

## FORMULATION AND EVALUATION AND DEVELOPMENT OF HERBAL MEDICATED CHEWING GUM AS AN ANTIPLAQUE AGENT

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### ABSTRACT

Medicated chewing gum (MCG) of MEDICATED CHEWING GUM was developed by different method with the goal to achieve quick onset of action and to improve patient compliance. Objective: Formulation development of MCG of DM and optimization of the formulation by screening of different excipients. Material and methods: MCG containing was prepared by screening different concentrations of sweeteners, flavouring agents, softening agents, lubricants and anti-adherents by changing one variable at a time. Performance evaluation was carried out by evaluating size, shape, thickness, taste, scanning electron microscopy, texture analysis, in vivo drug release study, ex vivo buccal permeation study and by studying statistical analysis for quality. Results and discussion: The statistical analysis showed significant improvement in organoleptic properties such as chewable mass, product taste, product consistency, product softness, total flavour lasting time and pharmaceutical properties like micromeritic properties after incorporation of appropriate excipients in an optimum amount in final optimized MCG formulation

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### INTRODUCTION

#### 1.1 PLAQUE

- **Dental plaque** is a biofilm of microorganisms (mostly bacteria, but also fungi) that grows on surfaces within the mouth.
- It is a sticky colorless deposit at first, but when it forms tartar, it is often brown or pale yellow. It is commonly found between the teeth, on the front of teeth, behind teeth, on chewing surfaces, along the gum line (supragingival), or below the gum line cervical margins (subgingival).
- Dental plaque is also known as microbial plaque, oral biofilm, dental biofilm, dental plaque biofilm or bacterial plaque biofilm. Bacterial plaque is one of the major causes for dental decay and gum disease.
- Dental plaque, a bacterial biofilm, is one of the major etiologic agents involved in the initiation and progression of dental caries, gingivitis and periodontal disease.
- Due to the strong association between oral microorganisms and caries, as well as periodontal diseases, the dental profession has been increasingly interested in the topical use of antimicrobial agents.
- Numerous studies have followed that herbal extract is one of the best investigated compounds in dentistry and to date remains the gold standard compared to other antimicrobials.

- For dental usage, herbal extract is marketed in various galenic forms such as mouth washes, sprays, and gums herbal extract was the antimicrobial agent shown to inhibit dental plaque and chronic gingivitis.

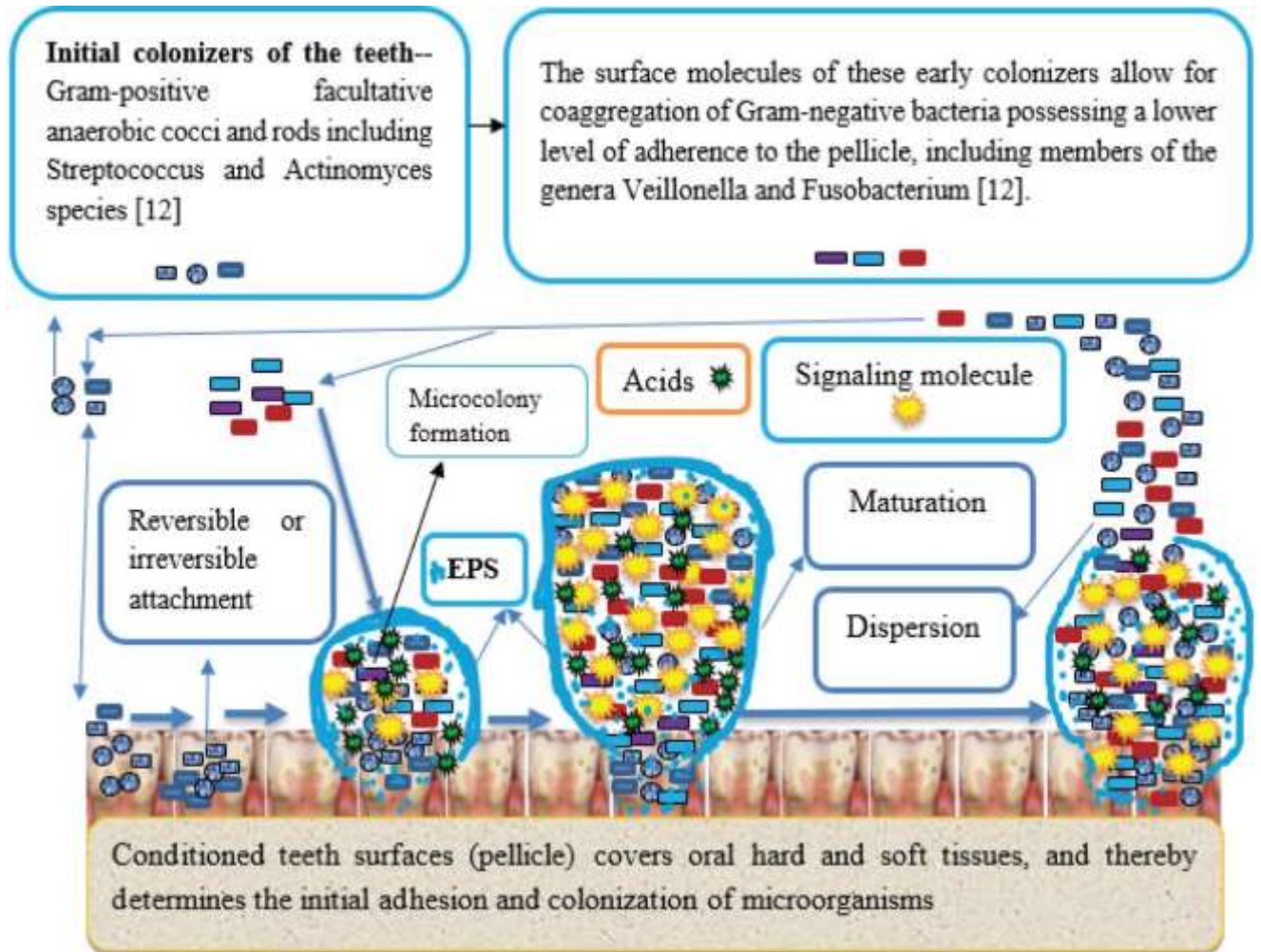


Figure 1.4 Schematic of bacterial biofilm formation process on teeth surface

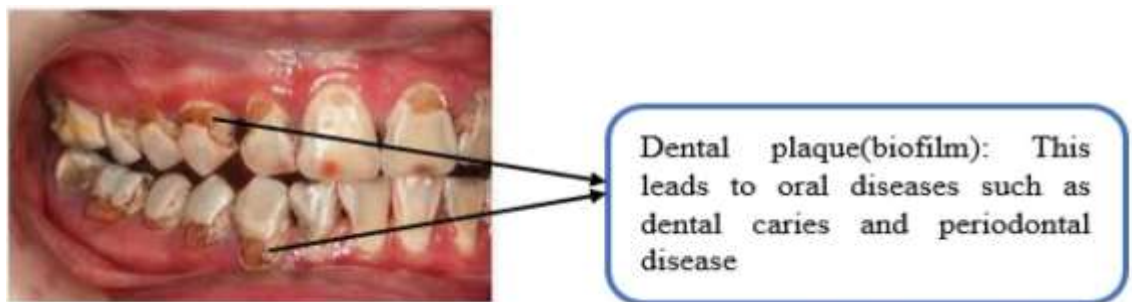


Figure 1.5 Dental plaque formation

### 1.1.1 Factors that determine bacterial growth and oral biofilm formation

oral bacterial communities may be influenced by physical and biological factors, nutrient availability, pH and oxy-reduction potential, as well as diet, smoking and drinking habits and the patient's overall health and oral hygiene. These

