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Traditional Herbal Remedies for Periodontitis

Amit V. Kakad*, Umesh D. Laddha, Sanjay J. Kshirsagar and Shubham J. Khairnar

MET's Institute of Pharmacy, Bhujbal Knowledge City, Affiliated to Savitribai Phule Pune University, Nashik, 422003, MS, India.

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Oral diseases developed because of poor oral hygiene are responsible for health burdens in many countries which may affect the person for a lifetime, lead to severe pain, and may cause death. Improper oral hygiene can also result in the development of oral cancer. As per the WHO facts sheet on 'Oral health', 3.5 billion population suffers from oral diseases globally. As per the Global Burden of disease, tooth decay is the most common condition. Poor oral hygiene and lack of awareness amongst the population of middle and low-income countries result in the formation of dental diseases. Additionally; diabetes and smoking increase the risk of dental diseases by many folds. Some phytoconstituent from plants we called as herbal remedies are found to be very effective and safe over conventional or synthetic medicines. Anti-bacterial, anti-inflammatory, and antioxidant properties of various herbal remedies are advantageous over the antibiotics used in periodontitis. Periodontitis is one of the most prevalent gum diseases in the world which affects the soft tissue and bone support to the tooth. Poor oral hygiene can lead to progressive loss of alveolar bone around the teeth. Various herbal remedies traditionally used for oral hygiene recently showed promising results against Periodontitis. This review provides detailed emphasis on the various herbal remedies and its components used for the treatment of diseases related to dental care, gum & teeth, and overall oral hygiene. Our goal is to discuss the overall views of researchers and the current useful strategy of herbal components for periodontitis.

Keywords: Anti-bacterial; Anti-inflammatory; Herbal remedies; Periodontitis; Traditional plant.

The periodontal term consists of the teeth which are supported by Gum and bone. Such teeth are affected due to poor oral hygiene and it causes the inflammation and formation of bacterial plaque which eventually losses the tooth. Gingivitis is one of the mildest forms of it.[1] Periodontitis based on specific etiology: chronic and aggressive. Sometimes it can be occurance by manifestation of systemic disease.[2] The main bacteria involved in the development of dental caries are *Streptococcus mutans* and *Lactobacillus acidophilus*.[3] Treatment for periodontitis seeks to lower the number of pathogenic bacteria in the mouth, eradicate diseased pockets, and heal inflammatory tissue.[1] For that treatment options may vary from cost-effective and costly surgical & non-surgical involving various antimicrobials, mouth rinsers, mouthwashes, antiseptic formulations, gels, and

*Corresponding author E-mail: amitkakad12@gmail.com

oral antibiotics prescribed by a periodontist. Surgeries are also available for periodontitis depending on the severity e.g flap surgery, guided tissue regeneration (GTR), tissue-stimulating proteins, soft tissue, and bone grafts.[4]

More severe periodontitis with bone loss and pocket formation, which could eventually lead to losing the tooth if not treated appropriately, may impact 40% to 45% of India's population, according to a report by the National Commission on Macroeconomics.[5] Traditional medicine has been used worldwide for centuries. Traditional herbal medicine is used by near about 70% of the total population in India and up to 90% of the population in Africa using for medical treatment.[4] Naturally occurring herbal components which having multiple bioactive constituents possess enormous medicinal value with few side effects and most important is maximum they are safe. The other synthetic antibiotics and antimicrobials have the disadvantages of being drug-resistant and numerous side effects. So, the natural phytoconstituent is a good and safest proven alternative for such oral diseases.[6] Various herbs are patented and have proven study for oral disease. In this review, introducing various herbal remedies that are useful for periodontitis. The following Fig.1 are shown comparison between Synthetic and Herbal drugs.

Commonly used herbs: overview

Due to the anti-plaque and anti-inflammatory properties of herbal medicine, they are strongly recommended in dentistry.[6] Some of them also act as precautionary, helping to prevent it from arising. Antimicrobial resistance and severe side effect are the disadvantages of synthetic drugs used in infection. Instead of them, phytoconstituents are the safe alternatives to control infections.[7] When applied to the gums, the aloe vera gel has been observed to reduce gum tissue irritation and pain. Clove oil lowers infection and relieves discomfort from pain. The methanolic extract of clove shows activity against anaerobic Gram-negative oral bacteria which cause tooth infection and periodontitis. From the literature, it is reported that Myricetin & Kaempferol have significant inhibitory activity against periodontal pathogens. Echinacea and goldenseal also have been reported to reduce inflammation and relief infection. A natural supplement of Coenzyme Q-10 promotes a healthy blood supply to the gums by increasing oxygen transport in the body. Clinical research data have shown that daily use of Coenzyme Q-10 improves plaque and calculus counts in patients with periodontal disease. Some nutraceutical product such as bioflavonoids along with Vitamin C helps to accelerate the healing process in oral issues. Some herbal components are patented for their action and uses. Among them are patented herbs like oral administration of a dried extract of Vinca rosea for reducing plaque. Which is a good oral hygiene method for the treatment of periodontal diseases. Acacia catechu has been used to remove tartar, plaque, and stains, as well as to cleanse and polish the tooth surface, which helps to enhance the condition.[1]

Miswak *(Salvadora persica)*

Miswak belongs to the *Salvadoraceae* family & also known as a chewing stick. Since ancient times miswak has been used for maintaining oral hygiene.[8] Researchers have suggested that miswak has over ten naturally occurring elements that are important for good dental, oral, and overall health like Fluoride, Silica, Benzyl isothiocynate, Essential oils, salvadorine, Salvadoraside, 1,8-Cineole, linalool, Piperidine, Isoterpinolene, Myrcenol, and sabiene.[6,9] In medicinal component Benzyl isothiocyanate shown in Fig 2 is a major volatile oils component of *Salvadora persica* which show bactericidal effect against many bacteria.[4] The important chemical constituent of miswak and their actions are shown in Fig 3. Another antimicrobial constituents & prophylactic components include alkaloids, fluoride, Sulphur compounds & glucosinolates, Methyl chavicol, etc.[5] Miswak is scientifically proven for its effectiveness against tooth decay and it is recommended to use as a successful oral hygiene tool by World Health Organization. It is a unique remarkable dental stick and cost effective solution for common people. Report from miswak users is that there is less gingival bleeding, better periodontal health, and interproximal bone loss when especially in comparison with common toothbrush users.[10,11].

Neem *(Azadirachata indica)*

The Neem tree is primarily grown in Asia and Africa's southern regions and because of its therapeutic characteristics, Asians have long utilized neem to treat a variety of ailments.

