



PUNICA GRANATUM; ANCIENT SEEDS FOR MODERN CURE IN MEDICAL AND DENTAL FIELD: AN OVERVIEW

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Article Info <i>Received 25/07/2015</i> <i>Revised 15/08/2015</i> <i>Accepted 18/08/2015</i> Key words: Pomegranate, Punica granatum, Ayurveda, Dentistry, Natural products, Complementary/Integrative medicine.	ABSTRACT Ayurvedic medications have stood the test of time and since time immemorial been used for various ailments. Recently there is renewed interest in use of various ayurvedic drugs for oral and dental health. Plants and natural products from time immemorial used for their pharmacological applications viz. antiulcerogenic, wound healing, anti-inflammatory, antimicrobial, antioxidant properties etc. One such natural product is the pomegranate tree i.e. Punica granatum, especially its fruit, possesses a vast ethno medical history and represents a phytochemical reservoir of medicinal values. This review is an attempt to highlight the potential of Punica granatum as a preventive and therapeutic aid for various systemic and oral diseases and also looks into the multitude prospects and perspectives.
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INTRODUCTION

A wide variety of plants possess enormous treasure of medicinal value. Majority of these medicinal plants have been used to treat various systemic conditions successfully. Over the recent years, use of these medicinal plants has resurfaced to treat oral conditions. Among the oral conditions, periodontal disease remains one of the most common. Alternative and preventive options has become the need of the hour in order to overcome the adverse effects of the antimicrobial agents used in large as an adjunct to mainstream periodontal treatment. Punica granatum is one of the oldest edible fruit which has a long history as a medicinal fruit. Punica granatum belonging to family Punicaceae is more commonly known as pomegranate. The genus name, Punica, was derived from the roman name for Carthage. The word Pomegranate means Apple ("pomum") and seeded ("granatus") [1]. The fruit of the pomegranate tree has been used extensively in

the folk medicine of many cultures. The healing property of pomegranates was discussed in one of the oldest medical texts, the Ebers Papyrus from ancient Egypt (1500 BC). The Punica granatum is a large shrub which grows 12-16 feet, has many spiny branches with lance shaped glossy leaves. The bark of the tree turns gray as the tree ages. The flowers are large, red, white, or variegated having a tubular calyx that eventually becomes the fruit. The ripe fruit is about five inches wide with a deep red, leathery skin, grenade shaped with a pointed calyx. The fruit contains many seeds separated by white, membranous pericarp. Each seed is surrounded by tart and red juice. 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. This fruit of nature has glossy leaves that are narrow and oblong in appearance. The tree/fruit can be divided into several anatomical compartments: (1) seed, (2) juice, (3) peel, (4) leaf, (5) flower, (6) bark, and (7) roots, each of which has interesting pharmacologic activity [2]. The phytochemistry and pharmacological actions of all Punica granatum components suggest a wide range of clinical

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applications for the treatment and prevention of cancer, as well as other diseases where chronic inflammation is believed to play an essential etiologic role. The latest research shows that the pomegranate hasn't been cultivated by mankind without reason for more than 5,000 years. In former times the skin and juice were often used as ink as well as dye for oriental carpets. The pomegranate has many positive effects on our health. A fatty acid appearing almost only in this fruit, which is demonstrably highly concentrated and has especially positive effects on our health, is important for all metabolism processes in the body. Of special importance to nutrition experts is the poly-phenol ellagic acid. An optimal anti-oxidative protection, the anti-oxidative effect of the pomegranate is 3 to 10 times higher than in well-known plants like bilberry (blueberry), cranberry or green tea [3].