## 1. 2 MEDICATED CHEWING GUM

- Medicated Chewing Gum (MCG) is a novel drug delivery system containing masticatory gum base with pharmacologically active ingredient and intended to use for local treatment of mouth diseases or systemic absorption through oral mucosa
- Medicated Chewing Gum (MCG) is a novel drug delivery system containing masticatory gum base with pharmacologically active ingredient and intended to use for local treatment of mouth diseases or systemic absorption through oral mucosa. MCG is considered as vehicle or a drug delivery system to administer active principles that can improve health and nutrition.
- MCG represents the newest system with potential uses in pharmaceuticals, over the counter medicines and nutraceuticals<sup>1</sup>. The drugs intended to act in oral cavity often have low water/saliva solubility and chewing gum constitute a valuable delivery system for such drugs.
- Medicated chewing gum is a solid or semisolid dosage form which consists of one or more active ingredient (water soluble or insoluble) incorporated in water insoluble base.
- Many scientific studies have explored the role of chewing gum in promoting healthy teeth. Gum chewing is a common habit in many countries .
- Chewing gum has been used for centuries to clean the mouth and freshen the breath. A MCG containing Acetyl Salicylic Acid was commercially introduced in 19283 .
- In 1991, Chewing gum was approved as a term for pharmaceutical dosage form by the commission of European Council. Approximately £80 to 100 million, 55% of it being sugar free gum. Seventynine percent of the chewing gums sold in Switzerland are sugar-free, 70% of the consumers are teenagers, and girls chew more gum than boys. Chewing gum was initially sweetened with sugar, which contributed to dental caries.
- Today, however, more than 50% of chewing gum sold in Europe is sweetened with sugar substitutes (polyols). Clinical evidence shows that sugar substituted chewing gum does not lead to caries, because the polyols do not lead to a clinically relevant production of metabolic acids in dental plaque.
- The objective of this systematic literature review is to appraise existing evidence concerning a possible therapeutic/ anti-carcinogenic effect of sugar- free chewing gum for patients. MCG represents the newest system with potential uses in pharmaceuticals, over the counter medicines and nutraceuticals

### 1.2.1. ADVANTAGE OF MEDICATED CHEWING GUM

- Does not require water to swallow. Hence it can be taken anywhere
- Advantageous for patients having difficulty in swallowing.
- Excellent for acute medication.
- Counteracts dry mouth, prevents candidiasis and caries.

- Highly acceptable by children<sup>10</sup>.
- Avoids first pass metabolism and thus increases the bioavailability of drugs.
- Fast onset of action due to rapid release of active ingredients in buccal cavity and subsequent absorption in systemic circulation.
- Stomach does not suffer from direct contact with high concentrations of active principles, thus reducing the risk of intolerance of gastric mucosa<sup>11</sup>.
- Fraction of product reaching the stomach is conveyed by saliva delivered continuously and regularly. Duration of action is increased.
- Aspirin, Dimenhydrinate and Caffeine shows faster absorption through MCG than tablets.
- Stimulates flow of saliva in the mouth.
- Neutralizes plaque acids that form in the mouth after eating fermentable carbohydrates.
- Helps whiten teeth by reducing and preventing stains

### 1.2.2 DISADVANTAGE OF MEDICATED CHEWING GUM

- Risk of over dosage with MCG compared with chewable tablets or lozenges that can be consumed in a considerable number and within much shorter period of time.
- Sorbitol present in MCG formulation may cause flatulence and diarrhoea.
- Additives in gum like flavouring agent, Cinnamon can cause ulcers in oral cavity and liquorice cause hypertension.
- Chlorhexidine oromucosal application is limited to short term use because of its unpleasant taste and staining properties to teeth and tongue.
- Prolong chewing on gum may result in pain in facial muscles.

#### 1.2.2.1.1 NOVEL MEDICATED DRUG DELIVERY SYSTEM (MCG)

- New formulations and technologies have been developed through oral drug delivery systems' researches. Such researches display significance of oral route amongst patients.
- Acceptance of medicated chewing gum has been augmented through years.
- The advantages and therapeutic benefits of chewing gum support its development as we can see new formulations with new drugs contained have been produced from past and are going to find a place in market by formulation of new medicated chewing gums.
- Potential applications of medicated chewing gums are highly widespread as they will be recognized in future.
- Nowadays standards for qualifying chewing gums are the same as tablets. Patient-centered studies include medicated chewing gums as a delivery system too which creates compliance for patients.
- Ability of chewing gums to release active ingredients into the oral cavity, steady and rapid action, capability of both systemic and local delivery, make it appropriate for extensive use in food and pharmaceutical industries.

### 1.1.2 COMPOSITION OF MEDICATED CHEWING GUM

- Chewing gum is a mixture of ingredients-either natural or synthetic-that comprises water-

soluble bulk portion and water insoluble gum bases.

- **Gum base** is the nonnutritive part of gum which is not dissolve while chewing, gum bases are mixture of natural gums, latex, plastics, solid paraffin, bees' wax but modern gum bases use no natural rubber at all or just a minimal amount, 15- 30% of chewing gum is gum base.
- **Elastomer** is a polymer with high elongation properties and elasticity, which make them flexible against its breaking or cracking. Natural and synthetic elastomers are two different materials applied in chewing gum formulations. The ability of formulation process depends on types and amounts of elastomers.
- **Plasticizer** is a material to make chewing gum composition softened and consumer-friendly. It promotes gum texture by applying plasticity and reducing brittleness and renders the elastomers.
- **Texturizer** supplies overall texture and facilitates blending and other processing stages. Cud size, chewing ability, and stretch are the effects of texturizers' level.
- **Rubber** is also associated with the manufacture of bubble gum, it's just the resin used in formulations which also acts as elastomeric plasticizer as well as a binding agent between elastomers and texturizers.
- **Sweeteners** provide the sweetness of formulation and improve the taste. Aqueous sweeteners which include corn syrup, hydrogenated starch, and sorbitol, help to retain moisture and freshness of the final product. They also act as a plasticizer or softening agent and binding agent.
- **High-intensity artificial sweeteners** also provide the sweetness, but a lower calorie is produced by them due to the partial absorbance in the intestine.
- **Flavoring agents** provide an acceptable flavor for the product and can act as taste-masking agents for bitter drugs to cover the taste of active ingredient.
- **Colorants** improve the color of the formulation by producing gentle and soft color.
- **Anti-oxidants** prevent the growth of microorganisms by inhibiting oxidation.
- **Anti-tack agents** eliminate self-adhesiveness known as blocking especially rubbers which have a tendency to stick together. It reduces fragmentation of the gum during mastication and prevents attaching to the teeth.
- **Anti-caking agents** are used to prevent caking and forming lumps. These materials improve flow ability and rehydration and help for good packaging.