The chemical composition includes Nimbin, nimbidin, azadirachtin, nimbolide, epicatechin, catechin, gallic acid, and margolone.[6] The bioactive compound of neem is shown in Fig 4. We found clinical study data showing the effect of Neem in the literature. In this study, 50 individuals with confirmed gingivitis were chosen, 40 of whom had significant bleeding and pustular discharges from their gums. Eight out of ten patients exhibited considerable improvement after brushing twice a day with a paste containing neem leaf extracts just for three weeks. The patients also experienced a decrease in bacterial populations as well as the removal of halitosis, all with no negative side effects.[8] Insoluble glucan production is prevented by aqueous extract of Neem, leading to bacterial aggregation. As a result, *streptococci's* ability to colonize tooth surfaces and the oral cavity will be reduced. It has been recommended that it be used to treat tooth plaque. The mucoadhesive dental gel has a composition of neem extract Compared to chlorhexidine gluconate mouthwash, it was found to be more effective at reducing bacterial count and plaque index.[12]

Water-soluble extracts of the *Azadirachata indica* affect some bacterial properties which may alter bacterial adhesion and also affect the growing ability to the colonization of tooth surfaces by *streptococci*. The most important thing is among the oral *streptococci* studied, neem has a broad bacterial aggregating effect.[13] Formulation of gel with neem extract combined with a mucoadhesive polymer can greatly shorten the time it takes to cure oral infections and manage the microorganisms that cause tooth problems.[14] Adyanthaya et.al[15] studied the antimicrobial effect of methanol extract of neem twig. They discovered that neem extract was effective in lowering cariogenic and periodontal disease-causing bacteria, and they proposed utilizing methanolic extracts of neem twig in oral care products. Following a daily dosage of 25, 50, or 100 mg/kg for 6 weeks, nimbidin caused subacute toxicity in adult rats; a hypoglycemia effect was also reported after administering

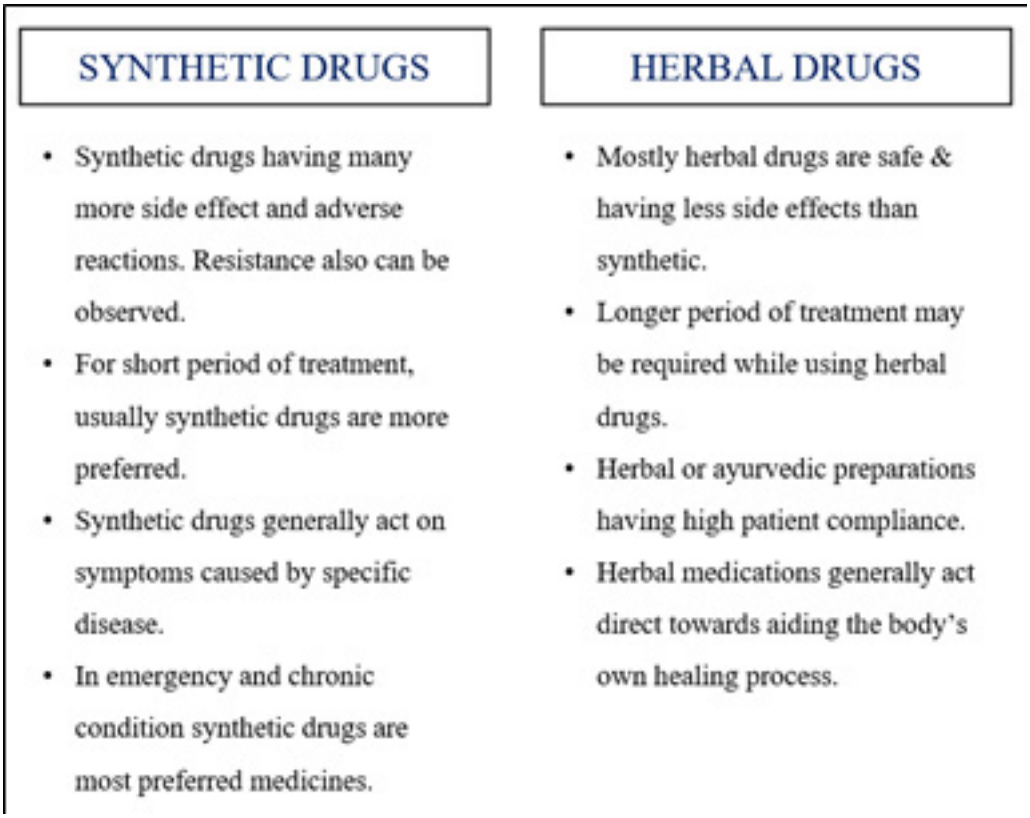

Fig. 1. The comparison between Synthetic drugs and Herbal drugs

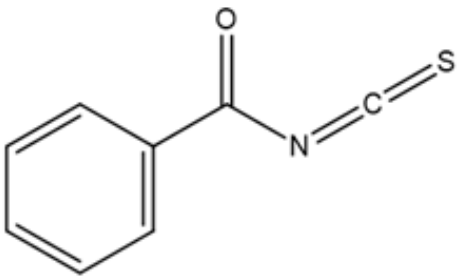

Fig. 2. The Structure of Benzyl Isothiocynate

nimbidin to fasting rabbits and on another side, when nimbolide and nimbic acid are injected intravenously or intraperitoneally they are found to be harmful to mice; however, these chemicals are less dangerous to rats.[16] Fig 5 shows the structure of Nimbolide. Fig 6 structure of Nimbidin.

Guava (*Psidium guajava*)

Guava primarily rich in Vitamin C (Ascorbic acid) shows an excellent antioxidant property. This ascorbic acid alters the fibroblast differentiation and modulates procollagen gene expression by the effect on the extracellular matrix, following collagen formation. Ascorbic acid, in