Phytochemistry and functional components The peel contains bioactive compounds that include phenolics, flavonoids, proanthocyanidin compounds and complex polysaccharides. The pomegranate is an excellent water and food supplier: it contains beta-carotene, vitamins B1, B2 and C, potassium, phosphorus, magnesium, calcium, iron, albumen and above all large quantities of antioxidants, secondary plant substances like polyphenols (flavonoids, tannins). 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. 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 [4]. The seeds also constitute protein, fibres, vitamins, minerals, pectin and estrone, among others. Arils, on the other hand, contain mostly water and a small amount of sugars, pectin, organic acid and bioactive compounds. 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. 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. Pomegranate juice contains anthocyanins, glucose, ascorbic acid, ellagic acid, gallic acid, caffeic acid, catechin, epigallocatechin, quercetin, rutin, iron and amino acids possessing anti-atherosclerotic, antihypertensive, antiaging and potent antioxidative properties. Seed oil is composed mainly of punicic acid and sterols having nephroprotective properties. The pericarp (peel, rind) contains punicalagins, flavones, flavonones, and other flavanols possessing anti-inflammatory, antimutagenic and antifungal activity [5]. Tannins including punicalin and punicafolin, and flavones glycosides like luteolin and apigenin form the major constituents of pomegranate leaves. The leaves are said to

have excellent antioxidant properties. The flowers contain ursolic acid, triterpenoids like maslinic acid and asiatic acid possessing antioxidant, hepatoprotective properties and are used as a remedy for diabetes mellitus. Ellagitannins and piperidine alkaloids are present in pomegranate roots and bark. The bark possesses molluscicidal properties. The bark and roots are known for its antihelminthic and vermifuge properties [6].

Phenolic Compounds and their Mechanism of Action

The main components responsible for most of the purposeful properties of this fruit are the phenolic compounds. Chemically, phenolic acids are defined as substances that possess an aromatic ring bound to one or more hydrogenated substituents. 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. 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. 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. However, there exist some differences in opinion regarding which compounds play the bigger role in performing this activity [7]. Tzulker et al concluded in their study that punicalagin is the cause for the antioxidant activity whilst anthocyanins play only a small role [8]. 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. As such, reducing properties are associated with the presence of reductones 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 precursor [9]. 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. Consequently there has been no specific ultimatum reached as to what component contributes most [10].

General therapeutics Pomegranate is considered "A pharmacy unto itself". Pomegranate has many potential effects including bactericidal, antifungal, antiviral, immune modulation, vermifuge, stimulant, refrigerant, astringent, stomachic, styptic, laxative, diuretic and antihelminthic. It has also been widely used in treatment of cardiovascular diseases, diabetes, diarrhea, dysentery, asthma, bronchitis, cough, bleeding disorders, fever, inflammation, acquired immune deficiency syndrome, dyspepsia, ulcers, bruises, sores, mouth lesions, skin lesions, malaria, prostate cancer, atherosclerosis, hypertension, hyper lipidemia, denture stomatitis, male



