, DiSilvestro DJ, DiSilvestro DJ. Pomegranate extract mouth rinsing effects on saliva measures relevant to gingivitis risk. Phytotherapy Research. 2009; 23(8): 1123-1127.
[49]. Sastravaha G, Gassmann G, Sangtherapitikul P, Grimm WD. Adjunctive periodontal treatment with Centella asiatica and Punica granatum extracts in supportive periodontal therapy. Journal of the International Academy of Periodontology. 2005; 7(3): 70-79.
[50]. Gould SWJ, Fielder MD, Kelly AF, Naughton DP. Anti-microbial activities of pomegranate rind extracts: enhancement by cupric sulphate against clinical isolates of S. aureus, MRSA and PVL positive CA-MSSA. BMC Complementary and Alternative Medicine. 2009; 9:23.
[51]. Life Extension Mouthwash. Available at: http://www.lef.org/Vitamins-Supplements/Item01279/Life-Extension-Mouthwash-with-Pomegranate.html. [Cited 11 October 2013]
[52]. Reddy MK, Gupta SK, Jacob MR. Antioxidant, antimalarial and antimicrobial activities of tannin-rich fractions, ellagitannins and phenolic acids from Punica granatum L. Planta Med. 2007; 73(5):461-467.
[53]. Thelma de B, Machadoa, Ivana C.R. Leala. Antimicrobial ellagitannin of Punica granatum Fruits J. Braz. Chem. Soc. 2002; 13(5): 606-610.
[54]. Gagari E, Kabani S. Adverse effects of mouthwash use: a review. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology.1995; 80(4), 432-439.
[55]. Gürgan CA, Zaim E, Bakirsoy I, Soykan E. Short-term side effects of 0.2% alcohol-free chlorhexidine mouthrinse used as an adjunct to non-surgical periodontal treatment: a double-blind clinical study. Journal of periodontology. 2006; 77(3), 370-384.
[56]. Mennella JA, Beauchamp GK. Optimizing oral medications for children. Clinical therapeutics. 2008; 30(11), 2120-2132.
[57]. Adhami VM, Khan N, Mukhtar H. Cancer Chemoprevention by Pomegranate: Clinical and Labratory Evidence. Nutr Cancer. 2009; 61(6): 811–815.
[58]. Jurenka J. Therapeutic Applications of Pomegranate (Punica granatum L.): A Review. Alternative Medicine Review. 2008; 13(2):128-144.
[59]. Dahlawi H, Jordan-Mahy N, Clench MR, Le Maitre CL. Bioactive actions of pomegranate fruit extracts on leukemia cell lines in vitro hold promise for new therapeutic agents for leukemia. Nutr Cancer. 2012; 64:100-110.
[60]. Dulcich MS, Hartman RE. Pomegranate Supplementation Improves Affective and Motor Behavior in Mice after Radiation Exposure. Evidence-Based Complementary and Alternative Medicine. 2013; Article ID 940830.
[61]. Viuda-Martos M, Fernández-López J, Pérez-Álvarez JA. Pomegranate and its Many Functional Components as Related to Human Health: A Review. Comprehensive Reviews in Food Science and Food Safety. 2010; 9(6): 635–654.
[62]. Schubert SY, Lansky EP, Neeman I. Antioxidant and eicosanoid enzyme inhibition properties of pomegranate seed oil and fermented juice flavonoids. J Ethnopharmacol. 1999; 66 (1): 11–17.
[63]. Aviram M, Dornfeld L, Rosenblat M, Volkova N, Kaplan M, Coleman R, Fuhrman, B. Pomegranate juice consumption reduces oxidative stress, atherogenic modifications to LDL, and platelet aggregation: studies in humans and in atherosclerotic apolipoprotein E–deficient mice. The American journal of clinical nutrition. 2000; 71(5), 1062-1076.
[64]. Aviram M, Dornfeld L. Pomegranate juice consumption inhibits serum angiotensin converting enzyme activity and reduces systolic blood pressure. Atherosclerosis. 2001; 158(1):195-198.
[65]. Komperda KE. Potential interaction between pomegranate juice and warfarin. Pharmacotherapy. 2009; 29:1002-1006.
[66]. Howell AB, D'Souza DH. The Pomegranate: Effects on Bacteria and Viruses That Influence Human Health. Evidence-Based Complementary and Alternative Medicine. 2013; Article ID 606212
[67]. West T, Atzeva M, Holtzman DM. Pomegranate polyphenols and resveratrol protect the neonatal brain against hypoxic-ischemic injury. Dev Neurosci. 2007; 29(4-5):363-372.
[68]. Macchia L, Giliberti LA, Lotti A. Allergy to pomegranate and artichoke, novel food allergens of the Mediterranean diet. Clin Transl Allergy. 2013; (s3): 75
[69]. Komperda KE. Potential interaction between pomegranate juice and warfarin. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2009; 29(8), 1002-1006.
[70]. Schneider, Hildegard. On the Pomegranate. small 3. 1945: 1il.