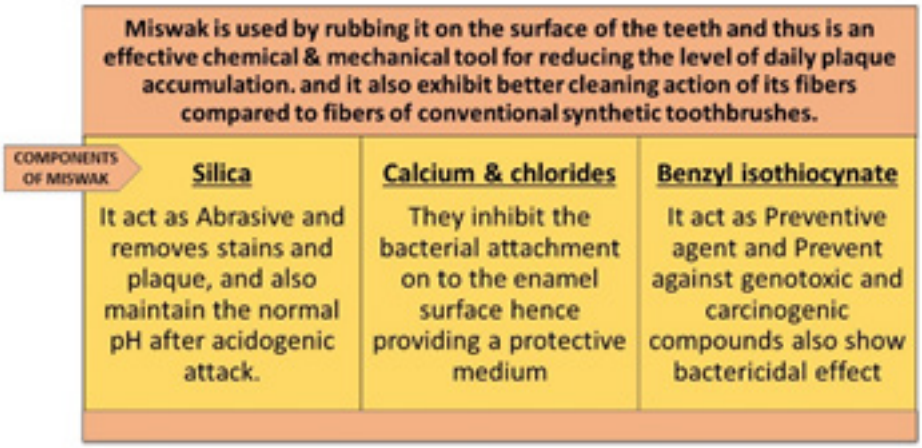

Fig. 3. The bioactive components of Miswak

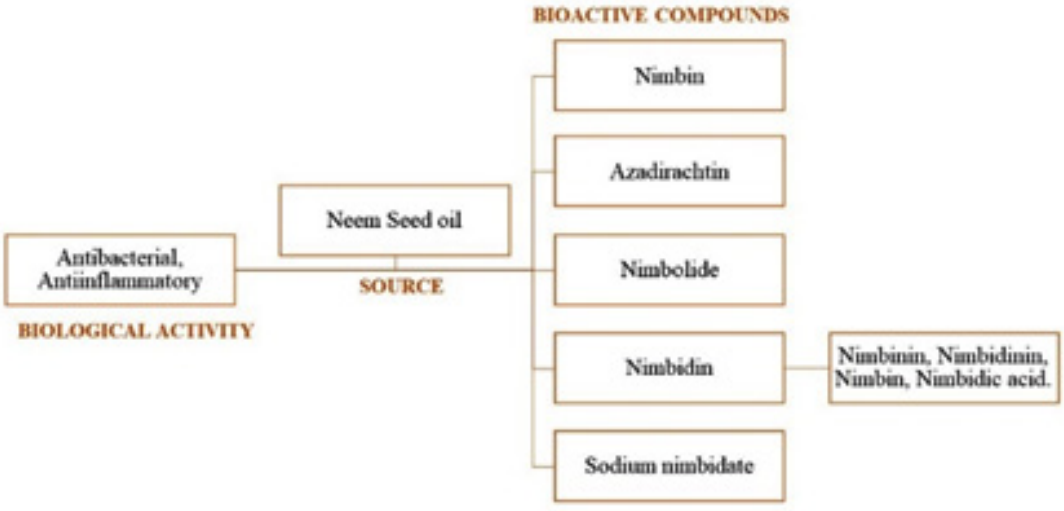

Fig. 4. List of bioactive compounds in *A. indica*

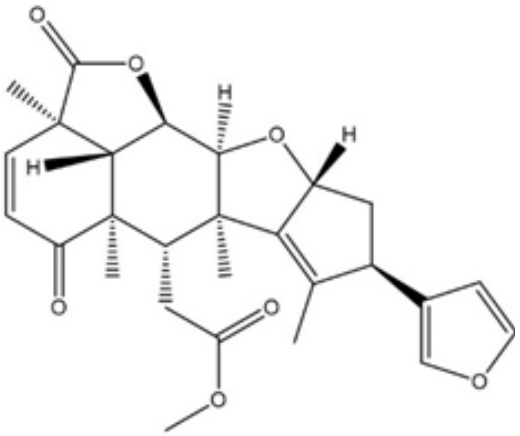

Fig. 5. The Structure of Nimbolide

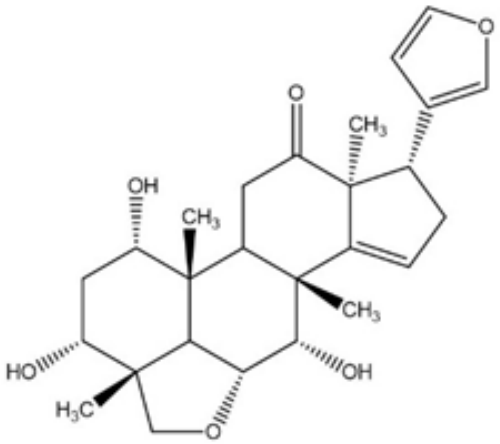

Fig. 6. The Structure of Nimbidin

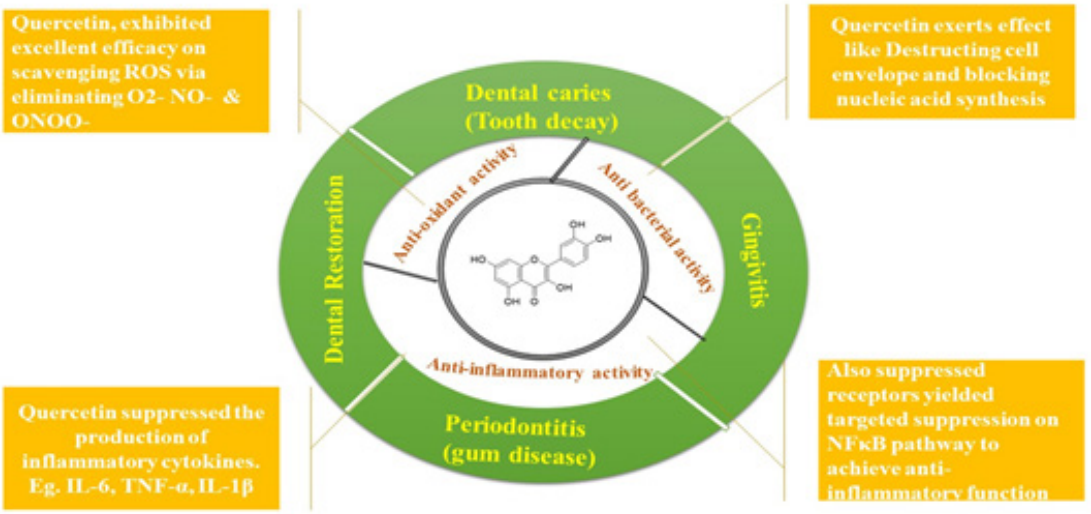

Fig. 7. The Structure of Quercetin with its various effect

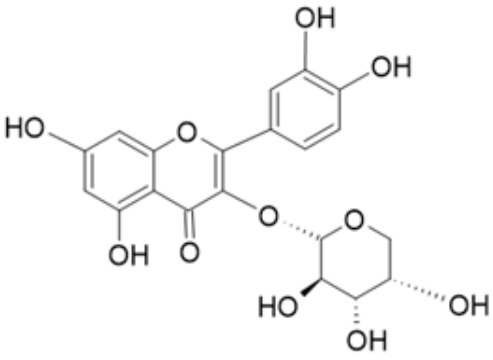

Fig. 8. The Structure of Guaijaverin

combination with bioflavonoids, assists in the healing process.[17] Phytoconstituent of guava mainly shows multifunctional effects like carotenoids, quercetin, and polyphenols which exhibit its antioxidant action, the antibacterial effect of guava is mainly associated to flavonoids, guaijaverin, and quercetin. One of the major flavanol quercetin has demonstrated good antimicrobial activity against periodontal pathogens *Aggregatibacter actinomycetemcomitans* (Aa), *Porphyromonas gingivalis* (Pg), *Prevotella intermedia* (Pi), *Fusobacterium nucleatum,* etc. and this activity of quercetin is thought to be related to the formation of irreversible complexes that disrupt

the membrane and inactivate extracellular proteins. The structure and MOA of quercetin are shown in Fig 7. Guava essential oils and leaf extracts can scavenge hydrogen peroxide and superoxide anion, as well as reduce the generation of hydroxyl radicals. The decoction of leaves can be used as a gargle for bleeding gums, while the decoction of roots and bark can be used as a mouthwash.[18,19] Quercetin's anti-inflammatory properties are due to its involvement in the NF-êB, JNK, and Nrf2 signaling pathways. NF-êB is a transcription factor that can influence the transcription of cell genes and thereby regulate the inflammatory response.[20] The existence of several essential oil compounds, such as monoterpenes, 1.8-cineol, and acetate of á-Terpenil along with guaijaverin and psidiolic acid contributes to *P. guajava's* antimicrobial activity.