infertility, vaginitis, erectile dysfunction, Alzheimer's disease, obesity, and neonatal hypoxic-ischemic brain injury [11]. From the fruit, the skin, the blossoms, the leaves of the pomegranate to its trunk everything can be used. The fresh juice has a stimulating impact on the blood in the body, helps for anaemia and improves digestion, especially the activity of the stomach. The pomegranate has a contracting quality and thus stops strong bleeding and sweating, heat flushes as well as diarrhoea. It soothes inflammation, increases the healing of wounds by regeneration of the tissue, is useful for the healing of the skin and mucous membranes, helps for bronchitis and tuberculosis, is effective against skin aging, has a proven, strengthening impact on epidermis, increases the firmness and elasticity of the skin, acts positively compensating on skin moisture and reduces wrinkles. At the same time the preventive as well as healing effect on cancer diseases like skin, breast and prostate cancer is to be stressed [12]. Juice and peels, for example, possess potent antioxidant properties, while juice, peel and oil are all weakly estrogenic and heuristically of interest for the treatment of menopausal symptoms and sequelae. Japanese studies from 2004 prove that because of its enormous quantities of phyto-estrogens (natural hormone treatment) the pomegranate provides for a noticeable soothing of frequent troubles of women in menopause like change of mood, osteoporosis and heat flushes. Also the typical pre-menstruation complaints will be diminished. The oil of the seeds and leaves shows a high substance of plant hormones [13]. The fatty acid of the pomegranate contributes to the formation of prostaglandins in the human body. Prostaglandins are hormones of utmost importance for the metabolism and immune system, which the body produces itself. The use of juice, peel and oil has also been shown to possess anticancer activities, including interference with tumor cell proliferation, cell cycle, invasion and angiogenesis. These may be associated with plant based anti-inflammatory effects. According to dietetic studies (Dr. Michael Avriam, 2004) the complete anti-oxidative protection in the blood rises by 130 % after having consumed pomegranate concentrate (10 ml per day) [14]. Furthermore, other controlled studies prove the optimal effect on the heart circulation system. The oxidation of the cholesterol Low Density Lipoprotein (LDL) could be reduced strongly after the consumption of pomegranates. Oxidized LDL cholesterol is more easily deposited in sediments and results in the so called arteriosclerotic plaque, which is known as the main reason for heart circulation problems [15-16]. Even a clear decrease of the sediments in the arteries could be seen. Regular consumption prevents anti-aging, arteriosclerosis and heart circulation diseases. 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. 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 [17]. On the other hand, punica granatum has also started to pave way for its use in preventing brain injuries. Simple juice consumption is also said to inhibit viral infections. A study by Syed et al (2006) suggests that pomegranate fruit extract (PFE) is effective for ameliorating UVA-mediated damages by modulating cellular pathways and preventing potential skin cancers [18]. When ingested, pomegranate juice could help patients with carotid artery stenosis, decrease carotid intima-media thickness, and their systolic blood pressure (Aviram, et al., 2004) [19]. An important potential application for the anti-microbial properties of Punica granatum is its use as a topical microbicide for HIV prevention. In vitro research indicates that an anti-HIV-1 microbicide could potentially be made from Punica granatum (Neurath, et. al. 2005) [20]. Research on lung cancer looked at the effect of PFE as a source of treatment (Khan et al., 2007). The results suggested that PFE can be a chemo preventative agent against lung cancer [21]. Flavonoid-rich polyphenols can be extracted from fresh and fermented pomegranate juice. These polyphenols were tested for their ability to induce differentiation in human HL-60 promyelocytic leukemia cells. Extracts from the fermented juice and pericarps promoted differentiation the best when compared to fresh juice and had similar inhibitory effects on proliferation of the cell line (Kawaii and Lansky 2004) [22]. Pomegranate tannin extract and punicalagin were found to suppress the COX-2 protein expression and inhibited phosphorylation and binding of the p65 subunit in HT-29 colon cancer cells indicating that these chemicals could play a major role in modifying the inflammatory cell signalling in colon cancer cells (Adams et al., 2006) [23].

Periodontal implication of pomegranate Dental plaque is a prerequisite for periodontal disease. Bacteria present in dental plaque have direct pathologic effect on the periodontal tissues. Periodontitis has been proven to occur due to various other indirect mechanisms apart from the direct effect of periodontal pathogens. Bacterial lipopolysaccharides stimulate production of catabolic cytokines and inflammatory mediators including arachidonic acid metabolites such as prostaglandin E2 (PGE2), Interleukin-1 (IL-1), Interleukin-6 (IL-6), TNF- α (Tumour Necrosis Factor- α). These cytokines and inflammatory mediators stimulate the release of tissue-derived enzymes, the matrix metalloproteinases, which cause destruction of the extracellular matrix and bone. Reactive oxygen species have also been considered as a major etiology of exaggerated inflammatory response in the pathogenesis of periodontitis. These reactive oxygen species along with direct tissue damage to the periodontium may also activate key nuclear transcription factors, such as receptor activator of nuclear factor kappa β (NF- κ B) and Activated Protein-1 (AP-1). These nuclear transcription factors possess a positive effect on gene



