Original Article

Periodontal Gel For The Targeted Drug Delivery In The Periodontal Cavity For Management Of Periodontitis And Gingivitis.

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Abstract

When medications are taken orally or through another route into the systemic circulation, their blood concentration steadily rises and peaks (C max) after a few hours. Based on the medication's physicochemical makeup, the drug's pharmacokinetics (ADME). A maintenance dose must be given when the medication level is expected to be reduced or close to the efficacy threshold after achieving the peak plasma concentration (C max) in blood [1]. We can now distribute medications to the systemic circulation in a controlled and precise manner for longer pharmacological action, minimize the frequency of dose and unpleasant effects, improve patient compliance, and give the desired impact. Since several processes occur after a medication is administered at the application site and before it reaches the target location in CDDS, its concentration in the blood is frequently affected by metabolism and excretion, making it difficult to notice the desired impact. This issue can be solved by injecting the medications right into the affected area, allowing a lower dose to produce the desired effect. Local drug delivery systems are more effective since they are less expensive, more stable, less toxic, biocompatible, and biodegradable. The proper management of a patient with periodontitis and gingivitis, the utilization of periodontal pockets as a site for the application of medication, the design of an appropriate dose form, and its potential benefits are the main topics of this review. A unique technique for treating diseases like periodontitis and gingivitis could be useful in a more effective treatment since the microorganisms in periodontal pockets could seriously destroy periodontal tissues.

Keywords: Periodontitis, gingivitis, Gel, Intra-pocket, periodontal, targeted delivery system

1. INTRODUCTION:

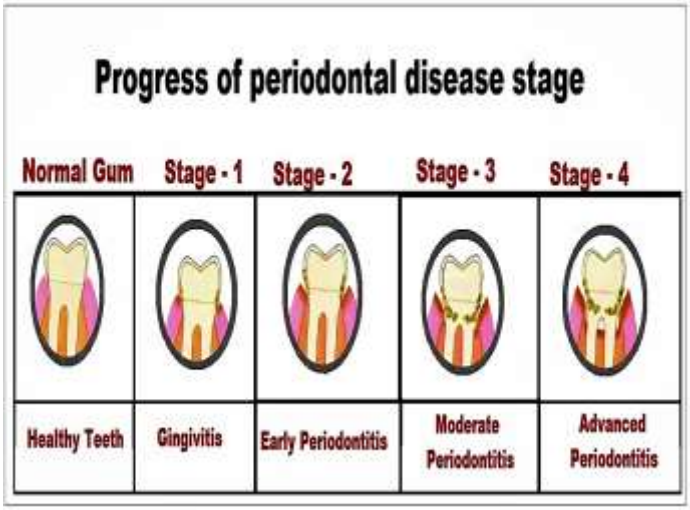
1.1 PERIODONTITIS

The most prevalent types of periodontal disease are gingivitis and periodontitis. The word periodontitis is derived from the Greek words "peri" and "odont," which mean "around" and "tooth," respectively. Many inflammatory diseases can affect the periodontium, the tissues surrounding and supporting teeth [1]. Progressive bone loss surrounding the teeth is a symptom of periodontitis, which can also lead to loosening and eventual tooth loss as well as the development of a periodontal pocket. Gingivitis is the term for gingival inflammation, while periodontal disease is the term for increasing periodontal tissue inflammation accompanied by the loss of alveolar bone. Periodontitis is caused by the accumulation of numerous layers of germs on a tooth's surface, which may trigger an overly aggressive immune response to the microorganisms [2,3,4]. Various anaerobic types of bacteria cause chronic periodontitis, such as Porphyromonas gingivalis, Aggregatibacter (Actinobacillus) Bacteroides forsythias, Treponema denticola, Prevotella intermedia, Fusobacterium nucleatum, and Eubacterium species. A significant part of chronic periodontitis is also played by microaerophile bacteria like Actinomyces actinomycetemcomitans, Campylobacter rectus, and Eikenellacorrodens. [5]. Plaque, a multi-layered microbial film made of bacteria, stays on the teeth for around two or three days. Over time, plaque hardens under the gum line and turns into tartar, also known as calculus. Tartar acts as a bacterial reservoir and is more challenging to remove than plaque [3,6,7]. Teeth surface damage from plaque and tartar buildup results from prolonged accumulation. Inflammation and irritation primarily affect the gingiva, and this causes pockets to form between the gums and teeth as a result of the accumulation of plaque, tartar, and germs. Long-term deposition increases the depth of the pockets because more bacteria are deposited there. This, together with early infection, promotes the loss of periodontal tissue and jaw bone [8,9,10]. Plaque deposition is typically the first sign of periodontitis. Periodontitis develops progressively if untreated. Plaques develop when food is deposited and interacts with bacteria. Plaque that has been let to accumulate over time is known as tartar or calculus. Periodontitis will result from this calculus. Caton and his colleague (2018) (6) established that there are two types of periodontitis. Tonetti, Greenwell, and Kornman (2018) state that the first category's (7) four stages are divided into groups based on the intensity and complexity of management. Periodontitis is

