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Potential of clove (syzygium aromaticum) in development of a therapeutic agent for periodontal disease and dental caries

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Abstract

Background: Syzygium aromaticum, also known as clove, has been traditionally used for its medicinal properties in various cultures for centuries. One of its therapeutic uses is in the prevention of dental caries, which is a common oral health problem caused by bacterial activity in the mouth that leads to the demineralization of tooth enamel.Eugenol has been found to be effective against the bacteria that cause dental caries, such as Streptococcus mutans, by inhibiting their growth and reducing their ability to adhere to tooth surfaces.

Aim: Syzygium aromaticum is plant derived spicies used for the treatment of various dental diseases and effects on periodontitis and dental caries

Methods: An online search was performed in PubMed and Google Scholar using a combination of key words which included clove buds, clove essential oil, eugenol, Eugenia caryophyllata, spices, medicinal plant, chemical composition, biological effect, therapeutic use,anti-bacterial, anti-fungal, anti-viral, anti-oxidant, anti-inflammatory, anaesthetic, periodontal,dental, and periodontitis.

Results: In vitro studies and also human trials have shown Syzygium aromaticum to have bacteriostatic, bactericidal, anti-viral, anti-mycotic, anti-oxidant, anti-

carcinogenic, anaesthetic and analgesic properties. Due to its ability to inhibit the cyclo-oxygenase-2 and lipo-oxygenase enzymes, clove oil possesses distinct anti-inflammatory properties.

Conclusion: The potential utilization of clove and its derivatives as targeted agents for combating plaque and inflammation could be considered for treating periodontal disease. Future research should concentrate on designing new formulations based on clove derivatives in the form of local drug delivery systems or topical agents for the treatment of periodontal diseases.

Keywords: Non Surgical periodontal therapy, Periodontitis, Syzygium aromaticum.

Introduction

Syzygium aromaticum, also known as clove, has been traditionally used for its medicinal properties in various cultures for centuries. One of its therapeutic uses is in the prevention of dental caries, which a common oral health problem is caused by bacterial activity in the mouth that leads to the demineralization of tooth enamel. Eugenol has been found to be effective against the bacteria that cause dental caries, such as Streptococcus mutans,Aggregatibacter actinomyc-etemcomitans, Porphyromonas gingivalis, Prevotella intermedia, Tannerella forsythia, and Treponema denticola ,by inhibiting their growth and reducing their ability to adhere to tooth surfaces.Periodontitis is referred to as inflammation of the periodontium , caused due to several local and systemic factors. Plaque ,a biofilm that is formed on the surface of our teeth and contains bacteria can cause periodontitis, a type of gum disease[1]. The bacteria such as Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, Prevotella intermedia, Tannerella forsythia, and Treponema denticola, are commonly associated with periodontitis[2]. When plaque is not removed through good oral hygiene practices such as brushing and flossing, these bacteria can colonize the gingival crevice and trigger an immune response that can lead to inflammation and destruction of the surrounding tissues and bone. This process can ultimately result in the development of periodontal pockets, gum recession, and tooth loss if left untreated. It has been proposed that incorporating natural products could serve as a supplementary approach to prevent and treat periodontal disease. Syzygium aromaticum, also known as clove, is a spice with a long history of use in traditional medicine for its analgesic, anti-inflammatory, and antimicrobial properties [3]. In recent years, research has focused on exploring the potential of clove and its bioactive compounds in the development of therapeutic agents for periodontal disease and dental care. This review summarizes the available evidence on the chemical composition, pharmacological properties, and mechanisms of action of clove extracts and essential oil in relation to periodontal health. The findings suggest that clove has significant antimicrobial, anti-inflammatory, and antioxidant properties that could be harnessed for the development of novel therapeutic agents for the prevention and treatment of periodontal disease and other oral health conditions. Further research is needed to fully elucidate the therapeutic potential of clove and its components and to establish their safety and efficacy for clinical use[4].The potential utilization of clove and its derivatives as targeted agents for combating plaque and inflammation could be considered for treating periodontal disease. Future studies should focus on the development of new formulations based on clove derivatives as topical drug delivery systems or topical treatments for periodontal disease[5].The proliferation of drug-resistant pathogens poses a critical challenge to the effective management of microbial