transcription for key pro-inflammatory mediators and osteoclastogenesis stimulation. The major ingredient of pomegranate fatty acids, punicalic acid, is an excellent anti-inflammatory compound with a property to suppress prostaglandin production [24]. Cold pressed pomegranate seed oil has inhibited both cyclooxygenase and lipoxygenase enzymes in vitro. Both these are key enzymes in production of various inflammatory mediators. Pomegranate fruit extract has a broad inhibitory effect on matrix metalloproteinases (MMPs) expression and IL-1 β induced tissue destruction. Apart from the above mechanisms, anti-inflammatory effect of pomegranate could be due its immunoregulatory action on macrophages and T and B lymphocytes. Pomegranate extract exhibited anti-inflammatory activity through inhibition of NF- κ B (nuclear factor kappa-B) activity and prevention of ERK-1 or ERK-2 (Mitogen activated protein kinase cascades) activation. It also decreased NO (nitric oxide) and PGE2 synthesis in human intestinal Caco-2 cells. Ellagic acid inhibited NF- κ B activation through a mechanism independent of I κ -B (inhibitor of nuclear factor kappa B) phosphorylation. Blocking NF- κ B, inflammatory cell signalling pathways that produce various destructive factors may be a potential strategy to prevent inflammation induced bone resorption and a promising mechanism to treat periodontitis. Oral ingestion of polyphenol rich extract of pomegranate fruit extract inhibited COX-1 and COX-2 enzymes. It also inhibited IL-1 β induced NO and PGE2 production [25]. A significant reduction of gingival bleeding was observed after using a dentifrice containing pomegranate. Pomegranate could be beneficial in treating periodontitis as it possesses excellent anti-inflammatory effect. Pomegranate extracts have the ability to scavenge free radicals and decrease macrophage oxidative stress and lipid peroxidation. Pomegranate could produce an anti-gingivitis effect as the flavonoids possess direct antioxidant properties and indirect effects by enhancing the free radical scavenging activity of hepatic enzymes catalase, super oxide dismutase and peroxidase. Sastravaha et al. concluded in their preliminary study that local delivery with *Centella asiatica* and *Punica granatum* extracts following scaling and root planing showed significant improvements in pocket depth and attachment level compared to placebo. *Punica granatum* extract may provide a synergistic action in collagen stabilization as tannins have the affinity for proteins, thus, forming bonds with collagen fibers. In their follow-up study, they observed there were significant improvement in the periodontal parameters and a decrease in the IL-1 β and IL-6 compared to baseline [26]. Pomegranate components could promote oral health, including reducing the risk of gingivitis. Thrice daily mouth rinsing with pomegranate extract dissolved in water increased the levels of antioxidant activity and decreased activities of aspartate aminotransferase. Aspartate aminotransferase is considered an effective indicator of cell injury and is elevated among periodontitis patients. Protein levels in

saliva are higher among periodontitis patients correlating with the plaque forming bacterial content. Saliva samples showed a significant decrease in protein levels after rinsing with pomegranate mouthwash indicating its antibacterial activity [27]. Pomegranate flavonoids have shown antibacterial action in vitro against gingivitis causing microbes. *Streptococcus sanguis* (*S. sanguis*) was sensitive to pomegranate extract and the inhibitory action was similar to chlorhexidine. *S. sanguis* is known to be the initial colonizer in dental plaque formation. The possible reason for this antibacterial effect are the tannins which increase bacteriolysis, interfere with bacterial adherence mechanisms onto the tooth surfaces. In contrast, fruit bark extract of pomegranate showed better inhibition of growth of *S. sanguis*, *S. sobrinus* and *Lactobacillus casei* when compared to chlorhexidine [28]. A hydro alcoholic extract pomegranate mouth rinse decreased colony forming units of plaque forming bacteria by 84% against chlorhexidine (79% inhibition) among 60 healthy patients. Pomegranate extract also suppressed the ability of plaque forming microorganisms to adhere to the surface of tooth. Pomegranate may be a possible alternate for the prevention of formation and treatment of dental plaque. A 10% *Punica granatum* extract gel was not efficient in preventing dental plaque formation and gingivitis. Whereas, a pomegranate gel (5g of carboxymethyl cellulose in 100mL of pomegranate juice) showed excellent anti-gingivitis effect and significant reduction in plaque scores when used as an adjunct to mechanical debridement. A recent study proved that pomegranate mouthwash had antibacterial efficacy against *Aggregatibacter actinomycetemcomitans* (*Aa*), *Porphyromonas gingivalis* (*Pg*), *Prevotella intermedia* (*Pi*), which are the most important periodontal pathogens [29]. *Punica granatum* has shown antimicrobial activity against *Eikenella corrodens*, which is a secondary colonizer in the biofilm formation on the tooth surface significantly more than chlorhexidine. Rinsing with 30 mL of pomegranate juice was effective in reducing colony forming units of dental plaque forming organisms by 32% [30]. Pomegranate mouthwash used two times daily for fifteen days resulted in more efficient reduction of gingival and bleeding on probing scores when compared to chlorhexidine. Pomegranate gel when used as an adjunct with mechanical debridement was efficient in treating gingivitis with an improvement in the clinical and microbiological parameters [31]. Significant improvement was observed in plaque, gingival and bleeding indices among 92 patients who were instructed to use toothpaste, which contained pomegranate along with various other herbs [32]. Pomegranate thereby could be an excellent adjunct to the conventional periodontal therapy as an anti-plaque agent due to its antibacterial properties. Deep periodontal pockets are said to be associated with *Helicobacter pylori* (*H. pylori*) infection. Increased levels of *H. pylori* have been detected from the oral cavities of patients with periodontitis. Pomegranate has demonstrated significant antibacterial activity against *H. pylori*. Hence,