divided into four stages: stage I, starting periodontitis; stage II, moderate periodontitis; stage III, severe periodontitis with the possibility of further tooth loss; and stage IV, severe periodontitis with the possibility of dentition loss. Based on the likelihood of rapid advancement and the anticipated response to treatment, the second group has three categories. Grading systems include grade A for sluggish progression, grade B for moderate progression, and grade C for quick progression. Periodontitis is still very common around the world, especially severe periodontitis, which is the sixth most common disease in humans. (8) Teeth may be lost as a result of severe periodontitis, which has an effect on both function and appearance. Any age may be impacted by different types of periodontitis. (9)

Fig: I Plaque formation in Periodontal cavity

Fig: II Progress of periodontal disease stage [1]

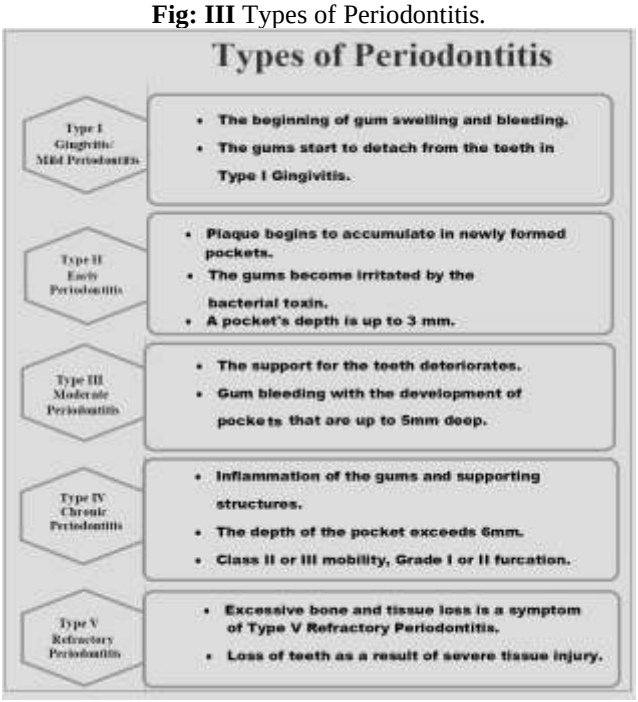


2. MOST COMMON APPROACH FOR THE TREATMENT OF PERIODONTITIS [38]

Oral medication delivery is employed to treat numerous local and systemic diseases. The soft tissues and bones that support the teeth are harmed by periodontitis, an inflammatory condition of the gums. To achieve a therapeutic effect during the treatment of periodontitis, the peak plasma concentration of antibacterial drugs should be maintained [11–14]. Periodontitis treatment focuses on suppressing and eradicating subgingival microorganisms that cause plaque formation. Using a variety of delivery devices, including strips, gels, films, and implants, it is possible to distribute medication in a targeted and regulated manner [15–16]. Antibiotic systemic administration may result in the development of host cell resistance to lessen these unwanted effects. A method that has to be investigated is using local drug delivery systems to give an adequate number of antibiotics that can sustain medication concentrations in the afflicted area to improve the effectiveness of periodontal disease therapy while also minimizing side effects [18]. Removing plaque and tartar from teeth is necessary for the treatment of periodontitis, as the diseased tissues near a tooth usually heal quickly on their own.

Periodontitis that has advanced stages is challenging to treat with standard dental techniques. Dental surgery can be used to remove dental plaque and tartar from the affected gum tissue. The main objectives of treatment for people with chronic periodontitis are to lessen inflammation, stop the disease from progressing by lowering etiologic variables that are less than the threshold value, and stop tissue disintegration so that tissues can heal. Direct drug application into the afflicted area, such as a periodontal pocket, is more advantageous in terms of preserving therapeutical concentration at the site of action and preventing negative drug effects like gastrointestinal intolerance, depression, etc. The pathogenic population and the symptoms of periodontitis can be defeated by direct distribution of the active ingredient at the afflicted area within the periodontal pockets.

Fig: III Types of Periodontitis.