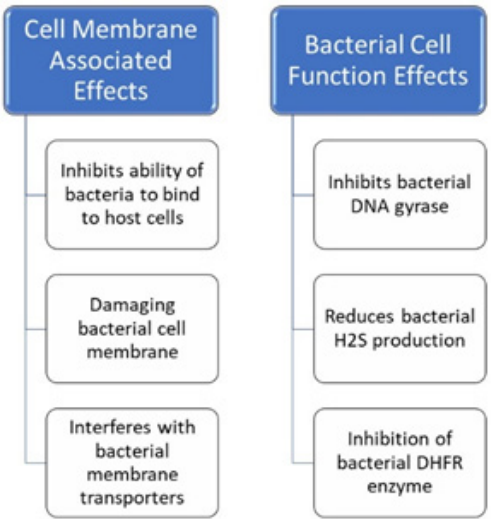

Fig. 9. Cell membrane associated effect and bacterial cell function effect of catechin

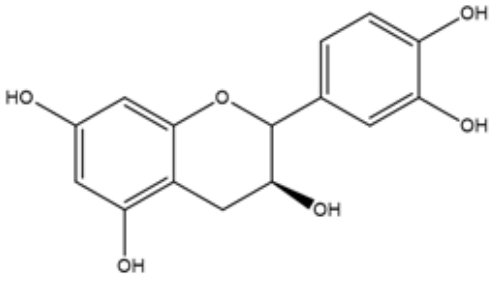

Fig. 10. The structure of Catechin

According to the literature, most of these medicinal plant extracts or their combinations could be used as herbal alternatives to chlorhexidine.[21] The second most important constituent is Guaijaverin which is a promising antiplaque component due to its bacteriostatic property by preventing the growth of *S. mutans* and *S. aureus*. Guaijaverin reduces the hydrophobicity of oral pathogenic bacteria, which is one of the most critical components in their ability to attach to the tooth surface. This activity could be due to guava extracts binding to cell surface proteins, lowering total cell hydrophobicity, and so guava could be developed as a natural antiplaque agent. The structure of guaijaverin is shown in Fig 8. Guava extract has been shown to suppress the growth, adhesion, and co-aggregation of dental plaque bacteria in *in-vitro*. Guava leaf extracts may reduce plaque bacteria formation without altering oral cavity balance.[19] From the literature author found that there was a significant reduction in full-mouth scores of plaque index (1.36 ± 0.04), gingival index (1.29 ± 0.047), gingival bleeding index (47.5±1.162), and PPD (0.71 ± 0.024mm) and gain in CAL (0.72 ± 0.052mm), at various time intervals. Thus, these indicated an overall improvement in gingival and periodontal health.[17] The presence of catechol at the B ring may have attributed to the flavanol compound guaijaverin which demonstrated growth-inhibitory effect against the test microorganisms. The bioactive compound in the extract of the guava leaf, such as flavonoids and tannins, are responsible for the prevention of bacterial adhesion. Flavonoids have anti-GTase properties. This enzyme is capable of converting sucrose to viscous insoluble glucan, which encourages *S. mutans* to stay firmly attached to the tooth's surface.[22]

Green Tea *(Camellia sinensis)*

Green tea is made from *Camellia sinensis* leaves that have been processed with minimal oxidation. It has the highest percentages of polyphenols, which are antioxidants in nature

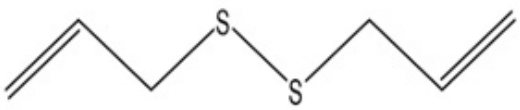

Fig. 11. The structure of Allicin

and categorized as catechins. Green tea has 6 major catechin components. : Catechin, gallocatechin, epicatechin, epigallocatechin, epicatechin gallate (ECg), and epigallocatechin gallate (EGCg). Among all the other chemicals, EGCg has been the subject of much research, and it is a particularly powerful antioxidant in action. Green tea is also found in tocopherols, selenium, carotenoids, ascorbic acid, chromium, and zinc as well as a variety of phytochemical substances. Catechins in green tea have demonstrated potential antibacterial activity on periodontal infections, as shown in Fig 9. The principal etiological agents in periodontitis are anaerobic bacteria such as

