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Catechin Or Chitosan…Next Antimicrobial In Periodontics ??

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ABSTRACT: Many alternative approaches have been researched in both recent and past studies for the inhibition of biofilm formation using different agents derived from plants, animals, microbes and chemical agent. Among these agents, chitosan and its derivatives have got a superior properties in their biodegradability, biocompatibility, antimicrobial activity, non-toxicity and moreover chitosan is a natural polysaccharide which shows a promising result. Catechins are polyphenol chemical compounds that are abundant in green tea and have shown to exhibit physiological effects, including antibacterial, antifungal, antiviral, antioxidative, and antitumor activities. Recent researches have considered chitosan and its derivatives as an effective agents to inhibit biofilm formation and alter the virulence properties of various pathogenic bacteria.

KEYWORDS: Chitosan, Virulence, Catechin, EGCG, Mushroom, Algae

I. INTRODUCTION

The oral cavity contains almost half of the bacterial population present in the human body as commensals. An increase in the number of these microorganisms may result in systemic diseases such as infective endocarditis and aspiration pneumonia as well as severe infections in oral cavity. Dental plaque composed of accumulated microorganisms and is a major pathogenic factor in the oral cavity.[1] More than 700 different bacterial species have been identified in oral cavity of humans and most of them are associated with the development of gingivitis and periodontits. There are strong evidence which proves the association between plaque and development of inflammatory periodontal disease.[2]

Chitosan is extracted by the partial deacetylation of chitin, creating a polysaccharide composed of glucosamine (2-amino-2-deoxy-D-glucose) and N- acetyl glucosamine (2- acetamido-2-deoxy-D–glucose) units linked by β(1→4) bonds. The structure of chitosan composed of amino groups which proves the cationic nature enabling it in low pH settings, ensuring biological activity by the interaction with negatively charged compounds such as proteins, polysaccharides and phospholipids which are present in the bacterial cell.[3] Chitosan exhibits antimicrobial activity against pathogenic bacteria as well as virus, fungi and yeasts. The mechanism associated with the antimicrobial property of chitosan has been linked to the positively charged amino groups present in its structure and this property is dependent on the degree of deacetylation, which upregulates the total positive charge of chitosan and increases the affinity for negatively charged surfaces of bacteria.[4] Moreover chitosan has shown to have an enhanced antibiofilm properties which enable it to prevent the biofilm growth in oral cavity and destruction of pathogenic microflora.

The catechins present in green tea are commonly called polyphenols. Fresh green tea leaves are enriched with catechins which are not fermented and are withered. Catechin oxidation by polyphenol oxidase is prevented by steaming or by panning, which play an important role in maintaining the polyphenols in monomeric forms.

Black tea leaves are undergone crushing and fermentation process where as catechin derivatives are undergone oxidation process which induce the formation of polymeric compounds, the arubigins and the aflavins. They act efficiently in medical field as a constituent for various purposes. The tea catechins are the most powerful antioxidants known among the plant phenols.[5] Epigallocatechin gallate (EGCG), which is the main constituent of green tea (Camellia sinesis) that exhibits anti-oxidative, anti-tumor and anti-bacterial properties. EGCG is effective against both gram-positive and gram-negative bacteria and most studies have proved that EGCG exert its antibacterial effects through altering the oxidative stress.[6]

NATURAL ANTIMICROBIALS IN PERIODONTICS

There are natural antimicrobials are from animals, microorganisms and plants.
Some examples of natural antimicrobials are from

Animal sources : milk eggs
crustaceans : lysozyme, lactoferrin, lactoperoxidase, chitosan, megainin, pleurocidin, curvacin A, spheniscin
freefattyacids.

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Microorganismsource : controlled acidification bacteriocins bacteriophage
Plant source : onion and garlic
spices cruciferae
phenoliccompounds hops
alkaloids
flavonoids – catechin essential oil and terpenes sugar alcohol

Algae and mushrooms : macroalgae (seaweeds) microalgae(diatoms) mushrooms

ANTIMICROBIAL FROM ANIMAL SOURCE

Natural antimicrobials from animal sources are milk, eggs, and crustaceans which composed of lysozyme, lactoferrin, lactoperoxidase, chitosan, megainin, pleurocidin, curvacin A, spheniscin and free fatty acids. Antimicrobials of animal origins are mostly in the form of enzymes/proteins and peptides. The lactoperoxidase system composed of lactoperoxidase, thiocyanate and hydrogen peroxide which acts as an antimicrobial system which is a natural component present in milk and other secretions mainly saliva and tear.[7]

CHITOSAN

Chitosan is a derivative of chitin which is the second most abundant natural biopolymer. It is a primary structural component of the exoskeleton of arthropods such as crustaceans, the cell wall of fungi and the cuticle of insects. Chitosan is extracted from chitin which is a biodegradable natural biopolymer with non-toxic and non-immunogenic property. Extraction of chitosan can be done by following methods :

1. **DEPROTEINIZATION -** Dried shells of crustaceans are treated with an alkali solution like NaOH for protein removal and are undergone centrifugation to separate alkali insoluble fraction which is followed by repeated washing with distilled water.