### 1.2.3 MANUFACTURING PROCESS FOR FORMATION OF MEDICATED CHEWING GUM

- **FUSION METHOD** The first step of a typical process for manufacturing chewing gum is to melt and soften the gum base at about 60°C and place it in a kettle mixer, in which blades soften the base, then other ingredients such as sugar, glycerin, sweeteners, taste- masking agent are added to the softened base, lately the flavoring agent is added in the mixing procedure at 40°C, then cooling and rolling steps would be done, and the rolled chewing gum would then be cut into pieces of desired shapes and sizes. To make a coated gum tablet, a coating agent should be sprayed to form a uniform surface.

➤ **Second type of this method is somehow different:**

- The primary step of preparation is to set up a mixer (the mixer could be sigma blade or other types of mixers), if a sugar containing gum is needed, the first step is to add corn syrup to the mixer, and then finely powdered sugar is added gradually. Sugar, used in this step, could be powdered sucrose, dextrose, fructose, corn syrup solids or combination of them. After adding these sweeteners, plasticizers are added to modify the texture and regulate the cohesiveness. Glycerin is the most preferably plasticizer used such as fillers, colorants, and flavorings. But it is recommended that flavorants being added to the matrix at the end of procedures when gum base is totally and completely homogenized because most flavorants are relatively volatile.
- The proportions of components in the matrix are variable between sources and depend to desired characteristics. But powdered sugar has approximately the most proportion. The mechanical forces of mixer, that is, compressive and shear and heat can ease the softening process.
- When no heat is applied, a higher power is demanded. The mixing process continues until a homogenous mass is formed. The mixing process should last about 8 min. Another way of mixing ingredients is to add sugar gradually till the end of adding other components.
- After matrix preparation and completely mixing it, the commercially prepared particles of gum base are added to the chamber all at once. But it is believed that these particles should have been heated and mixed before adding all other ingredients to the mass of gum base.

➤ **COOLING GRINDING AND TABLETING METHOD**

- One other method to provide a chewing gum with desired taste, color, and flavor is to mix gum base with favorable and suitable sweeteners, corn syrups, starches, flavoring agents, and colorants, and then refrigerate and cool it by a freezer apparatus or by contacting with a coolant like carbon dioxide to a temperature below  $-15^{\circ}\text{C}$  which is therefore crushed and pulverized with a cutter or grinding apparatus to obtain minute particles then these finely ground particles are heated to a temperature which makes them adhere to each other and form a slick and uniform bulk with consistent texture and low specific gravity.

➤ **DIRECT COMPRESSION**

- A new technology to make a chewing gum tablet is direct compression and tableting at high-speed standard machine, but as explained in a patent, this way of forming chewing gum tablets provides a quickly dissociable chewing gum, but after a few seconds of chewing, particles adhere together to form a uniform and homogenous mass. In this method; we need a granulating agent, most preferably that is sorbitol which can also act as a sweetener.
- A lubricant such as magnesium stearate, talc, stearic acid, hydrogenated vegetable oils, and sodium stearyl fumarate is added to formulation before tableting. First step of this method is dry mixing of gum base, granulating agent and at least one processing material then adding active ingredient, sweeteners, and other needed ingredients to the formulation in free flowing form of materials then directly compressing the chewing gum into tablets. In the first step, the temperature should not raise higher than the melting point of the gum base.

- After obtaining a uniform and slick mass, the temperature would lower to add other ingredients
- We can formulate many sensitive active substances in model of compressed chewing gum that is advantage over previous methods, other significant benefits are: 1. Fast release. 2. fast absorption, and 3. high content uniformity. Bi-layered compressed chewing gum tablets are now found in new pharmaceutical products.

### ➤ CHEWING GUM PACKAGING

- The advantages of chewing gum packaging are clear to the world since it extends shelf-life of the product by preventing aroma and flavor to disappear. It also provides moisture retention and gum stability.
- There are too many packaging methods with a wide range of options. In almost all of packaging types, we need a wrapping machine that receives and wraps the sticks of gums; in some cases, the wrapper machine seals the end of the package. In the following, a formed blister pack may be used then a foil will be heat-sealed at the back or a traditional packaging may be applied by lining the pellets up in a row and wrapping then sealing the both ends. The manufacturing and packing steps should be performed at about 20-25°C and relative humidity of 57%.
- Packaging has a substantial portion in the whole process both in terms of cost and time. Undoubtedly, packaging influences attraction of product among consumers, thus a well-favored and stylish design can attract more consumers to buy the specific product.
- Therefore, besides protecting the content, avoiding impurity, expediting transport and improving storage, packaging can influence consumers' willingness to buy the product and capture his attention during purchase competition.

#### 1.12 THERAPEUTIC USE OF MEDICATED CHEWING GUM

1. The use of sugar free gum to counteract dental caries by stimulation of saliva secretion has led to a more widespread use and acceptance of gums. It has been proved that chewing non-MCGs increases plaque pH, stimulates saliva flow, and decrease decay. Prevention and cure of oral disease are obvious targets for CG formulations. It can control the release rate of active substances providing a prolonged local effect
2. Fluoride containing gums have been useful in preventing dental caries in children and in adults with xerostomia
3. MCGs containing chlorhexidine (CHX) for treatment of gingivitis and plaque have been available. The use of MCG in the treatment of oral infections has also been reported. CHX CG offers numerous flexibility in its formulation as it gives less staining of the teeth and is distributed evenly in the oral cavity. The bitter taste of CHX can be masked quite well in a CG formulation

4. For systemic effect in conditions such as Vitamin C deficiency, pain and fever alertness, motion sickness, as well as for local effect in the conditions such as plaque acid neutralization, fresh breath, disinfection, anticaries, antiplaque, antifungal, and antibacterial are available
5. Obesity- Active substances such as chromium, guaran, and caffeine are proved to be efficient in treating obesity. Chromium is claimed to reduce craving for food because of an improved blood-glucose balance. Caffeine and guaran stimulate lipolysis and have a thermogenic effect (increased energy expenditure) and reduce feeling of hunger
6. In addition, gums are available for smoking cessation.

### 1.3 MEDICATED CHEWING GUM USING HERBAL EXTRACT

- The use of botanicals to treat health ailments is in practice from the beginning of recorded human history. The Egyptian Ebers Papyrus dated around 1550 BC contains herbal remedies for over 876 illnesses. It is reported that Hippocrates, the “Father of Medicine,” whose writings contain references about 250 medicinal plants and herbs.
- Many other ancient Indian, Chinese, medicines also have references proving the use of medicinal herbs to treat various diseases.
- Hence, the use of various herbal extracts for the treatment of plaque-induced.
- Herbal extracts are more efficient and effective than chemical compounds in treating plaque-induced gingivitis. Moreover, the natural components are much biocompatible and harmless to the body. Organic compounds found in the extracts have several other properties which are good to human body.
- They are safer and economical. Their mechanisms of action are unique, and hence, development of resistance to herbal extracts by the microorganisms is rare. Hence, herbal extracts can be used to treat plaque-induced gingivitis in the form of mouthwash and toothpaste

#### ❖ NEEM AS HERBAL DRUG

- *Azadirachta indica* Meliaceous family tree, has been used in India for several decades for the treatment of several diseases in medicine and dentistry.
- *Azadirachta indica*, commonly known as **neem**, **nimtree** or **Indian lilac**,<sup>[3]</sup> is a tree in the [mahogany](#) family [Meliaceae](#).
- It is one of two species in the genus [Azadirachta](#), and is native to the [Indian subcontinent](#) and most of the countries in [Africa](#).
- It is typically grown in [tropical](#) and semi-tropical regions. Neem trees also grow on islands in southern [Iran](#).
- Its fruits and seeds are the source of [neem oil](#).
- The purpose of the present study was to assess the efficacy of neem based mouth rinse regarding its antingivitic effect.