illnesses. Over time, there has been significant interest in essential oils and plant extracts as potential sources of natural products for the treatment of various infectious diseases. These natural remedies have been extensively evaluated for their ability to serve as alternative treatments.[6]. Clove oil is extracted from the buds, leaves or stems of the tree Syzygium aromaticum by steam or water distillation.Clove leaf oil has been conventionally employed to address cuts and burns, and even in dental care, to alleviate infections and toothache.[7].The major constituent of clove oil, eugenol, exhibits properties that include antioxidant and anti-inflammatory effects.[8].Research has demonstrated the effectiveness of clove in combatting bacteria linked to periodontal disease and dental caries, as well as a broad range of other bacterial strains.[9].Furthermore, research has indicated that Syzygium aromaticum exhibits anti-fungal, anti-carcinogenic, anti-allergic, and anti-mutagenic properties[10]. The objective of producing a paper on the potential of Syzygium aromaticum in the development of a therapeutic agent for periodontal disease and dental caries is to review and summarize the available evidence on the chemical composition, pharmacological properties, and mechanisms of action of clove extracts and essential oil in relation to periodontal health. The paper aims to explore the potential of clove and its bioactive compounds in the development of therapeutic agents for periodontal disease and dental care. The review will examine the antimicrobial, anti-inflammatory, and antioxidant properties of clove and its components and how they could be harnessed for the prevention and treatment of periodontal disease and other oral health conditions. Ultimately, the paper aims to contribute to the growing body of knowledge on the use of natural products in the prevention and treatment of oral health conditions and provide insights into the development of safe and effective therapeutic agents for periodontal disease and dental caries.

Materials and Methods

The development of Syzygium aromaticum as a therapeutic agent for periodontal disease and dental caries involves several methods, including:

Extraction of bioactive compounds: The first step is to extract the bioactive compounds from clove using appropriate solvents. The extraction method can affect the yield and quality of the extracted compounds and can be optimized based on the type of bioactive compounds being targeted.

Characterization of bioactive compounds: Once the bioactive compounds have been extracted, they need to be characterized using various analytical methods such as gas chromatography, mass spectrometry, and high-performance liquid chromatography. This step is important to identify the compounds responsible for the pharmacological properties of clove.

Evaluation of pharmacological properties: The next step is to evaluate the pharmacological properties of the extracted bioactive compounds using in vitro and in vivo experiments. In vitro experiments involve testing the compounds on cultured cells or microorganisms, while in vivo experiments involve testing on animal models. The pharmacological properties evaluated include antimicrobial, anti-inflammatory, and antioxidant properties.

Clinical trials: If the safety and efficacy tests are successful, clinical trials can be carried out to determine the safety and effectiveness of the therapeutic agents in humans. The clinical trials should be designed to determine the optimal dose, safety, and effectiveness of the therapeutic agents.

Regulatory approval: Finally, regulatory approval needs to be obtained from the relevant regulatory agencies before the therapeutic agents can be marketed for the prevention and treatment of periodontal disease and dental caries

Inclusion Criteria

- Original articles
- Articles on the effect of Syzygium aromaticum as a therapeutic agent for prevention and treatment of patients with plaque induced periodontitis and dental caries

Exclusion criteria

- Review articles
- Articles without open access

Search Strategy

MEDLINE/PubMed and Google-Scholar was searched for appropriate articles using the following keywords in various combinations: "clove", "Syzygium aromaticum", "eugenol", "clove essential oil", "Eugenia caryophyllata", "spices", "medicinal plant", "herbal medicine" "chemical composition", "biological effect", "therapeutic use", "antioxidant", "anti-inflammatory", "anti-bacterial", "anti-viral", "anti-mycotic". "periodontal", "periodontitis" and "dental". All articles on human, animal, in vitro and in vivo studies and reviews published in English were selected. Preference was given to articles that described the composition, pharmacological effects and toxicity of clove.Following the Prisma guidelines, the Mesh terms were modified in each search engine if the search yielded excessive or insufficient results. The titles and abstracts of articles that met the eligibility criteria were then scrutinized for coherence.

Results

The search generated a collection of articles, which were subsequently evaluated individually for eligibility. Figure I depicts the flow of the review process, from identification and screening of reports to the final inclusion and exclusion of articles.

