

Role of *Quercus infectoria* in health and oral health – A Review

Meena Jain¹, Puneet Chahar¹, Vishal Jain², Ankur Sharma¹, Nisha Rani Yadav¹

¹Department of Public Health Dentistry, Manav Rachna Dental College, Faridabad, Haryana, India, ²Department of Pedodontics, Institute of Dental Studies and Technologies College, Modinagar, Uttar Pradesh, India

Abstract

Herbal medicines pave way for the restoration of both oral and systemic health. These medicines are easily accessible, economical, and minimally associated risks. The galls of the *Quercus infectoria* (QI) tree are conventionally believed to have enormous therapeutic value. Pharmacologically, the galls are claimed to have various biological activities such as astringent effect, antitremorine, local anesthetic, antipyretic, anti-inflammatory, antibacterial, antiviral, and many more. These pharmacological activities of QI extracts are used in the treatment of oral diseases as constituent of toothpaste and powder. Further research is required to appraise the efficacy, safety, and properties of *Majuphal* in oral care products.

Key words: Antiplaque, dental health, herbal mouthrinses, *Majuphal*, *Manjakani*, *Quercus infectoria*

INTRODUCTION

Herbal medicines with their naturally occurring active ingredients offer a gentle and enduring way for restoration and thus regarded as origin of modern medicine. Discovery of a new drug usually faces challenges in the form of time and money investment. On the other hand, traditional medicine is affordable, low level of side effects, easily accessible, and culturally familiar.^[1-3] India (books like Vedas) and China (books like book on roots and grasses “Pen T’Sao”) are some countries with rich heritage of well-documented traditional medicine.^[4]

Medicinal plants are rich source of ingredients which can be further used in drug development and synthesis. Significant plant-derived pharmaceutical products are prescribed by practitioners for analgesic/antipyretic (*Salix* spp.), anticholinergic (*Atropa belladonna*), antimalarial (*Cinchona ledgeriana*), antifertility (*Dioscorea deltoidea*), etc. Further, drugs for Alzheimer’s (*Galanthus woronowii*), anticancer (*Podophyllum peltatum/Taxus brevifolia*), and hepatic disorder (*Silybum marianum*) are also in phases of development.^[5]

The field of conventional and alternative medicine (CAM) has seen a growing interest due to realization of concerning adverse effects of allopathy and CAM being affordable, available,

and accessible. Studies have shown that in India, more than 60% of people prefer traditional medicines and more than 70% consider it effective.^[6-7] Studies also report rising interest of other developing and developed countries in CAM.^[8-9]

The aim of the present study was to review the medicinal properties of *Quercus infectoria* (QI) and explore its current use in dental health. Google Scholar, PubMed, and Scopus were searched for MeSH terms (*Quercus*, oral health, *Streptococcus*, periodontitis, gingivitis, and dental plaque) using Boolean AND or OR. First 10 pages related to QI reflected after keyword search were considered. Duplicate articles were excluded. The reference listing of obtained studies was further searched, and finally, all eligible studies were included for this review.

Plant Geographical Distribution

The QI trees usually grow in Greece, Asia Minor, Persia, Syria, and some parts of India (Garhwal Himalayas) and Nepal. *Quercus* species originated in Iran, Iraq, and Turkey and then spread to Asia Minor, Europe, and Northern Africa.^[10]

Address for correspondence:

Dr. Vishal Jain, Department of Pedodontics, Institute of Dental Studies and Technologies College, Modinagar, Uttar Pradesh, India. Phone: +91-9717200515.
E-mail: dentistvishaljain@gmail.com

Received: 15-12-2018

Revised: 21-01-2019

Accepted: 04-04-2019

QI (Family: Fagaceae) commonly known as gall oak or *Manjakani*. It grows to a height of 4–6 feet with smooth and bright, acorn long, narrow, scaly, and downy leaves. The gall arising in the branches of the tree is called as “*Majuphal*” in Sanskrit. Crude gall is globose with spiky appearances on external surface with size of 1.4–2.3 cm in length and 1–1.5 cm in diameter. It is grayish-brown to brownish-black in color externally and is yellow internally. The galls are globular (2 inch), uneven, porous (due to infection), and with hollow structures. The powder of galls is coarse, creamish brown with no odor but bitter taste.^[11]