Figure 1.7 NEEM

- **The medicinal utilities** have been described especially for neem leaf. Neem leaf and its constituents have been demonstrated to exhibit immunomodulatory, anti-inflammatory, antihyperglycaemic, antiulcer, antimalarial, antifungal, antibacterial, antiviral, antioxidant, antimutagenic and anticarcinogenic properties.
- A teeth-cleaning twig (in India: *datun*<sup>[1]</sup>) is an [oral hygiene](#) tool made from a twig from a tree. It can help to prevent [tooth decay](#) and [gum disease](#)
- **TEETH CLEANING TWIGS** can be obtained from a variety of tree species. Although many trees are used in the production of teeth-cleaning twigs, some trees are better suited to clean and protect the teeth, due to the chemical composition of the plant parts. The tree species are:



- [Salvadora persica](#)

- [Cinnamon Bark](#)
- [Sassafras](#)
- [Gumtree<sup>\[16\]</sup>](#)
- Lemon grass oil
- [Garcinia mannii](#) in West Africa
- [Orange tree](#) (*Citrus × sinensis*)
- African laburnum ([Cassia sieberiana](#))
- [Tea tree](#)
- [Neem](#) in the Indian subcontinent
- [Vachellia nilotica](#), also called *babool* or *kikar* in the Indian subcontinent
- [Dalbergia sissoo](#), also called *sheesham* in the Indian subcontinent
- [Liquorice](#)
- [Gouania lupuloides](#)
- [Cinnamon](#)
- [Dogwood](#)
- [Olive](#)
- [Walnut](#)
- [Acacia catechu](#)
- [Acacia nilotica](#) bitter roots

#### ➤ MECHANISM OF ACTION

- Antimicrobial role through inhibitory effect on microbial growth/potentiality of cell wall breakdown.
- Free radical scavenging properties due to rich source of antioxidant.
- Concentration-dependent antiradical scavenging activity and reductive potential of active constituents Azadirachtin and nimbolide.

#### ➤ NEEM IN DENTAL CARE

- The tree is known for its anthelmintic, antifungal, antibacterial, antiviral, pest-control, sedative and many more effects
- In 1942, scientist Salimuzzaman Siddiqui was the first person to find that the nimbidin compound in the neem oil is primarily responsible for the antibacterial property
- Based on this research fact, neem oil is the main ingredient in commercial toothpaste sold by advertising the dental benefits of neem
- A research study was carried out at the Department of Public Health Dentistry, People's College of Dental Sciences and Research Centre, Bhopal, India
- The study aimed at comparing the effects of neem stick with a toothbrush in removing plaque and improving gingival health
- 30 participants belonging to the age group of 18-25 years underwent this study for three weeks
- At the end, the researchers found that neem stick is equally effective in removing plaque and reducing gingival inflammation as a toothbrush

- The study recommended the use of a stick of neem as the primary source of dental care in rural areas where commercial toothbrushes and toothpaste are not available easily
- It fulfils all the requirements of primary dental care and can serve as an excellent alternative for commercial toothbrushes and pastes
- The research also recommended a stick of neem as a health promotion tool in developing countries in the Asia continent where there are limited oral health care facilities
- The benefits can be obtained by chewing the neem stick for 10 – 15 minutes
- The juices released from the stick contain all the essential chemical ingredients and reach every nook and corner of the mouth to provide the above-mentioned benefits
- However, the researchers mentioned that enough care should be taken while using the stick to ensure no damage is caused to the oral mucosa through any trauma or injury.

### ➤ CINNAMON AS HERBAL DRUG

- **Cinnamon** is a [spice](#) obtained from the inner bark of several tree species from the genus [Cinnamomum](#).
- Cinnamon is used mainly as an aromatic [condiment](#) and flavouring additive in a wide variety of [cuisines](#), sweet and savoury dishes, [breakfast cereals](#), [snack foods](#), [bagels](#), [teas](#), [hot chocolate](#) and [traditional foods](#).
- The aroma and flavour of cinnamon derive from its [essential oil](#) and principal component, [cinnamaldehyde](#), as well as numerous other constituents including [eugenol](#).



- [Cinnamomum verum](#), from Koehler's Medicinal-Plants (1887)  
Close-up view of raw cinnamon bark.
- various related species are also cultivated as a source of cinnamon spice, including [Chinese cassia](#) (*Cinnamomum cassia*), Vietnamese, or Saigon, cinnamon (*C. loureiroi*), Indonesian cinnamon (*C. burmannii*), and Malabar cinnamon (*C. citriodorum*).
- Cinnamon is the name for several species of trees and the commercial spice products that some of them produce.
- All are members of the genus *Cinnamomum* in the family [Lauraceae](#). Only a

few *Cinnamomum* species are grown commercially for spice. *Cinnamomum verum* (alternatively *C. zeylanicum*), known as "Ceylon cinnamon" after its origins in [Sri Lanka](#) (formerly Ceylon), is considered to be "true cinnamon".

- ❖ **CINNAMALDEHYDE** *Trans*-Cinnamaldehyde (*t*-Cinnamaldehyde or (*E*)-Cinnamaldehyde) was reported to be the main constituent of cinnamon EO and extracts. This molecule provides a major contribution to cinnamon's organoleptic and antibacterial properties.

- Cinnamaldehyde was the most active against the two oral pathogens (*S. mutans* and *Streptococcus sobrinus*), with inhibition zones ranging from 4.2 to 5.7 cm.

- From a pharmaceutical point of view, if precise active ingredient concentrations is the goal, using pure compounds like cinnamaldehyde and eugenol seem to be the best alternatives. These substances could be included in certain formulations by dental material manufacturers. Since the effects of the EO depend on the interaction of all its ingredients, not only its main components, further investigations should be conducted to determine the synergetic effects between the pure compounds .

- Cinnamon EO, cinnamon extracts, and the main components show significant antimicrobial activities against oral pathogens and could be beneficial in caries and periodontal disease prevention, endodontics, and candidiasis treatment.

#### LEMON GRASS OIL AS HERBAL DRUG



Figure 1.9 of Lemon Grass

- Lemongrass oil is rich in vitamin C, A and E. This oil has antibacterial, antifungal, antimicrobial and anti-infectious properties. Its aroma is rejuvenating and adds a lot to the health benefits.
- India's best toothpaste makers - [Dabur](#), recommend the use of lemongrass. This is because it cures many dental problems such as plaque, tooth decay, periodontitis.
- Lemon grass oil removes bacteria from the oral cavity and prevents teeth and gum diseases.