2. **DEMINERALIZATION-**Deproteinized shells are treated with dilute solution of a mineral acid like HCl to remove minerals and centrifugation is done followed by washing with distilled water. It is dried overnight to yield chitin.

3. **DECOLORIZATION-**The chitin is then decolorized by treating with anoxidizing agent like potassium permanganate, washed with oxalic acid solution and purified chitin is obtained.

4. **DEACETYLATION –** Done by treating it with concentrated alkali solution for several hours to convert it into chitosan.[8]

BIOLOGICAL PROPERTIES OF CHITOSAN :

a. **ANTIBACTERIAL ACTIVITY OF CHITOSAN**

Chitosan is considered to be a bactericidal or bacteriostatic compound against a wide variety of organism including bacteria. A number of studies demonstrated that chitosan is capable of inhibiting both Gram-negative and Gram-positive bacteria, depending on the molecular weight of chitosan. Effects of chitosan on two oral pathogens, Actinobacillus actinomycetemcomitans and Streptococcus mutans were evaluated in vitro which showed that chitosan inhibits Actinobacillus actinomycetemcomitans at very low concentration.[9] The antibacterial action of chitosan is that it interacts with outer membrane of microorganisms and inhibit their growth in the biofilm. A key feature of chitosan is that it can form a polycationic structure which differentiate it from others.

Many studies have provided sufficient evidences that the chitosan would bound to anions on bacterial surface and suggested that the interaction with the positive charge of chitosan and anionic components of Gram- negative bacteria may weaken the barrier function of the outer membrane of microorganisms in the biofilm.[10] Decker et al explained the synergistic anti-plaque effect of chlorhexidine and chitosan based on the adhesive property of chitosan. Water-soluble derivatives of chitosan, obtained by replacing N-alkyl groups with disaccharides, have showed significant anti-bacterial activity against Escherichia coli and Staphylococcus aureus.[11]

b. MUCOADHESIVE PROPERTIES OF CHITOSAN

The mucoadhesion property of chitosan is based on the theory of its hydration with water molecules in the presence of mucus through hydrogen bonding and electrostatic interaction of positively charged quaternized groups of chitosan with negatively charged components of mucus gel. The cationic amino groups is linked to third position of the glucopyranose ring and the chitosan is being characterized by weak cohesion between macromolecular chains and mucoadhesion to the anionic mucus substructures.[12] The mucoadhesion properties of chitosan can be increased by eliciting its hydrophilicity through the quaternization of the primary amino groups. The thiolation of chitosan

was considered as a more powerful way to increase both the mucoadhesion property and cohesion of chitosan. Recent studies have suggested that the molecular weight, the degree of deacetylation, and the solvent nature, hydrodynamic stability and mucoadhesion of chitosan microparticles which are electrosprayed can be used as oral drug delivery systems.[13]

c. ANTIOXIDANT ROLE OF CHITOSAN IN PERIODONTICS

Reactive oxygen species (ROS) and reactive nitrogen species (RNS) are generated during oxidative stress and show harmful effects such as cancer, aging and inflammatory diseases. Antioxidants show beneficial health effects by protecting body against the adverse effects of ROS, which has shown to cause oxidative damage to membrane phospholipids, protein and DNA. The chitin, chitosan and its derivatives can be used effectively as a major ingredients in food compound to improve overall health and to promote the shelf life of food. It can be added to invitro and invivo activities for their action of free radical-scavenging and protective the body from the destructive action.[14]

d. ANTI FUNGAL ACTIVITY OF CHITOSAN

Chitosan has been suggested to have antifungal activity against different fungi in free form. The antifungal activity of chitosan depends on many factors like its molecular weight, concentration, degree of substitution, types of fungus and also the presence of functional groups in the chitosan derivatives. It has been explained from different studies that the antifungal activity is shown by the polycationic nature of the chitosan. Chitosan does not possess any chemical modification and possess natural antifungal activity and shows effective action against fungal organisms.[15]