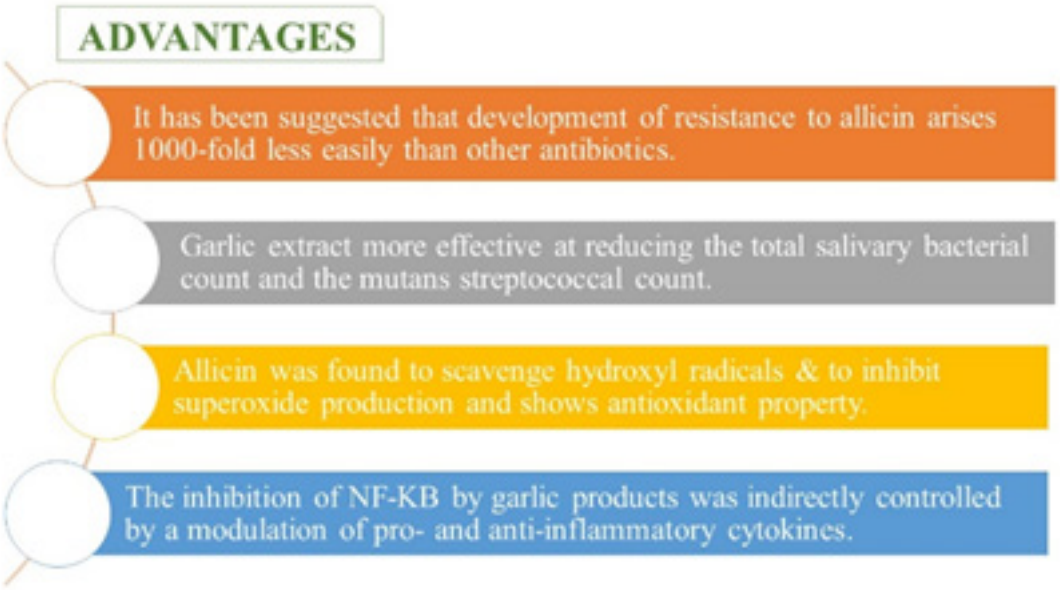

Fig. 12. Various Advantages of Allicin

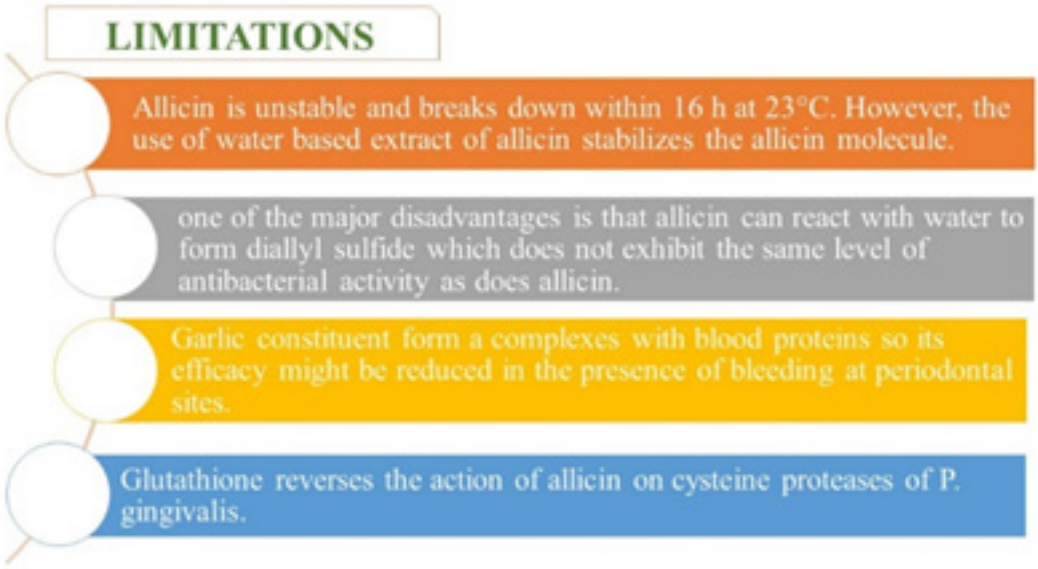

Fig. 13. Limitations of Allicin

Porphyromonas gingivalis and *Prevotella spp*. The *in-vitro* experiment demonstrated that these herbal medicinal compounds prevent the growth of *P. gingivalis*, and *Prevotella nigrescens*. This further inhibits *P. gingivalis* from adhering to human buccal epithelial cells.[23]

The catechin from green tea had a bactericidal action against black-pigmented Gram-negative anaerobic rods (BPR), and the combination of mechanical therapy and green tea catechin application using a local drug delivery system improved periodontal condition. Green tea catechin was tested for its minimum inhibitory concentration (MIC) and bactericidal action against BPR. As a method of slow-release local delivery, the hydroxy propyl cellulose patches containing catechin were placed in dental pockets of the patients. Dosing like once in a week for eight weeks. The clinical, enzymatic, and microbiological effects of catechin were investigated. Green tea catechin demonstrated a bactericidal effect against *Porphyromonas gingivalis* and *Prevotella spp.* in the investigation, with MIC was found to be1.0 mg/ml reported by *in-vitro* method.[24] The structure of catechin shown in Fig 10.

The goal of this study was to see how epigallocatechin gallate (EGCg) affected developed biofilms and it's development through *Porphyromonas gingivalis,* a common periodontal disease pathogenic bacteria. The

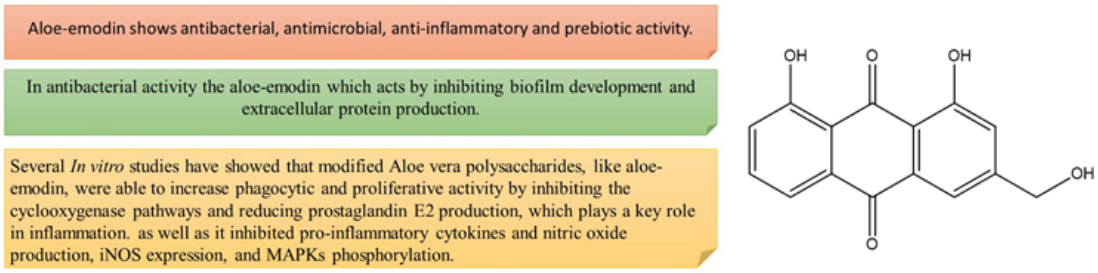

Fig. 14. The structure of Aloe Emodin and its action

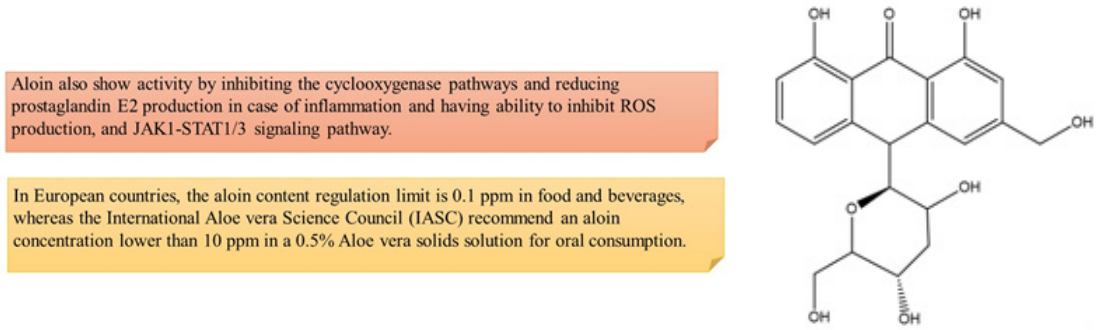

Fig. 15. The structure of Aloin and its action

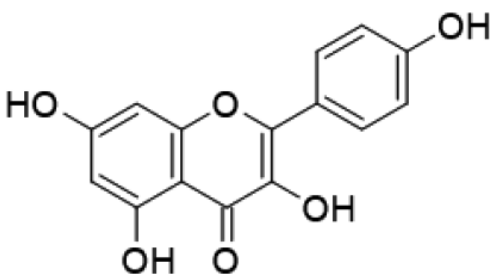

Fig. 16. The structure of Kaempferol

primary polyphenolic component of tea, (-) epigallocatechin-3-gallate (EGCg), has the greatest bactericidal and biological effects among catechins. EGCg inhibited the growth of P. gingivalis in a dose-dependent manner and shown bactericidal action on *P. gingivalis* at 500 mg l1 (99.9% decrease) and 1 g l1 (100% decrease).[25] The antibacterial action of green tea extract on the periodontic pathogen examine by standard agar disk diffusion (ADD) test was found to be, the *P. gingivalis*, *P. intermedia* and *A. actinomycetemcomitans* were sensitive at

Table 1. List of some important herbal remedies with their active component and pharmacological actions