- The gums are strengthened due to astringent properties. Hence, teeth are healthier and problems such as tooth fall and bleeding gums can be avoided. The oil also lends freshness of breath because of its aroma. Lemongrass oil can be used in mouth washes in order to prevent plaque formation and also to remove plaque.
- Thereby it will inhibit caries formation.
- Lemongrass is effective in busting through the tough biofilm of plaque and hence it can be used as a mouth wash and toothpaste to remove biofilm, which ultimately forms plaque.
- Lemongrass oil has anti-oxidant properties, which helps in prevention and treatment of periodontitis hence by increasing the level of thiol anti-oxidants and also by reducing the bacteria. Apart from curing dental problems, lemongrass has properties that can help cure other ailments as well:
  - **Antiseptic:**  
Lemongrass oil is used for application on external and internal wounds as well as an ingredient of antiseptic lotions and creams as the properties of this oil do not let the wounds become septic.
  - **Pain relieving:**  
Lemongrass helps to alleviate muscle spasms by relaxing the muscles thereby leading to the reduction of pain-related symptoms. It is useful for abdominal pain, headaches, joint pains, muscle pains, digestive tract spasms, muscle cramps, stomach ache and others.
  - **Nervine:**  
Lemongrass has antidepressant properties and is beneficial for nervous and stress-related conditions. It helps to strengthen the nervous system and may thus be useful for conditions such as Parkinson's disease. It is also helpful in alleviating anxiety and depressive symptoms.
  - **Cholesterol controller:**  
The regular consumption of lemongrass helps in sustaining healthy levels of triglycerides and reducing the cholesterol in the body. This helps in preventing various cardiac disorders such as atherosclerosis.
  - **Skin care:**  
Lemongrass helps in strengthening the skin tissues and toning up the pores while also sterilizing them.
  - **Women care:**  
Lemongrass is very useful for lactating mothers since it helps in better milk generation and improves quality of milk. Lemongrass oil relieves pain and muscle aches caused during delivery and menstrual cramps.

### **CHLORHEXIDINE**

- Chlorhexidine is a medication used to help treat **periodontal disease** (a disease of your gums), which is caused by bacteria growing beneath the gum line.
- Chlorhexidine works by killing the bacteria. Up to eight chlorhexidine implants are placed between your teeth and gums in places where the gum has a deep pocket.
- Your dentist will place the chlorhexidine implants after your teeth have been thoroughly cleaned<sup>1</sup>.

- It is important to note that chlorhexidine is not a cure for periodontal disease, but rather a treatment to help manage the symptoms. It is also important to follow your dentist's instructions on how to use chlorhexidine properly, as it can cause side effects such as tooth discoloration and changes in taste.
- Because of its antimicrobial and anti-inflammatory activity, it was hypothesized that rinsing with cinnamon-containing mouthwash could probably lead to a reduction in dental plaque and gingival inflammation.
- A study conducted by Devanand Gupta and Ankita Jain found that cinnamon extract may prove to be an effective agent owing to its ability to reduce plaque level and gingivitis .
- In conclusion, cinnamon extract may have **antiplaque and gingivitis properties**.



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## 2. REVIEW OF LITERATURE

### 2.1 LITERATURE REVIEW OF DISEASE

#### 1) Zoya Ahmad, Dr. Rupali Kalsi, Dr. Sachit Anand Arora (2022)

<sup>(23)</sup> Dental plaque is the sole reason for dental caries and periodontal disease. Few antibacterial agents might counterbalance the inadequate mechanical plaque removal. Antimicrobial agents are best indicated in secondary and tertiary prevention as the objectives are to restore health and to prevent disease recurrence. The rationale behind it is to prevent or delay subgingival recolonization by pathogenic microorganisms. Delmopinol is a chemical plaque control agent which can be used as an adjunct to mechanical plaque control. It is an antiplaque agent that aids in reduction of plaque and gingivitis while possessing the property of inhibiting the adhesion of oral microorganisms to the tooth surface. Long term use of such compound can preserve the biological environment of the oral cavity.

2) Vyas, Taru Bhatt, Garima Gaur, Abhishek et al (2021)<sup>(24)</sup> Dental plaque is a complex microbial population of bacterial and salivary polymers present on the

tooth surface. It is understood that human diseases must be avoided and a high social concern for the population as a whole. The argument for the implementation of successful prevention measures is strong for life-threatening diseases or those with serious morbidity. However, regardless of seriousness, the case for avoiding any disease may be based on the belief that it is easier to be healthy than dead or sick. Thus plaque prevention is an efficient way to both treat and avoid periodontal diseases, it is an important component of gingival and periodontal diseases' primary management.

3) **C.J .Jaya Seneviratne et al ( 2011)** <sup>(25)</sup> Dental plaque is an archetypical biofilm composed of a complex microbial community. It is the aetiological agent for majordental diseases such as dental caries and periodontal disease. The clinical picture of these dental diseases is a net result of the cross-talk between the pathogenic dental plaque biofilm and the host tissue response. In the healthy state, both plaque biofilm and adjacent tissues maintain a delicate balance, establishing a harmonious relationship between the two. However, changes occur during the disease

process that transform this 'healthy' dental plaque into a 'pathogenic' biofilm. Recent advances in molecular microbiology have improved the understanding of dental plaque biofilm and produced numerous clinical benefits. Therefore, it is imperative that clinicians keep abreast with these new developments in the field of dentistry. Better understanding of the molecular mechanisms behind dental diseases will facilitate the development of novel therapeutic strategies to establish a 'healthy dental plaque biofilm' by modulating both host and microbial factors. In this review, the present authors aim to summarise the current knowledge on dental plaque as a microbial biofilm and its properties in oral health and disease.

4) **Graham F Cope , Anwen Cope (2018)** <sup>(26)</sup> Gingivitis is arguably the commonest conditions seen by dental professionals, yet the risk factors are often ignored and the underlying causes are poorly understood. Most of the adult population have varying degrees of chronic gingivitis and the condition can affect all ages. The causes can be classified as local; relating to accumulation of micro-organisms and food deposits around the teeth, and systemic, whereby particular diseases, altered hormonal conditions and certain lifestyle factors increase the risk of the disease. It is important that dental professionals can effectively identify, treat and prevent recurrence of gingivitis.

5) **Paul .S. Rosen (2009)** <sup>(27)</sup> The inflammatory components of plaque induced gingivitis and chronic periodontitis can be managed effectively for the majority of patients with a plaque control program and non- surgical and/or surgical root debridement coupled with continued periodontal maintenance procedures. Some patients may need additional therapeutic procedures. All of the therapeutic modalities reviewed in this position paper may be utilized by the clinician at various times over the long-term management of the patient's periodontal

condition.

**6) Vyas .T. ,Bhatt G ,Sharma.C. (2021)<sup>(28)</sup>** Dental plaque is a complex microbial population of bacterial and salivary polymers present on the tooth surface. It is understood that human diseases must be avoided and a high social concern for the population as a whole. The argument for the implementation of successful prevention measures is strong for life- threatening diseases or those with serious morbidity. However,

regardless of seriousness, the case for avoiding any disease may be based on the belief that it is easier to be healthy than dead or sick. Thus plaque prevention is an efficient way to both treat and avoid periodontal diseases, it is an important component of gingival and periodontal diseases' primary management.