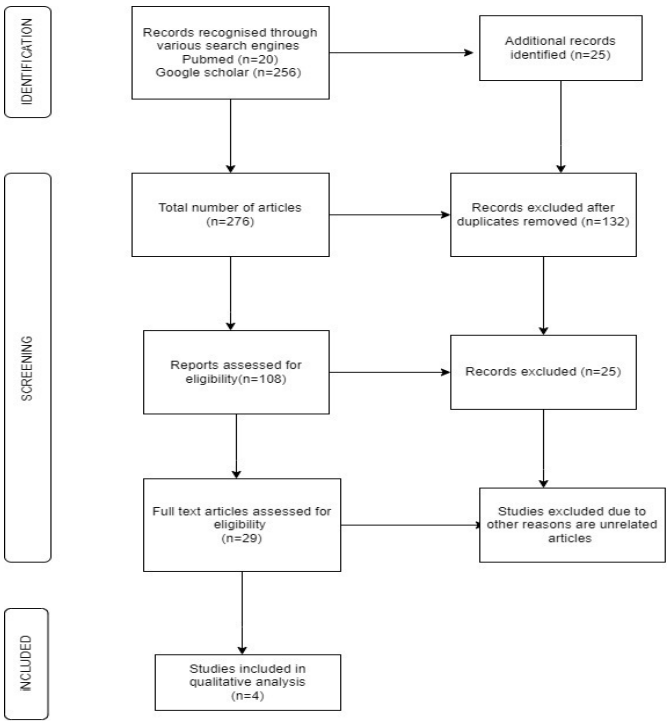

Fig. 1: Flow diagram showing the number of studies of studies identified, screened, assessed for eligibility and included for systematic review

Table 1 presents the characteristics of the studies that were selected for the systematic review. The included articles exclusively focused on the potential of Syzygium aromaticum, or clove, as a therapeutic agent for periodontal disease and dental caries. The table provides information on the authors, year of study, and sample size of each article investigated.

Table 1 characteristics of intervention in the study:

Author name	Year	Total number of the sample used	Preparation used	Interventions
Dibua Esther Uju, Anna mani Petra Obioma1	2011	Samples from 31 patient were taken with tooth decay	These samples were investigated with use of sterile blood agar Muller Hinton agar (MHA) by spread inoculation and the samples were incubated at 37.C for 24 hours. The colonies were reinoculated with sterile Mitis salivarius agar (MSA) and incubated at 37.c for 24 hours. Catalase test and gram staining were done . Plant extracts like tobacco leaves, clove seeds and they were grounded into powder dried , stored in clean containers and closed with cork. Phytochemistry investigation were performed on the plant extract,minimum inhibitory concentration (MIC), minimum cidal concentration (MCC) and compared with common antibiotics used for dental caries and atlast antibiotic sensitivity was done and results were analysed.	18 samples were found to be catalase positive. 13 samples were found to be catalase negative 13 samples were confirmed to be gram negative 18 samples were confirmed to be gram positive.
Olugbenga Oludayo Oluwasina et.al2	2019	NA	sterile amber bottle were used to obtain J.curcuma as liquid exudate from the stalk of leaves and stem of j curas grown in ilara Molina. S.aromaticum buds bought from kings market ondo state. The entire chemical used in this research are analytical grade	photochemical components such as alkaloids,phenolic,and flavonoids were detected in s.aromaticum. All these shows effective interventions.

			obtained from sigma aldrich. All these components were made into a toothpaste and given to a random number of people	
Kamel chaieb, Hafedh Hajlaoui,Tarek Zmantar, Amel Ben Kahla-nakbi, Mahmoud Rouabhia, Kacem Madouani,Amina Bakhrouf3	2007	Various microorganisms and parasites were examined to determine the biological activity of S. aromaticum and Eugenia caryophyllata.	A topical application is made using the oil that is extracted from the dried flower buds of S. aromaticum.	The essential oil used against the pathogenic bacteria shows anti microbial,antioxidant,anti fungal,antiviral and also possess anti inflammatory, cytotoxic, insect repellent and anaesthetic property.
Mamta besra and Vipin Kumar4	2018	Inhabitants of rural regions of Dhanbad district,Jharkhand,India.(Numbers were not mentioned)	An essential oil from plant samples was extracted by hydro-distillation techniques using clevenger apparatus. The plant samples were dried shed and ground into powder using grinde and Soxhlet apparatus with 200ml of solvent for 10h. The solvents used are methanol and distilled water. The solvent extracts was evaporated under reduced pressure at 40°C using a rotator evaporator and preserved at 4°C for further anti microbial test. Bacterial stains used are Streptococcus mutants (MTCC 497), Lactobacillus acidophilus (MTCC 10307) The growth media employed were brain heart infusion broth.	The essential oil extracted from S.aromaticum possess anti microbial , anti inflammatory and anti cariogenic also possess other systematic effects.

Table 2: shows the impact measures that the tests are taken to analyze the effects of syzyium aromaticum in dental caries.