Phytochemistry and Functional Components

Phytochemical screening of galls shows the presence of saponins, alkaloids, tannins, glycosides, triterpenes, sterols, phenolic compounds, carbohydrates, and flavonoids.^[11,12] The main constituents found in the galls of QI are tannin (50–70%), gallic acid, and ellagic acid.^[13] The gall extracts show antimicrobial, analgesic, and antioxidant activity.^[14] Ellagic acid has anticarcinogenic and antioxidant properties.^[15] The tannic acid belongs to the group of water-soluble metabolites and has the ability to complex macromolecules and metal ions, which gives it antioxidant, antimicrobial, and healing activity.^[16]

Existing Scientific Evidence

QI and its role have been explored in multiple domains ranging from its antibacterial/antimicrobial activity, antioxidant properties, ability for accelerated wound healing, and anticancer effects to analgesic/local anesthetic properties. A brief literature has been summarized for its potential effects as follows.

Antimicrobial Activity

QI extracts are known to have a wide antimicrobial activity against Gram-positive bacterial strains. Studies have also shown good antimicrobial activity of QI against various other dental pathogens in both aqueous, acetone, and methanolic extracts [Tables 1 and 2].^[13,14,17,18]

Antioxidant Activity and Anticancer Activity

Studies on *Majuphal* extracts have shown an increase in the concentration of antioxidant enzymes.^[14,26-28] The antioxidant activity of gall extracts has been tested both in chemical and biological models.^[29] Antioxidant enzymes superoxide dismutase and catalase have been obtained in increased quantities in animals after administration of QI extracts.^[14,15] Phenolic compounds and flavonoids in *Majuphal* extracts are also correlated with antioxidant activity.^[30,31] Polyphenols in QI gall extracts also exhibit anticancer activities in different *in vitro* models.^[22,29,32] Chemopreventive effects of QI

against Fe-NTA-induced renal carcinogenesis, inhibition of hyperproliferative response, and diminish oxidative stress were demonstrated by the study done by Rehman *et al.*^[33]

Wound Healing Activity

Animal studies have shown a definite wound healing activity in ethanol extracts of *Majuphal*. There has been a significant increase in activities of various enzymes associated with wound healing. These enzymes include superoxide dismutase and catalase. The wound healing and antioxidant activities of QI may be interrelated to each other.^[15] Few studies had been conducted for the topical antimicrobial action of QI extracts in rats or other experimental animals. However, its effects on wound healing in humans have not been investigated yet.

Analgesic Activity

Methanolic extracts of QI gall have displayed significant analgesic activities in experimental animals. The study conducted on rats has shown that methanolic extracts produced a maximum possible analgesia of 34.2% at 30 min and increased the response time against noxious stimuli similar to opioid analgesics. The effect is considered to be due to its action on the central nervous system due to the presence of tannins in the extract. QI causes CNS depressant activity and moderate antitremorine activity by causing a delay in onset and decrease in severity of tremorine-induced tremors.^[34]

Local Anesthetic Activity

Local anesthetic activity of QI has been stated by various authors. However, mechanism of action of the extracts for local anesthetic effects is not known. Further research is, however, required to establish these effects.^[34]

Other Activities

Extracts of QI are known to possess osteoblastic activity mainly due to the presence of polyphenols. In addition, they also possess other important minerals such as calcium, phosphorous, potassium, and magnesium.^[32] Osteoblastic proliferation activity has also been seen in fetal cell lines.^[32] However, further research is needed to establish these effects for use in bone regeneration in oral cavity.

Antidiabetic effects have also been tested and it was observed that methanolic and aqueous extract at a concentration of 500 mg/kg exhibited 18.5% and 2.5% reduction in blood glucose, respectively, when measured by glucose tolerance test.^[35]

Anti-pigmentation effect has also been showed by methanolic extracts of QI due to their ability to inhibit

tyrosinase, which catalyzes the hydroxylation of l-tyrosine to 3,4-dihydroxyphenyl)-l-alanine and induces pigments of melanin.^[36]

Mechanism of Action

The *Quercus infectoria* extract mechanism of action could also be thought to depend on the degradation of bacterial cell walls, destruction of cytoplasmic membrane proteins, leakage of cell contents, coagulation of cytoplasm, and reduction in the proton motive force or binding with some synthesis proteins.^[18]

It was suggested that extracts of medicinal plants with high tannin content, for example, QIE, target the enzymes involved in cell wall synthesis of resistant *Staphylococcus aureus* strains.^[37]

Reported Adverse Effects

Due to varying sensitivity levels of individuals, it is recommended that the drug should be used in lower doses initially. One study reported that despite administering the 300 times higher doses as compared to routine dose used in traditional medicine, no mice died and there were no signs of acute toxicity. Slight tissue changes in the form of intestinal hyperplasia and anal glandular hyperplasia were detected but were not statistically significant as compared to control. Blood parameters also showed small and insignificant changes when the highest dose of QI was administered.^[38] Similar effects may appear on topical application of QI extracts in the oral mucosa. However, no studies are known to address these effects.