## **2.2 LITERATURE REVIEW OF DOSAGE**

**1) Priya Gupta , Madhvi Jain, Sonu Sharma (2020)<sup>(29)</sup>**Medicated chewing gum is an innovative approach which is used as a drug delivery vehicle for pharmaceutical and nutraceutical ingredients. Medicated chewing gum is a solid, single dosage form which release drug slowly in oral mucosa by the help of mechanical strength of chew. Medicate chewing gum does not dissolve in mouth but it release therapeutic agent in oral mucosa. Distinct from chewable tablet, medicated chewing gum have to remove from mouth so medicated chewing gum always labeled as not to be swallowed. Medicated chewing gum contains gum base with one or more than one active ingredients and suitable excipients. Medicated chewing gums are brilliant mobile drug delivery systems for self-medication and it can be administered discretely without water. Medicated chewing gum is used in systemic as well as local disease condition like Smoking cessation, travel illness, freshening of breath, vitamin or mineral supplementation, vomiting, pain relief etc. Other than therapeutic benefits medicated chewing gum offers many advantages like it give attractive and elegant look, acceptable taste and odour, it can formulate in many flavours which give joy to patients and most important it is highly acceptable by children and patients who have problem to swallow tablet.

**(2) Abofalz Aslani ,Farna Rostani et al (2015)<sup>(30)</sup>** According to the benefits of chewing gum as a novel drug delivery, like concurrently supporting both local and systemic delivery, protection against acids and enzymes, low first pass metabolism, elevating alertness and cognitive function, good stability and a lot more; we can conclude that chewing gum will be much more familiar to patients and market in the next few years. However, their new and old applications prove our statement as it can be seen that there are treatments for motion sickness, pain, smoking,

dental caries, tooth decay, otitis media, GI problems, oral fungi, inflammatory



problems etc., by formulating efficient chewing gums that contain at least one drug as active agent. Treatment of fungal diseases, prevention of caries and other dental health issues, smoking cessation, etc., are common health work of MCGs. But remineralization of teeth, cold relief, energy enhancing, anti-nausea and so many new advantages of this novel drug delivery system are going to play an important role through future studies. MCGs are admissible alternatives of chewable or standard tablets and oral disintegrated dosage forms.

**(3) Vipul patel (2011)<sup>(31)</sup>** It can be concluded that the chewing gum can be used, as a carrier for vast categories of drugs where extended release and the local action is desired. Chewing gum can be used without water, at any time. Medicated Chewing gums can produce both local effects as well as systemic effects in the oral cavity. They can be used for the purpose of taste masking of certain drugs too. Chewing gums are mobile drug delivery systems. It is a potentially useful means of administering drugs either locally or systemically via, the oral cavity. The medicated chewing gum has through the years gained increasing acceptance as a drug delivery system. Several ingredients are now incorporated in medicated chewing gum.

**4) Jinendra Kr. Kochar Jain, Soma Das, Deepika Khatiwara (2022)**

<sup>(32)</sup>The study and development of oral medication delivery systems has seen advancements in both medicine and technology in recent years. Due to greater patient compliance, not only in geriatric and paediatric patients but also in the general population, medicated chewing gum has attracted attention on a global scale throughout the year. This distribution mechanism for drugs since it is easy to use and works without water, self- medication. The invention of medicated chewing gums (MCGs) heralds a revolutionary new era in oral transportable medication. It is described as a solid single-dose formulation with a base of gum that must be effortlessly chewed for a set amount of time. It may also have more than one active component. Additionally, because the official Pharmacopoeias only suggest a small number of tests, there aren't many assessment parameters available.

**5) Jyoti Kiran Sahu, Suruchi Prasad (2023)<sup>(33)</sup>** Oral medication delivery system research has resulted in the development of new formulations and technology. Such studies demonstrate the importance of the oral route among patients. We've gone through all of the benefits and drawbacks of medicated chewing gum as a contemporary medication delivery system, including the history, benefits and drawbacks, production processes, composition variations, assessment tests, and samples of different medicated chewing gum kinds. The acceptance of medicated chewing gum has grown over time. Chewing gum's advantages and therapeutic benefits encourage its development, as shown by the fact that new formulations including new pharmaceuticals have been generated in the past and

will be found in the market by the formation of new medicated chewing gums. Medicated chewing gums have a broad range of potential uses that will be identified in the future. Chewing gums now have the same qualification criteria as pills. Patients' compliance is improved by using medicated chewing gums as a delivery strategy in patient-centered research.

**6) Deepika Khatiwara, Priyanka Ranabhat, Moumita Paul et al**

(2021)<sup>(34)</sup> Many advances in research and technology have been made in the oral route of drug delivery system in recent years. Because of increased patient compliance not only in geriatric and paediatric patients, but also in the general population, the oral channel of drug delivery system- medicated chewing gum has received worldwide recognition throughout the year. Chewing gum can be used as a mobile medication delivery device for both local and systemic drug administration via the oral route. Because of its ease and ability to be administered without water, it is an exceptional drug delivery device for self-medication. Because of its simplicity, improved patient compliance, and ease of administration without water, chewing gum can be considered an exceptional drug delivery system for self-medication. It can be used for both local and systemic medication delivery. Chewing gum has the potential to become a first-choice medicine delivery method for conditions requiring a quick onset of action, such as motion sickness, nausea, allergy, pain, headache, and infections. In light of the advantages of medicated chewing gum as a novel drug delivery system, such as

protection against acids and enzymes, increased alertness and cognitive functions, low first pass metabolism, taste masking of many drugs, smoke cessation, dental caries, mouth ulcer, and so on, we can conclude that chewing gum will gain more acceptance by patients in the future, including geriatric, paediatric, and general populations.

**7) kumar et al (2022)<sup>(35)</sup>** Medicated chewing gum of Ondansetron can be successfully prepared by melting method using different concentrations of plasticizer and synthetic gum base. On the basis of different evaluation parameters, formulation F1 was the optimized formulations are kept for stability studies. Thus, it's the better option to prepare Ondansetron into a medicated chewing gum to achieve better patient compliance and improved drug release.

**8) Jyoti Kiran Sahu<sup>1</sup>, Suruchi Prasad (2023)<sup>(36)</sup>** Compared to traditional dosage forms, modified release dosage forms have been greatly improved upon in terms of formulation development and product design, making them much more acceptable. The use of modified dosage forms is increasingly accepted and is drawing the attention of academics throughout the globe. Newer technologies are being developed to change standard, ordinary tablets in order to boost bioavailability and increase acceptance. Oral disintegrating pills, lozenges, medicated chewing gums, effervescent tablets, sublingual and buccal tablets, extended-release tablets, etc., fall within the category of modified-release dosage

forms. Gum may be utilized to deliver drugs in an innovative and practical way. These days, medicated gum is just as safe and effective as pills, and it can even be designed to have a variety of drug release patterns and therefore be used with certain populations in mind. Mankind has been chewing gum since prehistoric times. At now, it is one of the most widely utilized dosage forms for administering a wide variety of therapeutic agent.