e. WOUND HEALING AND BURNS

Chitin and chitosan plays an important role in tissue engineering due to their unique structural, physicochemical and functional properties and beneficial effects in wound healing. Antibacterial resistance is one of the major drawback in the field of wound care management as it may cause infection and interfere with wound healing. Chitosan derivatives interact with quaternary ammonium groups having high antimicrobial efficacy and are biocompatible, promote the growth of dermis and helps in wound healing. Another mechanism is that chitosan and its derivatives interact with red blood cells and become sticky due to positive-negative charges resulting in enhanced healing of wounds. Several studies suggested the use of chitosan scaffolds and membranes for the treatment of patients with deep burns and wounds.[16]

f. AS DRUG DELIVERY SYSTEMS

Chitosan is considered as a novel agent in medical field characterized by improved biological properties such as hemostatic, bacteriostatic, anticholesteremic, anticarcinogenic and fungistatic properties. Several studies proved that it can be considered as the most suitable candidates for biomedical applications including drug delivery. It is a natural biopolymer with biocompatibility and lack of toxicity which are greatly accepted in medical application.[17] Chitosan has a property of controlled release of antibiotics, protein or peptide drugs and vaccines inadequate amount. Colloidal particles formed by chitosan entraps bioactive molecules through a number of mechanisms of chemical crosslinking, ionic crosslinking and ionic complexion.

g. CHITOSAN IN PERIODONTAL REGENERATION

In GTR and GBR, chitosan can be used as an active membranes that release growth factors with improved tissue proliferation capacity and bone regeneration. Novel biodegradable chitosan scaffolds were prepared, and the study suggested that chitosan scaffolds induced higher amount of mineral deposits and would be essential for alveolar bone regeneration.[18]

ANTIMICROBIAL FROM PLANT SOURCE

Natural antimicrobials from microbial sources are nisin, natamycin, diplococcin, acidophilin, and pediocins, in which most of components are cationic, amphiphilic, and membrane-permeabilizing peptides (bacteriocins) which are mostly produced by Gram-positive bacteria. Nisin and natamycin have been used commercially for various purposes in dentistry. Nisin is one of the bacteriocins used by the food industry in the form of cheese, liquid eggs, and sauces. It shows a broad-spectrum antibacterial action against Gram-positive bacteria such as Listeriamonocytogenes. Natural antimicrobials can be obtained by means of fermentation process and can be applied as partially purified or purified concentrates. Reuterin is also an anti microbial compound produced by some strains of Lactobacillus reuteri and has antimicrobial activity towards a broad spectrum of food borne

pathogens.[19]

CATECHIN

Catechin plays an important role in the field of dentistry. Green Tea catechin is a product obtained from the leaf and bud of the plant Camellia sinensis, and is a non-fermented green tea produced by drying and steaming the fresh leaves to inactivate the polyphenol oxidase. One of the major components of green tea is catechin.Green tea seems a promising natural material for oral health due to its polyphenols and other ingredients. Catechin are polyphenol chemical compounds that are most abundant in green tea and have been shown to exhibit physiological effects including antibacterial, antifungal, antiviral, antioxidative and antitumor activities.[20] Recent studies have suggested that catechins can promote oral health and reduces risk of systemic disease.

BIOMEDICAL APPLICATION OF CATECHIN

a. ANTIMICROBIAL PROPERTIES OF GREEN TEA

Antimicrobial effects of catechins include destruction of bacterial cell membrane, inhibition of fatty acid synthesis and alteration of enzyme activity. Catechin show antimicrobial effects by inhibition of inflammation caused by oxidative stress and by increasing the synthesis of nitric oxide. It also inhibits the angiotensin II, IL-6 and C-reactive protein and causes the suppression of IL-6 and RANKL production in infected osteoblast-like cells. Adcocks et al in 2002 suggested that catechin inhibit IL- 8 production and alter the hyaluronidase activity which will stimulate the chronic inflammation.[21]

b. EFFECT OF GREEN TEA ON PERIODONTAL DISEASE

Periodontal disease progress due to the presence of large number of microorgansim in the periodontal pocket. It was followed by destruction of periodontal ligaments, resorption of bone, tooth mobility and tooth loss.One of the direct effects of tea catechins arebinding of catechin to bacterial lipid bilayer cell membrane causing damage to the membrane. This damage can then lead to lysis of bacteria. They exhibit antioxidant, anti-inflammatory, cytoprotective, as well as antimicrobial activity and are important in the prevention and treatment of periodontal disease. Shah et al suggested that catechin causes damage to the bacterial membrane by inhibiting the secretion of toxins.[22]

EGCG (epigallocatechin gallate), an extract from green tea suppress the growth and prevent the adherence of the Porphyromonas gingivalis to the epithelial cells by their action within the phenolic compound of the EGCG. Catechin and proanthocyanidins alter the production of gingipains which inhibit the attachment of Porphyromonas gingivalis and invade the host tissue. EGCG can also cause destruction to the biofilms produced by bacteria and inhibit their gene expression causing suppression of virulence factor produced by Porphyromonas gingivalis, which would have involved in host colonization, tissue destruction, and heme acquisition.[23] Indirect effects of catechins on bacteria is that they have the ability to modify antibiotic sensitivity and can elevate the expression of factors that determine bacterial virulence.