Sr No	Common Name	Botanical Name	Active Component	Pharmacological Effect	Dosage Form
1	Meswak[8](Roots)	*Salvadora persica* twigs, stem	Fluoride, alkaloids, sulphur compounds, glucosinolate, volatile oils	Anti-microbial, antiplaque	Toothpaste& Used as Toothbursh
2	Guava[34](Leaves)	*Psidium guajava*	Guaijaverin, QuercetinAscorbic acid, flavonoids	Anti-oxidant, Anti-microbial, antiplaqueAnti-inflammatory	Powder, Gel Toothpaste
3	Turmeric[35](Rhizome)	*Curcuma longa*	Curcumin, curcuminoid Desmethoxycurcumin	Anti-inflammatory, Antimicrobial, Astringent, anti-septic, Anti-oxidant and Analgesic.	Tablet & Toothpaste
4	Aloe Vera[36](Leaves)	*Aloe barbedens*	Vitamins, minerals, enzymes, polysaccharides, phenols, organic acids	Anti-microbial, Anti-inflammatory	Oral gels toothpaste
5	Neem [6](Leaves)	*Azadirachta indica*	Azadirachtin, nimbin, gallic acid, catechin, margolone	Antibacterial, Antioxidant, Anti-inflammatory, Host immune-modulatr, Anti-plaque	Toothpaste,Gel
6	Bee glu[6](Leaves, flower & barks)	Propolis Resin	Flavanooids, phenols, aromatics, caffeic acid, phenethyl ester	Anti-inflammatory, Anti-bacterial, local anesthetic, Antioxidant, Anti-calculus	Oralcleaner, Powder, Tablet
7	Clove[6](Dried flower buds of clove)	*Eugenia caprophylatta*	Eugenol, gallic acid, sesquiterpenes, furfural, flavonoids, kaempfero; myricetin	Anti-oxidant, Antiseptic, Anti-bacterial, Analgesic, Bacteriostatic	Oil & Gel
8	Babool[6] or Indian gum Arabic(Bark, root)	*Acacia nilotica*	Tannins, phenols, essential oils, flavanoids	Anti-bacterial, Antiplaqu	Toothpaste
9	Tulsi[37](Leaves)	*Ocimum sanctum*	Vitamin A, Iron, Zinc, calcium and Vitamin C.	Anti-inflammatory expectorant, analgesic, anticancer, antiasthmatic, antiemetic, diaphoretic, antidiabetic	Powder
10	Lemon grass[38](Leaves)	*Cymbopogon citratus*	Citronellol Geranio	Anti-oxidant, Anti-bacterial, anti-fungal, Anti-inflammatory and antiseptic.	–
11	Eucalyptus[39](Leaves)	*Eucalyptus globulus*	Essential oil	Antibacterial	Gel
12	Mango[40](Leaves)	*Magnifera indica*	Ascorbic and phenolic acids	Antibacterial properties.	–
13	Kalonji[41] or black cumin(Seed)	*Nigella sativa*	Carvone, terpene, alpha- pinene and p-cymene thymoquinone, di thymoquinone, thymohydroquinone and thymol	Anti-oxidant, antiinflammatory, anti-fungal, Anti-bacterial and antiparasitic.	–
14	Cranberry[42](Berries)	*Vaccinium macrocarpum*	Anthocyanins, peonidin-3-arabinoside, cyanidin-3-arabinoside, benzoic acid	Anti-inflammatory, Anti-bacterial, and anti-cancer.	–
15	Cinnamon[43] or Daarchini(Bark)	*Cinnamon zeylanicum*	Essential oil	Anti-bacterial, Anti-septic	Toothpaste, mouthwash, or chewing gum
16	Triphala[44](Fruit)	Amalaki (Emblica of icinalis), Haritaki	Vit c, carotene, phyllemblic acids. Anthraquinone glycoside, tannic acid, chebulagic acid	Antimicrobial, antioxidant and anti-collagenase	Powder form
17	Ginkgo[23](Leaf)	*Ginkbo biloba*	Ginkgo flavone glycosides, terpenoid Ginkgolic acid	Scavenging free radicals, lowering oxidative stress, anti-inflammation.	–

12.5, 25, and 50 mg/ml concentrations and zone of inhibition found in the rang from 10 to 30 mm in diameter. The most antioxidant component like epigallocatechin-3-gallate (EGCG) has been found to diminish acid generation in dental plaques by inhibiting *S. mutans* proliferation, interfering with bacterial attachment to the enamel, and suppressing glucosyltransferase and amylase activities.[26].

Garlic (*Allium sativum*)

Allicin, is the main phytochemical chemical constituent, has antibacterial activity against various Gram-negative and Gram-positive bacteria, including *Mycobacterium tuberculosis, Escherichia, pneumonia, Lactobacilli, Helicobacter pylori, Pseudomonas aeruginosa and Klebsiella* as well as antifungal action, specifically against *Candida albicans* and also exhibit some antiparasitic activity and antiviral activity.[26] Garlic is the plant materials that had a lot of research done on it because of its composition and therapeutic properties. The antibacterial activity of allicin, structure shown in Fig11 is due to a main compound called allicin (diallyl thiosulfinate). It is, however, exceedingly thermo-labile, and when heated, it forms a variety of disulfide compounds.[27] The advantage of allicin shown in Fig 12.

The many inhibitory effects that allicin shows on diverse thiol dependent enzymatic systems account for allicin's broad antibacterial spectrum. Allicin's principal antimicrobial impact is owing to its interacting with key thiol containing enzymes, specifically its capacity to interact with a model thiol molecule (L-cysteine) to produce the S-thiolation product which is S-allylmercaptocysteine.[28] The extract of garlic was found to be potent against all bacterial strains tested. Unfortunately, pharmaceutical companies have shown little interest in converting garlic into a medicine and conducting clinical studies. The important fact is, because of allicin's for so long presence in the public domain, no patents may be filed on it.[29] Limitation of allicin shown in Fig 13. Because of its powerful efficacy, garlic extract could be a viable periodontitis treatment and having effective action against both *P. gingivalis* and *A. actinomycetemcomitans* and also on the proteases of *P. gingivalis*. However, therapeutic medicines for periodontitis should preferably to be effective against biofilms rather than only planktonic cells in order to transfer into effective *in vivo* therapies. Garlic extract, on the other hand, has been shown to prevent *Staphylococcus epidermidis* from forming biofilms, even at sub-MIC levels.[7]

Aloe vera *(Aloe barbadensis)*

The *Aloe barbadensis* plant, also known as Aloe vera*,* is a member of the Lily family. It's a xerophyte type plant means that can adapt to less or erratic water availability with the ability to store a large amount of water. Aloin, Aloe emodin, barbaloin, aloetic acid, isobarbaloin, chrysophanic acid, anthracine, ethereal oil, anthranol, cinnamonic acid esters & resistannol are some of the plant's natural anthraquinones that have antimicrobial properties.[6] Structure of aloe emodin and its action shown in Fig 14.