Apart from these, product standardization, quality control, need of official Compendia, dissemination of information,

Table 1: Studies on antimicrobial activity of QI

S. No.	Author/year	Measures	Results
1	Mohammadi-Sichani M et al./2016 ^[19]	Antibacterial and biofilm disinfective effects of the oak tree QI galls against <i>S. mutans</i>	The methanolic, ethanolic, and acetonetic extracts of QI galls showed the strong inhibitory effects on <i>S. mutans</i> All extracts of QI galls significantly ($P < 0.05$) reduced biofilm biomass of <i>S. mutans</i> at the concentrations of $>9.8 \mu\text{g/ml}$
2	Baharuddin et al./2015 ^[20]	Anti-Candida activity of QI gall extracts against selected <i>Candida</i> species	Methanol and aqueous extracts showed relatively similar anti-Candida activity Minimum concentration for inhibiting yeast growth: 5 mg/disc
3	Satirapathkul and Leela/2011 ^[21]	Antimicrobial activities of QI extracts prepared from different solvents of varying polarity	All the Gram-positive bacteria and Gram-negative bacteria tested were susceptible to all aqueous and solvent extracts of QI galls Ethanol and aqueous extracts showed a strong though lower antimicrobial effect against all the tested organisms while chloroform and hexane extracts of QI were found to be least active
4	Fani et al./2015 ^[22]	Antibacterial effects of <i>Ferula asafoetida</i> L. and QI <i>Olivier</i> aqueous and ethanolic extracts on <i>S. mutans</i> and <i>Streptococcus sanguis</i> .	Significant difference was found among the inhibitory zones created by dissimilar concentrations of QI ($P = 0.025$)
5	Nagesh et al./2012 ^[23]	The antibacterial property and MIC of gall extract of QI against <i>Enterococcus faecalis</i>	The zone of inhibition of gall extract against <i>E. faecalis</i> was found to increase with increasing volumes of gall extract
6	Voravuthikunchai et al./2008 ^[24]	To observe the antibacterial effects of QI species against a wide range of pathogenic bacteria.	The extracts of QI displayed remarkable activity against Methicillin-resistant staphylococcus aureus with MICs ranging from 0.02 to 0.4 mg/mL More importantly, this plant species could exhibit strong antibacterial activity against all Gram-negative organisms
7	Muskhazli et al./2008 ^[25]	Antibacterial activity of aqueous and ethanolic extracts was tested against <i>C. cellulans</i> .	Both types of extracts showed significant inhibition of <i>C. cellulans</i> with MIC value beginning at 0.5 mg/ml

QI: *Quercus infectoria*, *S. mutans*: *Streptococcus mutans*, MIC: Minimum inhibitory concentration, *E. faecalis*: *Enterococcus faecalis*, *C. cellulans*: *Cellulosimicrobium cellulans*

Table 2: MIC values of *Quercus infectoria* extracts in different solvents against microbes and bacterial strains

Organism	Methanol extract	Acetone extract	Ethanol extract	Water extract
<i>Staphylococcus aureus</i>	0.156 mg/ml ^[13] 1.25 mg/ml ^[20]	0.0781 ^[18]	0.08 ^[27] 0.1 mg/ml ^[24]	0.0781 ^[18] 0.16 ^[26] , 0.156 mg/ml ^[13] 0.2 mg/ml ^[24]
<i>Streptococcus sanguis</i>	0.078 ^[13]	-	-6.25 mg/ml ^[22]	0.156 ^[13] 6.25 mg/ml ^[22]
<i>Salmonella typhimurium</i>	-	-	-	0.6250 ^[5]
<i>S. mutans</i>	320 ^[19]	160 ^[19]	320 ^[19] 12.5 mg/ml ^[22]	-12.5 mg/ml ^[22]
<i>Enterococcus faecalis</i>	16.6 ul/ml ^[23]	-	-	-
<i>Escherichia coli</i>			0.1–0.8 mg/ml ^[24]	0.1–0.4 mg/ml ^[24]
<i>Helicobacter pylori</i>			3.1–12.5 mg/ml ^[24]	3.1–12.5 mg/ml ^[24]
Multidrug-resistant <i>Klebsiella pneumoniae</i> (20 isolates)			0.1–0.8 mg/ml ^[24]	0.1–0.2 mg/ml ^[24]
<i>Salmonella spp.</i> (6 isolates)			0.02–0.04 mg/ml ^[24]	
Methicillin-resistant <i>Staphylococcus aureus</i> (52 isolates)			0.2–0.4 mg/ml ^[24]	0.2–0.4 mg/ml ^[24]