2.1. Conventional/ Nonsurgical Periodontal treatments therapy:

The purpose of treatment is to halt bone degradation by preventing and treating contaminated tissue, reducing the number of contagious bacteria, and shallowing pockets. Scaling and root planing are the mechanical, predictable methods of pocket exclusion that are targeted at getting rid of plaque, diseased and dead tissue lining from the gingival and periodontal gaps. Due to a lack of instruments that can effectively remove pathogens from deeper tissues, the mechanical approach alone is unable to completely eradicate hazardous germs; considerable amounts of trace bacteria are left behind and are therefore likely to recur. After scaling and root planning, harmful flora traces continue regenerating colonies. After a single periodontal debridement procedure, a pathogenic subgingival microorganism may regrow with good oral hygiene in 42 to 60 days. Even after numerous sessions of subgingival cleaning and meticulous supragingival plaque control, pathogen regrowth within deep periodontal gaps occurs in 120–240 days.

2.2. Antibiotic Systemic therapy:

Antibiotics can be used locally by either directly inserting the active ingredient into the subgingival cavity or by placing the active ingredient inside a periodontal cavity-appropriate device. To provide prolonged release, local administration of the active ingredient requires a high-loading dose and many applications [39]. The use of antibiotic medication in the treatment of periodontitis aids in reducing or eliminating microorganisms that are challenging to eradicate using instrumentation techniques. Tetracyclines, imidazole derivatives, fluoroquinolones, and other regularly used antibiotics can be given either systemically or locally. The two primary categories of antibiotics used to treat periodontitis are broad-spectrum antibiotics and narrow-spectrum antibiotics. Penicillin, amoxicillin, cephalexin, macrolides, and tetracyclines are a few examples of narrow-spectrum drugs. They are not very efficient against aerobic and anaerobic -lactamase producers and other pathogens since they have low antibacterial efficacy against pathogenic flora. Based on the idea that a pathogen causes periodontitis and that the presence of the active ingredient in the afflicted area can maintain the necessary level of medication to eliminate infections, systemic therapy against periodontitis-causing substances. The systemic administration of antibiotics can cause several serious issues, including irregular drug activity caused by factors like poor oral absorption, drug loss from first-pass metabolism, the need for more concentration at the application site during systemic circulation, and bacterial resistance to the antibiotic. Amoxicillin, ciprofloxacin, metronidazole, tetracyclines/doxycyclines, erythromycin, and clindamycin are among the antibiotics that can be administered systemically to treat periodontitis. However, systemic antibiotic administration has drawbacks. Since gingival tissues are poorly perfused organs, they absorb less of the active ingredients rich in infected tissue, and regular use of systemic antibiotics increases pathogen resistance to medication, high concentrations are necessary for effective therapy. However, we can reduce the danger by applying antibacterial medications locally. Systemic administration of antibiotics may encounter risks, particularly resistance and superinfections after long-term applications, and may deliver a low benefit-to-risk ratio that is intolerable. By keeping a therapeutic concentration of the active component at the site of action for the necessary amount of time to eradicate all infections, periodontitis can be effectively treated. For the treatment of periodontitis, controlled-release devices that apply the active component directly to the affected area have significant advantages over systemic applications.