Aloe vera mouth rinse was found to be effective for the reduction of gingivitis and accumulation of plaque in clinical study.[26] Polysaccharides from aloe vera have also been linked to direct bacterial activity via phagocytic leukocyte activation, which kills bacteria.[5] The cyclooxygenase pathway is inhibited by aloe vera, which lowers the formation of prostaglandin E2 from arachidonic acid. Structure of aloin and its action shown in Fig 15. C-glucosyl chromone, a novel anti-inflammatory component isolated from gel extracts, was recently discovered. Lupeol, urea nitrogen, salicylic acid, cinnamonic acid, sulphur & phenolsare six antiseptic compounds found in aloe vera that fight fungi, bacteria, and viruses.[30] Aloe vera shows several properties like anti-inflammatory, analgesic, wound healing, stomatitis, gingival health, immunostimulant and also effective against varicella-zoster virus & herpes simplex types 1 and 2.[30,31]

Clove *(Syzygium aromaticum)*

Clove is a highly valuable spice which has been utilised in the food industry as a preservative and for a variety of therapeutic uses for ages. Oil that is highly volatile (16-21) % likely Phenols. In which particularly Eugenol near about (80-88) %, acetyl eugenol (10-15) %, á and â -Caryophyllene, Pyrogallol tannins (10-13) %, Methyl furfural and dimethyl furfural are important compounds. Clove oil is most commonly used in dental and oral care. The oil's germicidal characteristics make it ideal for treating dental pain, toothaches, mouth ulcers and sore gums. Clove oil majorly contains eugenol, a substance that has long been utilised in dentistry since many years.[32] The extract showed

potential activity against *Actinobacillus Sp.* In an *in-vitro* antibacterial study, with show an effective zone of inhibition in the aqueous extract compared to a moderate zone of inhibition in the acetone extract.[33] Antioxidant polyphenolic substances kaempferol and myricetin have been shown to be bacteriostatic against periodontal infections. Structure of Kaempferol shown in Fig 16.

CONCLUSION

As demonstrated by various traditional herbal remedies the in given review, they are found to be a wide range of biological & medicinal properties like antibacterial, antioxidant, and anti-inflammatory effects and are useful in the prophylactic purpose or maintenance of various dental diseases like periodontitis condition. Herbal remedies are also called ancient medicines hence those having high patient acceptance. Diseases like periodontitis are less aware to common people and because of unawareness it may create several health problems. Synthetic drugs like painkillers and antibiotics are not advised to take for a longer period, they are more preferred in chronic conditions or an emergency condition or at the time of surgery. Hence from the literature, it was found that there are several herbal remedies having potent medicinal components which are useful for the prevention, treatment, and maintainance of dental diseases like periodontitis. Likewise, this is one of the thrust areas for researcher to develop novel drug delivery by using herbal components or making a combinatorial formulation that shows highly effectiveness over synthetic medicines.

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Conflict of Interest

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REFERENCES

1. Kumar P, Ansari S.H and Ali J. Herbal Remedies for the Treatment of Periodontal Disease-A Patent Review. Recent. Pat. Drug. Deliv. Formul., 2009. Vol. 3: 221-228.
2. Kassebaum N.J, Bernabe E, Dahiya M, Bhandari B, Murray C.J.L and Marcenes W. Global burden of severe periodontitis in 1990-2010: A systematic review and meta-regression. J. Dent. Res., 2014. Vol. 93 :1045–53.
3. Chandrashekar B.R, Nagarajappa R, Jain R, Singh R, Thakur R and Shekar S. Antimicrobial efficacy of Acacia nilotica, Murraya koenigii (L.) Sprengel, Eucalyptus hybrid, *Psidium guajava* extracts and their combination on Streptococcus mutans and Lactobacillus acidophilus. Dent. Res. J., 2016 Mar 1;13(2):168–73.
4. Jacob P. S, Zade R.M and Das M. Prevalence of periodontitis in the Indian population: A literature review. J. Indian. Soc. Periodontol., 2011 Jan-Mar; 15(1): 29–34.
5. Dhalkari C., Wagatkar J. and Ingle K. Herbal Remedies in Periodontics. Indian. J. Dent. Adv. 2015; 7(4): 255-258.
6. Hassan G. and Ghafoor S. Herbal medicines : An Adjunct to Current Treatment Modalities for Periodontal Diseases. Biomedica. 2020 Vol. 36(1). 15-22.
7. Shetty Y.S., Shankarapillai R., Vivekanandan G., Shetty R.M., Reddy C.S., Reddy H. and Mangalekar S.B. Evaluation of the Efficacy of Guava Extract as an Antimicrobial Agent on Periodontal Pathogens. J Contemp Dent Pract 2018 ;19(6):690-697.
8. Dhalkari C., Wagatkar J. and Ingle K. Herbal Remedies in Periodontics. Indian. J. Dent. Adv. 2015; 7(4): 255-258.
9. Niazi F., Naseem M., Khurshid Z., Zafar M.S. and Almas K. Role of *Salvadora persica* chewing stick (miswak): A natural toothbrush for holistic oral health. Eur. J. Dent. 2016;10:301-8.
10. Salehi P. Momeni D.Sh. Comparison of the antibacterial effects of persica mouthwash with chlorhexidine on streptococcus mutans in orthodontic patients. DARU J. Pharm. Sci., Vol. 14, No. 4 2006.
11. Al-Bayaty FH, AI-Koubaisi AH, Ali NA and Abdulla MA. Effect of mouth wash extracted from *Salvadora persica* (Miswak) on dental plaque formation: A clinical trail. J. Med. Plant Res. 2013 Sep 30 ;4(14):1446-58.
12. Lakshmi T, Krishnan V, Rajendran R and Madhusudhanan N. Azadirachta indica: A herbal panacea in dentistry - An update. Pharmacogn Rev. 2015 Jan;9(17):41.
13. Wolinsky L.E., Mania S., Nachnani S and Ling S. The inhibiting effect of aqueous *Azadirachta indica* (Neem) extract upon bacterial

properties influencing *in-vitro* plaque formation. J. Dent. Res Intern. 1996 Feb;75(2):816-22.