pomegranate could be beneficial in treating periodontitis. The group of Thai researchers conducted another study and found that pomegranate extracts, when combined with the extract from an herb called gotu kola, are effective for gingivitis. In an effort to see if the extracts of pomegranate and gotu kola could make a difference deep inside the gingival and the root of the tooth, they filled tiny chips with both extracts and then inserted the chips in the open area between the gum and tooth root. They discovered that the gingiva and the tooth attached more quickly and were healthier with the addition of the extracts [33].

Pomegranate extracts have been found to be effective against herpes virus. Recently, it has been suggested that herpes viruses could be a trigger for periodontal tissue destruction. Herpes viruses may initiate and accelerate progression of periodontitis due to its potential to stimulate cytokine release from host cells, impair host defense mechanisms, resulting in increased virulence of resident periodontopathic bacteria. Hence, pomegranate with its antiviral property could cure periodontitis as well. A recent study concluded that pomegranate peel extract had a remarkable effect on *Trichomonas tenax* and could be used in the treatment of acute ulcerative gingivitis [34]. Pomegranate extract is known for its wound healing properties. It is known to induce increased fibroblast migration and proliferation, formation of collagen and angiogenesis. 5%, 10% and 15% methanol peel extract ointment of pomegranate resulted in a complete and faster wound healing. The wound healing properties can be attributed to the presence of tannins and polyphenols. Quorum sensing is the capacity of bacteria present in a biofilm to communicate with each other. Dental plaque is a biofilm. Quorum sensing plays an important role in gene expression for development of antibiotic resistance, promoting growth of bacteria essential for biofilm and discouraging growth of competitors. Interfering with quorum sensing signals could be a potential strategy for disease control. Pomegranate extract inhibited quorum sensing in *Chromobacterium violaceum* (*C. violaceum*) and *Pseudomonas aeruginosa*. This was demonstrated by inhibition of violacein (purple pigment) production in *C. violaceum* and interference with swarming in *Pseudomonas aeruginosa*. Pomegranate may be a rich source of compounds to overcome pathogenic bacteria and development of antibiotic resistance. Pomegranate has positive effects on enteric probiotic bacteria. It has shown enhanced growth of *Bifidobacterium* species and *Lactobacillus* species. These probiotic microorganisms are known to have effect on periodontal pathogens by affecting their growth, adhesion and colonization. They also decreased the IL-1 and TNF- α level in the gingival crevicular fluid and interfered with the activity of tissue destructive enzymes like elastase, myeloperoxidase and metalloproteinase. Probiotic bacteria could be beneficial in treating periodontitis by decreasing the periodontal pathogen burden in the oral biofilm and strengthening

epithelial barrier function, thus enhancing resistance to infections. Synergistic action was observed between methanolic pomegranate extract and antibiotics like chloramphenicol, gentamicin, tetracycline, ampicillin and oxacillin against Methicillin resistant staphylococcus aureus (MRSA). The antibiotic activity of ciprofloxacin was enhanced by methanolic peel extract of pomegranate. Pomegranate because of its property of improving antibiotic sensitivity could be a promising adjunct in the treatment of periodontitis [35].