**9) Vijay Metkari, Ishwari Duddu, Rohit Shah et al (2023)<sup>(37)</sup>** Herbal chewing gum is a novel drug delivery system containing gum base with pharmacological active ingredient and intended use for local treatment of mouth diseases or systemic absorption through oral mucosa. Herbal chewing gum is considered as a vehicle or a drug delivery system to administer active principles that can improve health and nutrition. Chewing gum is a soft, cohesive substance designed to be chewed

without being swallowed. Modern chewing gum is composed of gum base, sweeteners, softeners/plasticizers, flavors, colors, and, typically, a hard or powdered polyol coating. Chewing gum helps to improve intestinal motility, also helps to increase saliva flow which promotes more frequent swallowing. This helps to prevent reflux of acid from the stomach back into the throat. The results of scientific research demonstrate that chewing gum is good for oral health and teeth specifically. The use of sugar-free gum provides a proven anti-caries benefit, but other oral health effects are less clearly elucidated.

## **2.3 LITERATURE REVIEW FOR DRUG**

### **1) Literature Review for LEMON GRASS OIL**

**(i) Ruckmani Rajesvari1 , T. Lakshmi (2016)<sup>(53)</sup>**Lemon grass oil can be used as an adjunct in mouth washes in order to prevent plaque formation and also to remove the plaque. Thereby it will inhibit the caries formation. A study published in the journal of ethno pharmacology proved that essential oil of lemon grass is effective in busting through the tough biofilm that *Candida* hides behind[3] and hence it can be used as a mouth wash and toothpaste to remove biofilm, which ultimately forms plaque .These researches concluded that lemon grass oil has anti-bacterial, anti-fungal, anti-oxidant, anti-proliferative, anti-viral and anti-inflammatory properties, which hints that it can be used to treat various diseases in human. The extract can be used as a mouth rinse or tooth paste or medicament to treat various dental issues. Further researches should be done in lemon grass oil in relation with oral cavity for the prevention and treatment of various dental diseases.

**(ii) Sree kumar Akula,,Javaniah Nagaratha (2021)<sup>(54)</sup>** Main Objective is Research is ongoing to find safe and effective oral hygiene aids for oral self-care in children. Mouthwashes are used to complete the process of mechanical plaque control. Lack of affordability and side effects of most commercially available

mouthwashes limit their use in children. Hence, the cost-effective and easily available essential oil, lemongrass oil, when formulated as a mouthwash, may possibly serve as an adjunct to oral hygiene maintenance. The main objective of this study was to compare the efficacy of lemongrass oil and chlorhexidine (CHX)

mouthwash in children. The results of the present study showed that both mouthwashes were effective in improvement of PI and GI. Also, 0.25% lemongrass oil mouthwash was found to be comparable to 0.2% CHX in reduction of gingivitis and as an antiplaque agent. Lemongrass oil mouthwash showed better results in the plaque pH scores in children than CHX. Thus, lemongrass oil mouthwash may be more beneficial for plaque control and gingival health, and it may be suitable for use as an alternative to CHX as an adjunct to mechanical plaque control.

**(iii) Sonia Ambade ,Neelima Deshpande (2022)<sup>(55)</sup>** The prepared mouth wash was found to have required stability in terms of physical and chemical parameters and has no cytotoxic activity. The study clearly demonstrated that the LGEO based mouthwash has considerable antimicrobial and anti-biofilm activity against the organisms responsible for dental plaque.

## **2) LITERATURE REVIEW FOR NEEM POWDER**

**(i) Niha Naveed ,Karthikayan Murthy Kumar (2014)<sup>(38)</sup>**Neem helps to prevent and heal gum disease, prevent cavities, eliminate bacteria that cause cavities and inflammation of the gums, prevent bacteria from adhering to your teeth (reduce plaque), enhance mouth immunity in general, and through all this freshen the breath. Neem, has pain-relieving compounds that can reduce the discomfort of a toothache. The vasodilatation and anti-inflammatory compounds in neem prevent cell adhesion and kill the bacteria that cause tooth decay. Neem alkalizes the gums and mouth, and kills the bacteria that cause Pyorrhea and Gingivitis. Neem obliterates the calcium-forming organisms and the organisms that cause cavities. Neem is 'arista,' which in Sanskrit means “perfect, complete, and imperishable.” Neem has been used in Ayurvedic traditions for thousands of years in agriculture, food storage, and medicine. Many research studies prove that neem is fungicidal, mitocidal, and antibacterial. Neem oil is an ideal remedy to eliminate periodontal and tooth infection. It can be applied locally around the teeth and gums and also benefits the gastrointestinal tract.

**(ii) Md Jalaluddin , UB Rajasekaran et al (2017)<sup>(39)</sup>** The present study aimed at evaluating the impact of neem containing mouthwash on plaque

and gingivities From the present study, it has been concluded that neem mouthwash can be used as an alternative to chlorhexidine mouthwash as the reducing scores are witnessed in both groups I and II. Neem mouthwash might have a better impact in maintaining oral hygiene, prevention as well as

pervasiveness of oral diseases as it is cost-effective and easily available.

**(iii) T.Lakshmi ,Vidya Krishnan et al (2015)<sup>40)</sup>** *Neem* which are responsible for antibacterial activity. *Neem* bark is used as an active ingredient in a number of toothpastes and toothpowders. *Neem* bark has anti-bacterial properties, it is quite useful in dentistry for curing gingival problems and maintaining oral health in a natural way. *Neem* twigs are used as oral deodorant, toothache reliever and for cleaning of teeth. The objective of this article is to focus on the various aspects of *Azadirachta indica* in dentistry in order to provide a tool for future research. Various parts of the *Neem* tree possess astringent and antiseptic activity. Leaf extracts have been widely used in both traditional and conventional times to manufacture toothpaste and mouthwash in the oral care dentistry. Its antibacterial properties due to the presence of nimbidin, Azadirachtin, and nimbinin help to remove many oral aerobic and anaerobic pathogens existing in the oral cavity.

### **3) LITERATURE REVIEW FOR CINNAMON POWDER**

**(i) Spartak Yanakair (2022)<sup>45)</sup>** Dental medicine is one of the fields of medicine where the most common pathologies are of bacterial and fungal origins. This review is mainly focused on the antimicrobial effects of cinnamon essential oil (EO), cinnamon extracts, and pure compounds against different oral pathogens and the oral biofilm and the possible effects on soft mouth tissue. Basic information is provided about cinnamon, as is a review of its antimicrobial properties against the most common microorganisms causing dental caries, endodontic and periodontal lesions, and candidiasis. Cinnamon EO, cinnamon extracts, and pure compounds show significant antimicrobial activities against oral pathogens and could be beneficial in caries and periodontal disease prevention, endodontics, and candidiasis treatment.

**(ii) J Anggono, M Damiyanti<sup>1</sup> and Y K Eriwati et al (2020)<sup>46)</sup>** Dental medicine is one of the fields of medicine where the most common pathologies are of bacterial and fungal origins. This review is mainly focused on the antimicrobial effects of cinnamon essential oil (EO), cinnamon extracts, and pure compounds against different oral pathogens and the oral biofilm and the possible effects on soft mouth tissue. Basic information is provided about cinnamon, as is a review of its antimicrobial properties against the most common microorganisms causing dental caries, endodontic and periodontal lesions, and candidiasis. Cinnamon EO, cinnamon extracts, and pure compounds show significant antimicrobial activities against oral pathogens and could be beneficial in caries and periodontal disease prevention, endodontics, and candidiasis treatment.