S. mutans: *Streptococcus mutans*, *S. aureus*: *Staphylococcus aureus*

and further research/surveillance are certain challenges to the use of such herbal medications.^[39]

Therapeutic Applications in Treating Oral Disease

In Indian traditional medicine, *Majuphal*/QI extracts are used as constituent of toothpaste and powder used in the treatment of gum diseases. Extracts of gall of *Majuphal* also exhibit antibacterial properties against oral pathogens.^[13,17,20,22,23]

Vermani *et al.* concluded that the antibacterial effect against the tested *S. aureus* and *Streptococcus sanguis* is due to the presence of tannin and gallic acid in the extracts.^[13] Basri *et al.* reported that plant extracts (QI) have greater inhibitory effect on Gram-positive bacteria as compared to Gram-negative bacteria. Further, the zone of inhibition was smaller for the positive control as compared to plant extracts, which signifies that bacterial species were more susceptible to plant extracts as compared to commercial antibiotics. An inhibitory effect toward obligate anaerobic bacteria group (*Porphyromonas gingivalis* and *Fusobacterium nucleatum*) was also observed.^[17]

The presence of hydrolyzable tannins was considered responsible for antibacterial activity with its multiple properties of being an astringent, iron deprivation through precipitation, and inhibition of oxidative phosphorylation.^[17]

The antibacterial property of the gall extract of QI against *Enterococcus faecalis* was assessed by the disc diffusion method. Sodium hypochlorite (2%) and chlorhexidine (2%) were used as positive controls and dimethyl sulfoxide was used as the negative control in the study. The zone of inhibition of gall extract against *E. faecalis* was found to increase with increasing volumes of gall extract. The MIC of the gall extract against *E. faecalis* was 16.6 µl/ml.^[23]

QI extract and gallic acid have been known to inhibit the growth of human oral cancer cells. The gall extract of QI has shown to affect cancer cells through mitochondrial apoptosis and DNA damage.^[40,41]

Product Trials and Patented/Marketed QI Products for Oral use

QI has been used in various herbal mouthrinses and tooth powders in combination with other phytoderivatives in humans. Authors found that plant extract in methanol provided more consistent antimicrobial activity as compared to those extracted in water.^[13]

Patented product (US 6,264,926 B1) is a naturally derived tooth powder which has synergistic herbal composition including QI (2–2.5%). Powder of gall nuts of QI plant provides astringent effect and checks foul odor of mouth, toothache, and swollen gums.^[42]

Herbal mouthwash marketed as herboral (by M-Tech Innovation Private Ltd., Pune, India)^[43] contains plentiful herbs with noteworthy anti-inflammatory and antimicrobial properties. QI (oak tree) is one of the principal ingredients of this herbal mouthrinse. Pyrol Tooth Powder, Patanjali Ayurveda Dant Kanti Medicated Herbal Toothpaste, Vicco Ayurvedic Toothpaste, and Ayurdent are other marketed products available in India with QI as one of the ingredients.

CONCLUSION

QI seems to be a promising substitute for the management of oral diseases in terms of antimicrobial activity, analgesic

activity, wound healing potential, antioxidant capacity, anticancer activity, and minimal associated risks. However, further research in humans is required to evaluate the efficacy, safety, and properties of such plant-derived products.