Other uses of pomegranate in dentistry: A 10% topical pomegranate gel was efficient in reducing recurrent aphthous stomatitis pain and time for complete healing of ulcers. This was attributed to its anti-inflammatory, antioxidant and antimicrobial properties of pomegranate. An 80% pomegranate peel extract lozenge was able to decrease gag reflex in soft palate up to 88.5% and in tonsils up to 92.5% [36]. This effect could be due to the presence of tannins which have anesthetic effects. A gel based *Punica granatum* bark extract was effective in treating denture stomatitis as effectively as miconazole. *Streptococcus mutans* (*S. mutans*) is considered as the chief dental caries causing pathogen. *S. mutans* has shown high sensitivity to pomegranate. Pomegranate fruit extract gel was active against *S. sanguis*, *S. mutans* and *Streptococcus mitis* (*S. mitis*) by controlling their adhesion on to glass surface and that it could be used to prevent adherence of various microorganisms in the oral cavity. In a recent in vitro study, pomegranate pulp extract gel showed highly significant inhibitory effect at 5%, 25%, 50% and 100% against *S. mutans* when compared to aloe vera and sorbitol. This action is probably due to the antimicrobial property of tannins. Pomegranate could be a potential anticariogenic agent due to its property to inhibit *S. Mutans* [37].

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 [38]. 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. 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. The arils, juice and peel extracts are said to have moderate anti-oxidant activity, whereas the pulp and the seeds exhibit high levels. 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, anti-inflammatory and anti-bacterial effects and complete removal of plaque from the surface of the tooth [14]. They have been able to bring about significant reduction in the activity of the enzymes aspartate aminotransferase and alpha glucosidase and increased activity of the antioxidant enzyme ceruloplasmin. 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, Mentha piperita (peppermint) oil, citric acid, menthol, poloxamer, colloidal silver and potassium sorbate. A similar combination of components with slight modifications to adjust flavour has been suggested in future products [16].

Advantages of using pomegranate (Punica granatum) as mouthwash: 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. 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. Moreover, it would be easier to convince children to use it because of its agreeable odour. 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. When used regularly in combination with toothpaste that has been reinforced with bioactive botanical extracts, pomegranate containing mouthwash may fight dental plaque and tartar formation by inhibiting the activities of the microorganisms that cause plaque. Additionally, pomegranate compounds possess anti-inflammatory properties that may help soothe irritated tissues [18].

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. Pomegranate juice may have potentially dangerous interaction with other medications. It is known to inhibit intestinal cytochrome P450 3A4. During rosuvastatin treatment for myopathy, it may increase the risk of rhabdomyolysis, the breakdown of muscle fibers resulting in the release of muscle fiber contents into the circulation and may result in kidney damage. However, rosuvastatin is not known to be metabolized by hepatic P450 3A4 (Sorokin, et. al. 2006). Some people are allergic to Punica granatum [39]. Several adverse reactions to pomegranate, including severe symptoms such as anaphylactic shock or laryngeal edema, have been described in recent years. Patients with pomegranate allergy are often sensitized to other allergens. Pomegranate should be considered a potential allergen in patients suffering anaphylaxis in autumn and living in countries where this fruit is consumed (Gaig, et. al. 1999). 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[40].

CONCLUSION

Pomegranate is slowly gathering interest as an exciting new medicinal product. 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. The authors are likely to sincerely encourage further research in this field, exploring more benefits of Punica granatum & revealing to clinicians along with evidence based study. Already 2,400 years ago Hippocrates said: "May your food be your medicine and your medicine your food!"

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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