14. Pai M.R., Acharya L.D and Udupa N. Evaluation of antiplaque activity of *Azadirachta indica* leaf extract gel-a 6-week clinical study. J. of ethnopharmacol. 2004 Jan 1;90(1):99-103.
15. Adyanthaya S, Pai V and Jose M. Antimicrobial potential of the extracts of the twigs of *Azadirachta indica* (Neem): an *in-vitro* study. J. Med. Plants Stud. 2014 ;2(6) :53-7.
16. Kumar R., Mehta S and Pathak S.R. Bioactive constituents of neem. In Synthesis of medicinal agents from plants. Elsevier. 2018 Jan(1):75-103.
17. Sharma H.M., Deepika P.C., Venkatesh M.P., Chandan S and Shashikumar P. Efficacy of 3% *Psidium guajava* local drug delivery in the treatment of chronic periodontitis : A randomized controlled trial. Int. J. Oral Health Dent. 2021 Jan 1;13(1):17–23.
18. Ramesh A., Varghese S.S., Doraiswamy J.N and Malaiappan S. Herbs as an antioxidant arsenal for periodontal diseases. J. Intercult. Ethnopharmacol. 2016 Jan ;5(1):92.
19. Wang Y., Tao B., Wan Y., Sun Y., Wang L., Sun J and Li C. Drug delivery based pharmacological enhancement and current insights of quercetin with therapeutic potential against oral diseases. Biomed. Pharmacother.2020 Aug 1;128:110372.
20. Chandrashekar B.R, Nagarajappa R, Jain R, Singh R, Thakur R and Shekar S. Antimicrobial efficacy of Acacia nilotica, Murraya koenigii (L.) Sprengel, Eucalyptus hybrid, *Psidium guajava* extracts and their combination on Streptococcus mutans and Lactobacillus acidophilus. Dent. Res. J., 2016 Mar 1;13(2):168–73.
21. Ravi K and Divyashree P. *Psidium guajava:* A review on its potential as an adjunct in treating periodontal disease. Pharmacogn Rev. 2014 Jul;8(16):96.
22. Prabu G.R, Gnanamani A., Sadulla and S. Guaijaverin - A plant flavonoid as potential antiplaque agent against Streptococcus mutans. J. Appl. Microbiol. 2006 Aug;101(2):487–95.
23. Ramesh A., Varghese S.S., Doraiswamy J.N and Malaiappan S. Herbs as an antioxidant arsenal for periodontal diseases. J. Intercult. Ethnopharmacol. 2016 Jan;5(1):92.
24. Hirasawa M, Takada K, Makimura M and Otake S. Improvement of periodontal status by green tea catechin using a local delivery system : A clinical pilot study. J. Periodont. Res. 2002; 37; 433–438.
25. Asahi Y, Noiri Y, Miura J, Maezono H, Yamaguchi M, Yamamoto R, et al. Effects of the tea catechin epigallocatechin gallate on Porphyromonas gingivalis biofilms. J. Appl. Microbiol. 2014 ;116(5):1164–71.
26. Araghizadeh A, Kohanteb J and Fani MM. Inhibitory activity of green tea *(Camellia sinensis)* extract on some clinically isolated cariogenic and periodontopathic bacteria. Med. Princ Pract. 2013 Jun;22(4):368–72.
27. Roy J, Shakleya DM, Callery PS and Thomas JG. Chemical constituents and antimicrobial activity of a traditional herbal medicine containing garlic and black cumin. Afr. J. Tradit. Complement. Altern. Med. 2006 Jan 12 ;3(2):1-7.
28. Ankri S, Mirelman D. Antimicrobial properties of allicin from garlic. Microb and inf. 1999 Feb 1;1(2):125-9.
29. Jabar M.A., Al-Mossawi A. Susceptibility of some multiple resistant bacteria to garlic extract. Afr. *J*. Biotechnol. 2007 ;6(6).
30. Tanwar R., Gupta J., Asif S., Panwar R and Heralgi R. Aloe Vera and its uses in Dentistry. Indian J. Dent. Adv. 2011 Oct 1 ;3(4) :656-8.
31. Lee SS, Zhang WU and Li Y. The antimicrobial potential of 14 natural herbal dentifrices : results of an *in-vitro* diffusion method study. *J*. Am. Dent. Assoc. 2004 Aug 1 ;135(8) :1133-41.
32. Kaur D. and Chandrul K.K. *Syzygium aromaticum L. (*Clove): A vital herbal drug used in periodontal disease. Indian j. pharm. biol. res. 2017 Jun 30 ;5(02) :45-51.
33. Sindagi A.S., Anmol G.K., Bellad A.S. and Kulkarni K. *in-vitro* antibacterial activity of neem, clove, and cinnamon against Actinobacillus sp., isolatedfrom chronic periodontitis patients. Biomedicine. 2020 Nov 11;40(2):214-9.
34. Lestari PM and Pamungkas ST. Tablet Kunyah Ekstrak Daun Jambu Biji *(Psidium guajava L.)* Dengan Amilum Sukun Sebagai Pengikat. J. *Jamu* Indones. a (2019) 4(1): 8-16.
35. Behal R, Mali A.M., Gilda S.S and Paradkar A.R. Evaluation of local drug-delivery system containing 2% whole turmeric gel used as an adjunct to scaling and root planing in chronic periodontitis: A clinical and microbiological study. J Indian Soc Periodontol. 2011 Jan;15(1):35.
36. Sanchez M, Gonzalez B.E, Iglesias I and Gomez-Serranillos M.P. Pharmacological update properties of Aloe vera and its major active constituents. Molecules. 2020 Jan ;25(6):1324.
37. Verma S. Chemical constituents and pharmacological action of Ocimum sanctum (Indian holy basil-Tulsi). J. phytopharm. 2016 ;5(5) :205-7.
38. Anand MK. Antibacterial effect of lemongrass oil on oral microorganisms : an *in-vitro* study. J. pharm. sci. 2013 ;2(2) :41-3.
39. Nagata H, Inagaki Y, Tanaka M, Ojima M, Kataoka K, Kuboniwa M, et al. Effect of

Eucalyptus Extract Chewing Gum on Periodontal Health : A Double-Masked, Randomized Trial. J. Periodontol. 2008 Aug.79(8) :1378–85.

40. Bairy I, Reeja S, Rao PS, Bhat M and Shivananda PG. Evaluation of antibacterial activity of Mangifera indica on anaerobic dental microglora based on in vivo studies. Indian J Pathol Microbiol. 2002 Jul 1 ;45(3) :307-10.
41. Ahmad A., Husain A., Mujeeb M., Khan S.A., Najmi A.K., Siddique N.A., et al. A review on therapeutic potential of Nigella sativa : A miracle herb. Asian Pac. J. Trop. Biomed. 2013 May 3(5):337–52.
42. Sanchez M. C., Ribeiro-Vidal H, Bartolome B, Figuero E, Moreno-Arribas M.V., Sanz M and Herrera D. New evidences of antibacterial effects of cranberry against periodontal pathogens. Foods. 2020 Feb 24;9(2):246.
43. Pandita V, Patthi B, Singh S, Singla A, Vashishtha V and Malhi R. Dentistry meets nature-role of herbs in periodontal care: A systematic review. J. Indian Assoc. Public Health Dent. 2014 ;12(3) :148.
44. Jagadish L., Anand Kumar V K. and Kaviyarasan V. Effect of Triphala on dental bio-film. Indian J Sci Technol 2009;2(1):30–3.