Green tea is considered as an antiplaque agent as it acts against gram positive and gram-negative microorganisms and has a wide range of antibacterial effects. Catechins maintains the salivary and plaque pH as neutral, which may prevent the bacterial colony growth and activity of Streptococcus mutans. EGCG may also inhibit the activity of matrix metalloproteinase-9 (MMP-9) and preventing the formation of osteoclasts in periodontal disease and hence inhibit alveolar bone resorption.[23]

c. HALITOSIS

Catechin plays an important role in reducing halitosis caused by volatile sulfur compounds. Green tea extract can be used as a natural herbal ingredient in oral hygiene products like toothpaste, mouthwashes etc. Morin et al. reported that ability of green tea extracts can inhibit the growth of Solobacterium moorei, a major bacterium playing major role in oral malodor. Catechin can be used as an effective ingredient of mouthwash which can neutralizing the halitosis caused by volatile sulfur compounds by inhibiting the bacterial growth.[24]

d. CATECHIN IN ORAL CANCER

Catechin play an important role in the prevention of cancer due to its anti inflammatory and antioxidant properties and it is also used in treating cancer. Catechin, mainly EGCG in green tea has been extensively studied as a potential chemotherapeutic agent for treating oral cancer. Literature has suggested the antitumor effects of EGCG in the initial stages of cancer development, preventing the tumor cell proliferation and preventing the metastasis of cancer. EGCG suppresses the expression of mRNA and transcription of genes that is involved in cancer

development.[25]

ANTIMICROBIAL FROM ALGAE AND MUSHROOM

Algae shows antimicrobial action against a wide variety of organism. Both macroalgae (seaweeds) and microalgae (diatoms) contain many pharmacological active compounds such as phlorotanins, fatty acids, polysaccharides, peptides and terpenes which interfere with bacterial invasion. It acts as a novel antimicrobial agent in the field of discovery of drugs.[26] Carrageenan derived from seaweed can be used in tooth paste which exhibits antimicrobial activity.[27]

Mushrooms can be used as an alternative medicine in many countries. It is also used in tea and as nutritional food. Lentinula edodes as shiitake mushroom is the most famous mushroom which composed of medical compounds. The components in shiitake mushroom are soluble dietary fibers such as heteroglycans, heterogalactans, heteromannans and xyloglucans and insoluble dietary fibers are heteroglycan, plyuronide, beta glucan and chitin.[28] Recent studies showed that extracts from shiitake mushroom has antimicrobial activity against periodontitis causing bacteria which helps to relieves inflammation. It has shown to inhibit Porphyromonas gingivalis and Tanerella forsythia and reduce their cell viability.[29]

II. CONCLUSION

Recent and past studies has shown that antimicrobial agents from plants, animals and microbes shows antimicrobial action and causes inhibition of biofilm formation. Chitosan is antimicrobial obtained from animal source shows superior action against periodontopathogen and it is considered as an ideal biomaterial due to its outstanding features of formability and fabricability when compared with other bioactive materials along with the properties of biodegradability and biocompatibility. Moreover, it occupies a higher position among the biomaterials due to its abundance, versatility, biodegradability, biocompatibility, non-toxicity, hydrophilicity, anti-bacterial and wound-healing effects. Apart from all these functions, certain limitations of chitosan are water insolubility, high viscosity, and tendencies to coagulate proteins at high pH. Catechin is considered as natural antimicrobial polyphenol components obtained from green tea which show an enhanced antimicrobial effects. It can also interfere with quorum sensing which is an essential component of biofilm formation by different bacteria. The superior function of green tea catechin is that it can be used as a local drug delivery agent in treating periodontal pockets and can act as an adjunct to scaling and root planning.

Many more studies have proved that the green tea catechin extracts can act efficiently as a local drug delivery agent at concentration of 1.0 mg/ml. Catechin also shown to cause an inhibitory effect on the collagenase activity suggesting that it can be used in the prevention of periodontal diseases. Hence chitosan and catechin can be used as an effective agent in treating periodontal disease by preventing its progression and enhancing destruction of bacteria. Evidence has shown that algae has antiviral, antifungal, anticancer and bone regenerative properties.

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