Table 2: Characteristics of outcome and effect measures

Author	Year	Outcome	Result
Dibua Esther Uju, Anna mani Petra Obioma[1]	2011	The n-hexane clove extract had the best anti microbial activity it has the largest and it has the largest inhibition zone diameter .	The n-hexane extract of clove seeds has preferential growth-inhibitory activity against the cariogenic pathogens in dental caries.Report says that clove extract be henceforth considered as a potential ingredient in toothpaste preparation.
Olugbenga Oludayo Oluwasina, Ifunanya Vivian Ezenwosu , Clement Olusola Ogidi, Victor Olusegun[2]	2019	Findings revealed that ethanolic extract of S.Aromaticum showed potential microbial activity against the highly caries inducing food borne bacteria namely S.Aureus and P.aeruginosa with MIC ranged from 2.5 to 5.0 mg/ml.	The anti microbial study showed that the toothpaste formulated using plant extracts had better performance than all the commercial toothpaste. The toothpaste made from extracts of S.aromaticum shows synergistic activity.
Kamel chaieb, Hafedh Hajlaoui,Tarek Zmantar, Amel Ben Kahla-nakbi, Mahmoud Rouabhia, Kacem Madouani,Amina Bakhrouf[3]	2007	Clove oil, which is derived from the dried flower buds, is applied topically to alleviate pain and enhance healing. Additionally, it serves as a source of fragrance and flavoring.	The findings indicate that the essential oil derived from S.aromaticum exhibits properties such as anti-inflammatory, cytotoxic, insect repellent, and anesthetic effects.
Mamta besra and Vipin Kumar[4]	2018	The essential oil destroys the cell membrane of caries causing bacteria.	Results shows that the extracted oil is more effective against or in the prevention of oral cavity from caries producing bacteria such as S.mutatans ,L.acidophilus and Actinomyces.

Table 3 shows the bias analysis of the studies included, which were categorized as high risk of bias, low risk of bias, and unclear risk of bias

Table 3: Analysis of Various Studies Included In The Review Revealed Distinct Biases.

Author	Random Sequence Generation	Allocation Concealment	Binding of Outcome	Incomplete Outcome	Selective Bias	Other Bias
Dibua Esther Uju, Anna mani Petra Obioma[1]	+	?	?	+	_	_
Olugbenga Oludayo		_	?	+	_	_

Oluwasina, Ifunanya Vivian Ezenwosu , Clement Olusola Ogidi, Victor Olusegun [2]						
Kamel chaieb, Hafedh Hajlaoui,Tarek Zmantar, Amel Ben Kahla-nakbi, Mahmoud Rouabhia, Kacem Madouani,Amina Bakhrouf[3]	_	_	_	+	+.	?
Mamta besra and Vipin Kumar[4]	+	_	_	+	_	+

+: Low-risk bias, -: high-risk bias, ?: unclear risk of bias

Discussion

Dibua Esther Uju, Anna mani Petra Obioma.et,al. collected Samples from 31 patient were taken with tooth decay hese samples were investigated with use of sterile blood agar Muller Hinton agar (MHA) by spread inoculation and the samples were incubated at 37.C for 24 hours. The colonies were reinoculated with sterile Mitis salivarius agar(MSA) and incubated at 37.c for 24 hours. Catalase test and gram staining test were done. Plant extracts like tobacco leaves, clove seeds and they were grounded into powder dried , stored in clean containers and closed with cork. Photochemistry investigations were performed on the plant extracts, minimum inhibitory concentration (MIC) minimum cidal concentration (MCC) and compared with common antibiotics used for tooth decay and atlast antibiotic sensitivity was done and results were analysed[1].Olugbenga Oludayo Oluwasina,et.al.,used terile amber bottle were used to obtain J.curcuma as liquid exudate from the stalk of leaves and stem of j curas grown in ilara Molina. S.aromaticum buds bought from kings market ondo state. The entire chemical used in this research are analytical grade derived from sigma aldrich . All these components were made into a toothpaste and given to a random number of people,photochemical components such as alkaloids,phenolic,and flavonoids were detected in syzygium aromaticum. All these shows effective interventions.Kamel chaieb et.al, assessed The biological activity of S.Aromaticum and Eugenia caryuphylata were investigated on several microorganisms and parasites,The essential oil used against the pathogenic bacteria shows anti microbial,antioxidant,anti fungal,antiviral and also possess anti inflammatory, cytotoxic, insect repellent and anaesthetic property[2].Mamta besra and Vipin Kumar Inhabitants of rural regions of Dhanbad district,Jharkhand,India.The essential oil was collected and extracted by hydro-distillation techniques using clevenger apparatus. The plant samples were dried shed and ground into powder using grinde and Soxhlet apparatus with 200ml of solvent for 10h.Solvents were used such as methanol and distilled water . The solvent extracts was evaporated under reduced pressure at 40°C using a rotator evaporator and preserved at 4°C for further anti microbial test[3].Bacterial stains used are Streptococcus