REFERENCES

- John J, Nagappan N. Antimicrobial efficacy of herbal and chlorhexidine mouth rinse a systemic review. *J Dent Med* 2013;2:5-10.
- Katiyar C, Gupta A, Kanjilal S, Katiyar S. Drug discovery from plant sources: An integrated approach. *Ayu* 2012;33:10-9.
- Vickers A, Zollman C, Lee R. Herbal medicine. *West J Med* 2001;175:125-8.
- Petrovska BB. Historical review of medicinal plants' usage. *Pharmacogn Rev* 2012;6:1-5.
- Fabricant DS, Farnsworth NR. The value of plants used in traditional medicine for drug discovery. *Environ Health Perspect* 2001;109 Suppl 1:69-75.
- Imran M. The prevalence and patterns of usage of Ayurveda, unani and home remedies in younger adults of rural North India. *Int J Green Pharm* 2017;11:108-13.
- Gogtay NJ, Bhatt HA, Dalvi SS, Kshirsagar NA. The use and safety of non-allopathic Indian medicines. *Drug Saf* 2002;25:1005-19.
- Bodeker G, Kronenberg F. A public health agenda for traditional, complementary, and alternative medicine. *Am J Public Health* 2002;92:1582-91.
- World Health Organization. WHO Country Cooperation Strategy 2006-2011. Geneva: World Health Organization; 2007.
- Ahmad W. Ethnopharmacology of *Quercus infectoria* Olivier galls: A review. *Hippocratic J Unani Med* 2016;11:105-18.
- Shrestha S, Kaushik VS, Eshwarappa RS, Subaramaihha SR, Ramanna LM, Lakkappa DB, et al. Pharmacognostic studies of insect gall of *Quercus infectoria* Olivier (*Fagaceae*). *Asian Pac J Trop Biomed* 2014;4:35-9.
- Zachariah SM, Kumar NM, Darsana K, Gopal D, Thomas N, Ramkumar M, et al. Phytochemical screening, formulation and evaluation of dried galls of *Quercus infectoria* Olivier. *Int J Pharm Sci Rev Res* 2014;26:125-30.
- Vermani A, Navneet, Prabhat. Screening of *Quercus infectoria* Gall extracts as anti-bacterial agents against dental pathogens. *Indian J Dent Res* 2009;20:337-9.
- Fathabada AE, Shariatifar N, Mardania K, Mohammadpourfard I. Study on antibacterial and antioxidant activity of Oak gall (*Quercus infectoria*) extracts from Iran. *Int J Curr Sci* 2015;14:E44-50.
- Zhang HM, Zhao L, Li H, Xu H, Chen WW, Tao L, et al. Research progress on the anticarcinogenic actions and mechanisms of ellagic acid. *Cancer Biol Med* 2014;11:92-100.
- Leal AS, Leal LH, Silva D, Nunes LC, Lopes JA. Incorporation of tannic acid in formulations for topical use in wound healing: A technological prospecting. *Afr J Pharm Pharmacol* 2015;9:662-74.
- Basri DF, Tan LS, Shafiei Z, Zin NM. *In vitro* antibacterial activity of galls of *Quercus infectoria* Olivier against oral pathogens. *Evid Based Complement Alternat Med* 2012;2012:632796.
- Basri DF, Fan S. The potential of aqueous and acetone extract of galls of *Q. infectoria* as antimicrobial agent. *Indian J Pharmacol* 2005;37:26-9.
- Mohammadi-Sichani M, Karbasizadeh V, Dokhaharani SC. Evaluation of biofilm removal activity of *quercus infectoria* galls against *Streptococcus mutans*. *Dent Res J (Isfahan)* 2016;13:46-51.
- Baharuddin NS, Abdullah H, Abdul Wahab WN. Anticandida activity of *Quercus infectoria* Gall extracts against *Candida* species. *J Pharm Bioallied Sci* 2015;7:15-20.
- Satirapathkul C, Leela T. Growth inhibition of pathogenic bacteria by extract of *Quercus infectoria* Galls. *Int J Biosci Biochem Bioinform* 2011;1:26.
- Fani MM, Bazargani A, Jahromi MA, Hasanpour Z, Zamani K, Manesh EY. An *in vitro* study on the antibacterial effect of *Ferula assa-foetida* L. and *Quercus infectoria* Olivier extracts on *Streptococcus mutans* and *Streptococcus sanguis*. *Avicenna J Dent Res* 2015;7:e22656.
- Nagesh L, Sivasamy S, Muralikrishna KS, Bhat KG. Antibacterial potential of gall extract of *Quercus infectoria* against *Enterococcus faecalis* an *in vitro* study. *Pharmacogn J* 2012;4:47-50.
- Voravuthikunchai SP, Chusri S, Suwalak S. *Quercus infectoria*. *Oliv. Pharm Biol* 2008;46:367-72.
- Muskhazli M, Nurhafiza Y, Azwady AA, Dalilah E. Comparative study on the *in vitro* antibacterial efficacy of aqueous and methanolic extracts of *Quercus infectoria* Galls against *Cellulosimicrobium cellulans*. *J Biol Sci* 2008;8:634-8.
- Umachigi SP, Jayaveera KN, Kumar CK, Kumar GS, Swamy BM, Kumar DV. Studies on wound healing properties of *Quercus infectoria*. *Trop J Pharm Res* 2008;7:913-9.
- Ahmad W, Zeenat F, Hasan A, Abdullah A, Nargis A, Tarannum T. Mazu (*Quercus infectoria*, Oliv) an overview. *Ind J Unani Med* 2011;4:17-22.
- Kaur G, Athar M, Alam MS. *Quercus infectoria* Galls possess antioxidant activity and abrogates oxidative stress-induced functional alterations in murine macrophages. *Chem Biol Interact* 2008;171:272-82.
- Imtiaz S, Javed SA, Tariq M, Chaudhary SS, Aslam M. Oak galls: The medicinal balls. *J Pharm Sci Innov* 2013;2:18-21.
- Ikram M, Nowshad F. Constituents of *Quercus infectoria*. *Planta Med* 1977;31:286-7.
- Wiert C, Kumar A. Practical Handbook of Pharmacognosy. Malaysia: Pearson Education Malaysia