- (iii) **B.Nandhini , K.Dharuna1 and B.Suresh (2023)<sup>(47)</sup>** Different crude medications are added to herbal tooth powders to assist clean the mouth. The physiochemical characteristics of allopathic and herbal powders may depend on the micromeritics of the particles as all of these ingredients are made up of fine particles (. Due to greater public knowledge of the poisonous and harmful effects of chemicals, people are becoming more interested in using substances that are natural, and the creation of cosmetics is a result of the long standing usage of herbal treatments. People used natural products in earlier days to maintain their oral hygiene and freshen their breath. The formulation and evaluation of the herbal tooth powder yielded promising results, suggesting its potential as a natural and effective dental care product. The use of carefully selected herbal ingredients provided antimicrobial properties, helping to maintain oral hygiene and prevent common oral health issues. The fine texture and pleasant aroma of the tooth powder enhance its user friendliness and consumer appeal. Overall, herbal tooth powders offer a natural and chemical-free alternative for maintaining oral hygiene. They can be an excellent option for individuals who prefer natural products and are looking to incorporate herbal remedies into their oral care routine. Further research and testing can be conducted to optimize the formulation and assess long-term effects.

#### **4) LITERATURE REVIEW FOR CHLORHEXIDINE**

- (i) **Setu Mathur , Tanu Mathur et al (2011)<sup>(56)</sup>** chlorhexidine to date is the most potent anti plaque agent. It is considered gold standard anti plaque agent, against which efficacy of other anti plaque and anti -gingivitis agents is measured. Its efficacy can be attributed to its bacteriostatic and bactericidal properties and its substantivity within the oral cavity. The antimicrobial properties of Chlorhexidine are attributed to its bi-cationic molecule, and this same property is the basis of its most common side effect, extrinsic tooth staining.
- (ii) **Alvi Fatima Arushi Goyal, Jaskaran Singh (2022)<sup>(57)</sup>** Diseases which are related to gums or periodontium are mainly caused by the inflammatory response of the bacterial products accumulation over the surface of the tooth or along with the gingival crevices. Most common bacteria responsible for the periodontal or the gum diseases are gram negative anaerobic bacteria's. Literature revealed that use of chemical agent such as chlorhexidine as an adjunct to mechanical aids such as tooth brushing or mechanical interdental cleaning helps in reducing the gums or periodontal inflammation. A study revealed that continuous use of chlorhexidine mouth rinse in the concentration of 0.2% for 4 to 5 weeks efficiently helps in reducing the clinical signs of periodontal inflammation. Chlorhexidine is not only an antiplaque agent but also possesses the property of

antimicrobial agent. Its wide variety of usage in the field of dentistry make its very much popular.

- (iii) **Zoe L.S Brooker ,Kamren Ali (2020)<sup>58</sup>** The use of CHX in dentistry and oral healthcare continues to be widespread and thus it is important that dental practitioners understand that, based on its differential mechanisms of action on different microbes, appropriate clinical and dental use of CHX should be oral disease specific.

### **Apparatus -II. Alternative Chewing Gum Apparatus**

**Noncompendial—Wennergren** One of the non-compendial apparatus commercially available was designed by Wennergren[79] . The schematic representation of the Wennergren chewing apparatus is shown in Figure 2. The chewing procedure consists of reciprocations of the lower surface in combination with a shearing (twisting) movement of the upper surface that provides mastication of the chewing gum and at the same time adequate agitation of the test medium. The upper jaw has a flat surface that is parallel to the central part of the lower surface. The small brim of the lower surface is angled upwards (45 degrees) so that the lower surface functions as a small bowl with a flat bottom. This bowl prevents the chewing gum from sliding during mastication. Investigations of the performance of the chewing apparatus with multiple drug products were published by Wennergren et al[79] . The influences of different operational parameters of the chewing gum apparatus on drug release have been carefully investigated **In-vitro Apparatus** An apparatus was specially designed and constructed for studying the release pattern of drug from the medicated chewing gums. The ability of the instrument to adjust settings such as temperature, chewing frequency, chewing time, volume of test medium, distance between the jaws and twisting angle increases the versatility of the apparatus. Selecting the test medium is also an important parameter. Each sample was kneaded mechanically in separate test chambers and the drug release was followed by sampling and HPLC analysis. Formulations prepared from different gum were tested and the obtained results demonstrate satisfactory release curves for a variety of formulations and active ingredients. The tested gum formulations include xylitol, nicotine, meclizine, and dimenhydrinate. The apparatus proved to be suitable not only in product control of commercial batches but also a useful tool in the research and development of medicated chewing gum formulations . General Comments about

**Apparatus I and Apparatus II** Both the apparatus described have been well studied and reported in the literature . The results show that the apparatus can provide strong mechanical forces that influence drug release and can prove to be a useful tool for drug release. In-vitro testing The absorption of active substances through the buccal mucosa can be examined by both in vitro and in vivo methods. The most common method utilizes chamber where excised buccal mucosa (either from human or animal) is placed as a barrier between two chambers. The active substances transported across the mucosa can be measured by withdrawal of samples from each chamber. Oral cavity made up of Porcine is recommended, as it is morphologically similar to human oral cavity . Likewise, a human TR146 cell culture model has proven a good invitro model for investigating permeability, permeability mechanisms, effects of chemical enhancers, and toxic effects [

## **CONCLUSION**

The study concludes the possibility of the formulation of the directly compressible MCG of DM

using HealthinGum(gum base) with the improved taste by using combination of the sweeteners. The first pass metabolism associated with DM can also be solved by the MCG, as the main site of absorption is buccal. The MCG formulation of DM is a novel approach for the treatment of nausea and vomiting associated with motion sickness and other pathophysiological conditions. MCG can increase patient compliance and patient acceptance as well as increase the bioavailability of DM as it showed significant permeation through buccal mucosa.

### Future Trends

For most drugs there are realistic possibilities of formulating them into a suitable chewing gum delivery system, although active agents with an extremely bitter taste may not be suitable candidates. Poorly water-soluble drugs require specialized formulation techniques to promote release, and these techniques are reasonably well developed. Dental health chewing gum for caries prevention has come to stay and the indications are that it will be accepted widely in future. Although, it has a good potential to become a convenient alternative approach to improve patient compliance, it still remains as a field to be explored to the fullest. Chewing gum not only offers clinical benefits but also an attractive, discrete and efficient drug delivery system. Nowadays more and more disease can be treated with Novel Drug Delivery Systems. Generally, it takes time for a new drug delivery system to establish itself in the market and gain acceptance and popularity by the patients, however chewing gum is believed to manifest its position as a convenient and advantageous drug delivery system as it meets the high quality standards of pharmaceutical industry and can be formulated to obtain different release profiles of active substances. Finally, in the future, we may see that more and more drugs formulated into chewing gum in preference to other delivery systems to deliver drugs locally to the oral cavity. The reason is simple that the chewing gum delivery system is convenient, easy to administer anywhere, anytime and its pleasant taste increases the product acceptability and patient compliance

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