mutants (MTCC 497), Lactobacillus acidophilus (MTCC 10307) ,The growth media employed were brain heart infusion broth.The essential oil extracted from S.aromaticum possess anti microbial , anti inflammatory and anti cariogenic also possess other systematic effects.Results shows that the extracted oil is more effective against or in the prevention of oral cavity from periodontitis and dental caries producing bacteria such as S.mutatans ,L.acidophilus and Actinomyces[4].Clove is a spice that contains essential oil, eugenol, eugenol acetate, and β-caryophyllene, which have various health benefits such as analgesic, antibacterial, antiviral, anti-inflammatory, and antioxidant properties. For centuries, clove has been used to alleviate toothache, treat periodontitis, act as an anesthetic, and cure bleeding gums. Avicenna, who was a renowned medical teacher in ancient times, used clove oil pills to treat rotting teeth and gums. In modern times, clove oil's germ-killing molecules have been used in dentistry for root canal treatment and other serious dental procedures since the 19th century. Furthermore, clove gel can be used as an alternative to benzocaine for topical anesthesia in dental practice, particularly in cases involving children or where access to pharmaceutical topical anesthetics is limited by cost or availability[5].The bacterial strains that were examined demonstrated notable vulnerability to oils such as cinnamon, clove, geranium, lemon, lime, orange, and rosemary. Prior studies have likewise affirmed the potent and reliable antimicrobial effects of cinnamon, clove, and rosemary oils against diverse pathogenic microorganisms.[6].Throughout history, natural products have been utilized in the treatment of microbial infections, and numerous essential oil molecules have shown the ability to inhibit the growth of various pathogens. At a concentration of 1,000 ppm, eugenol was observed to inhibit bacterial growth, and complete inhibition was achieved against P. aeruginosa at a higher concentration of 2,000 ppm. This level of inhibition was higher than that of ampicillin (1 mg/mL), which was used as a positive control[7].Research has found a correlation between the capacity of natural anticarcinogens to stimulate detoxifying enzymes and their effectiveness in preventing chemical carcinogenesis. As a result, these sesquiterpenes exhibit potential as anticancer agents[8].An extract of Syzygium aromaticum (clove) obtained using methanol showed significant growth-inhibitory activity against Gram-negative anaerobic periodontal oral pathogens, such as Porphyromonas gingivalis and Prevotella intermedia. Through bioassay-directed chromatographic fractionation, eight active compounds were isolated from the extract and identified based on spectroscopic evidence. These compounds include 5,7-dihydroxy-2-methylchromone 8-C-β-d-glucopyranoside, biflorin, kaempferol, rhamnocitrin, myricetin, gallic acid, ellagic acid, and oleanolic acid. These findings suggest that these compounds could potentially serve as effective agents against these pathogens[9].Indonesians use cloves to add a strong clove aroma to tobacco, which is called "Kretek". Additionally, the essential oils of cloves are utilized in dental treatment[10].

Conclusion

There are several studies that have shown the potential of Syzygium aromaticum in the development of therapeutic agents for periodontal disease and dental caries. Here are some of the results from these studies:Antimicrobial properties: Clove oil and extracts have been shown to have potent antimicrobial activity against a wide range of bacteria, fungi, and viruses that are associated with periodontal disease and dental caries.Anti-inflammatory properties: A study published

in the Journal of Medicinal Food investigated the potential anti-inflammatory effects of clove oil in rats with periodontitis. The results showed that the therapeutic effects of clove oil significantly reduced inflammation in the gingiva.Antioxidant properties: Antioxidant property of clove helps to protect the body from oxidative stress and damage caused by free radicals.Dental plaque inhibition: Clove oil has been shown to inhibit the formation of dental plaque, which is a major causative factor for the development of dental caries and periodontal disease.The results showed that the clove oil mouthwash was effective in reducing dental plaque, with a significant reduction observed after two weeks of use. Overall, these results suggest that Syzygium aromaticum has significant potential in the development of therapeutic agents for periodontal disease and dental caries.

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