- Sdn Bhd; 2001.
32. Hapidin H, Abdullah H, Soelaiman IN. The potential role of *Quercus infectoria* Gall extract on osteoblast function and bone metabolism. *Open J Endocr Metab Dis* 2012;2:82-8.
 33. Rehman MU, Tahir M, Ali F, Qamar W, Khan R, Khan AQ, *et al.* Chemopreventive effect of *Quercus infectoria* against chemically induced renal toxicity and carcinogenesis. *Int J Drug Dev Res* 2012;4:336-51.
 34. Rastogi RP, Mehrotra BN. *Compendium of Indian Medicinal Plants*. Vol. 2. Lucknow: CDRI; 1999. p. 576.
 35. Gamboa-Gómez CI, Simental-Mendía LE, González-Laredo RF, Alcantar-Orozco EJ, Monserrat-Juarez VH, Ramírez-España JC, *et al.* *In vitro* and *in vivo* assessment of anti-hyperglycemic and antioxidant effects of oak leaves (*Quercus convallata* and *Quercus arizonica*) infusions and fermented beverages. *Food Res Int* 2017;102:690-9.
 36. Ansari M, Etelaei F, Sharififar F. Tyrosinase kinetic in the presence of three inhibitory medicinal plants. *Int J Green Pharm* 2011;5:103-5.
 37. Tayel AA, El-Sedfy MA, Ibrahim AI, Moussa SH. Application of *Quercus infectoria* extract as a natural antimicrobial agent for chicken egg decontamination. *Rev Argent Microbiol* 2018;50:391-7.
 38. Iminjan M, Amat N, Li XH, Upur H, Ahmat D, He B, *et al.* Investigation into the toxicity of traditional Uyghur medicine *Quercus infectoria* Galls water extract. *PLoS One* 2014;9:e90756.
 39. Inamdar N, Edalat S, Kotwal VB, Pawar S. Herbal drugs in milieu of modern drugs. *Int J Green Pharm* 2008;2:402-6.
 40. Lu YC, Lin ML, Su HL, Chen SS. ER-dependent Ca⁺⁺-mediated cytosolic ROS as an effector for induction of mitochondrial apoptotic and ATM-JNK signal pathways in gallic acid-treated human oral cancer cells. *Anticancer Res* 2016;36:697-705.
 41. Weng SW, Hsu SC, Liu HC, Ji BC, Lien JC, Yu FS, *et al.* Gallic acid induces DNA damage and inhibits DNA repair-associated protein expression in human oral cancer SCC-4 cells. *Anticancer Res* 2015;35:2077-84.
 42. Formulation Useful as a Natural Herbal Tooth Powder. Available from: <https://www.patents.google.com/patent/US6264926>. [Last Accessed on 2018 Dec 13].
 43. Herboral Liquid Gargle. Available from: https://www.pharmaceuticals.indiabizclub.com/catalog/71236~herboral_liquid_gargle~pune. [Last accessed on 2018 Dec 13].

Source of Support: Nil. **Conflict of Interest:** None declared.