2.3. Local Medicament Delivery:

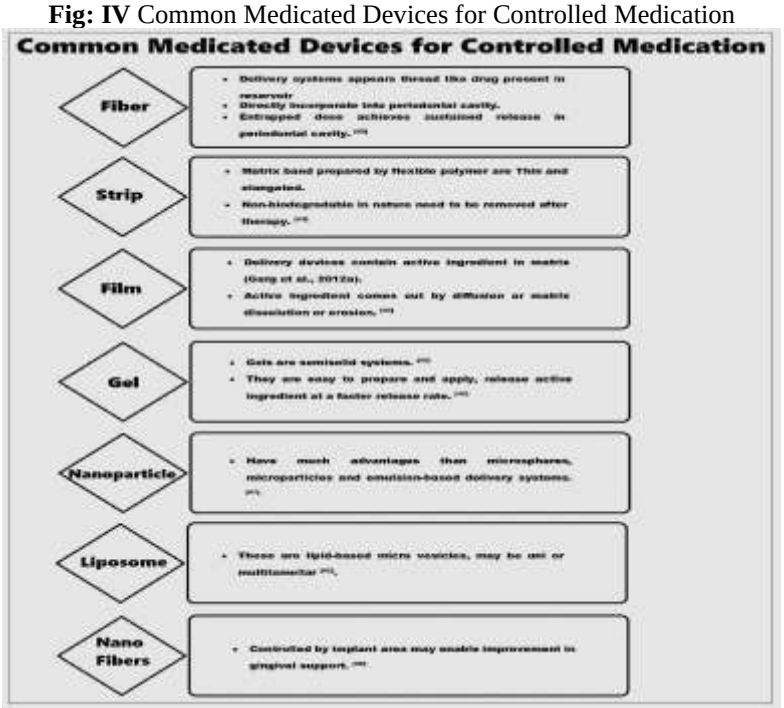
Local delivery systems are intended to deliver the active ingredient directly to the site of action within the periodontal gap, but in the absence of a release and retention mechanism that is suitable, it is challenging to maintain the therapeutic level of the active ingredient for a longer period to achieve a more effective treatment strategy. The medication concentration at the site typically increases and decreases exponentially with such devices. Antimicrobial medications delivered locally provide focused use, require a smaller dosage than when administered systemically, and release medication in a regulated manner over an extended period. Less medication is needed in these systems, and there is no evidence of antibiotic resistance. Local applications (such as mouthwash, gels, toothpaste, etc.) only stop supragingival plaque and pocket formation; high initial concentrations and frequent use are needed to offer persistent benefits. Direct subgingival application of the active ingredient can be accomplished, as can inserting the active ingredient in a suitable device that can hold the active ingredient at the diseased location for a long enough amount of time. Many medications, including tetracycline and chlorhexidine, are used as mouthwashes in the treatment of periodontitis. Direct delivery of the active ingredient by subgingival administration is possible, however regulated release is not possible. There are two different types of drug delivery systems used to apply the active component locally. First is intended to transfer the active component directly to the region's tissue, known as the periodontal gap, however without the proper drug delivery mechanism, drug recantation devices are unable to demonstrate a greater impact. Large variations in drug concentration are produced at the application site by local delivery systems. Devices of the second kind, controlled release local delivery systems, serve to keep the antibacterial effect at the site of infection for a longer period. Today's key area of interest in controlled-release drug delivery systems is the development of devices that are loaded with active ingredients and are placed directly in the periodontal cavity. Such delivery methods show great promise for the treatment of periodontitis. With the use of an appropriate carrier, the active ingredient is directly incorporated into delivery systems to allow sustained release. Agent effects on other body parts are reduced by the direct delivery of active components into the periodontal cavity. Devices used for local medication delivery for periodontitis can either impart a continuous or a sustained release of the medication. Non-sustained administration methods release additional medication into the subgingival cavity and keep high pocket concentrations there for a considerable amount of time.

Subgingival irrigation can be used to provide antimicrobials in various dose forms, such as fiber, gel, or films, to the per iodontal cavity and tooth surfaces.

2.4. Controlled Drug Delivery System (CDDS):

Controlled ejection Fibers, films, or strips are appropriate local drug delivery methods for this purpose because they retain the concentration of the active component with a carrier to offer regulated releases at local tissue for a prolonged length of time at the site of infection. Utilizing technology, these devices assist in achieving regulated release and guarantee sustained concentrations of the active substance in local tissue after a single administration. There are numerous varieties of delivery systems for local deliveries (i.e., intra-pocket devices)

Fig: IV Common Medicated Devices for Controlled Medication



2.5 Different types of Controlled Medicament Delivery Devices

The controlled release devices are classified into the following groups [22, 23]

2.5.1 Reservoir devices:

The membrane diffusion system comprises a dialysis tube that is ready to be inserted into the periodontal cavity for roughly a week and contains a solution of the active ingredient. Reservoir devices that slowly and carefully release the active substance from hollow fibers, gels, and dialysis tubing. [22] Reservoir systems can be divided into two groups: immediate-release devices, which release the active component slowly over time, and sustained-release devices, which release the medication more quickly.

2.5.2. Monolithic devices:

Devices with a single active component spread throughout a solid polymer matrix, such as acrylic or ethylene-vinyl acetate. About 0 to 2 mm thick acrylic strips make up this product. About 10 to 14 days after the active ingredient is released, the medication concentration in the local tissue is maintained. Strips composed of cross-linked collagen sheets, polyethylene glycol, hydroxypropyl methylcellulose, and [24] ethyl cellulose are examples of monolithic devices. [25] Materials that are bioabsorbable and biodegradable are used to include active ingredients and limit the risk of elimination from the application site. They also lessen the likelihood that risks will arise from polymer retention. Through the diffusion of the active ingredient, a drug from monolithic devices is released. Non-erodible monolithic devices with polymers that maintain their integrity even after the medication have been entirely withdrawn. Monolithic structures that degrade cause the release of active substances.

2.5.3. Others:

White petrolatum and polyethylene oxide make up gels. Gels are simple to use to fill syringes and implant in periodontal cavities, but a drawback is that the medicine releases quickly at the site, which means it can drain out of the cavity. Hybrid devices have certain extra qualities that allow them to stay in cavities for a longer period, such as microencapsulated polymer spheres that are monolithic devices with a diameter of around 0.2 mm and packed with the active ingredient. The formulation contains medicine inserted in a cavity and is made of thermosetting gel, which after application at body temperature, becomes more viscous and releases the active component by producing a thin film. Other processes involve "calendaring," in which polymer is mixed with heated rollers to create a film. Polymers are dissolved in a solvent using the solution casting method to generate a viscous solution. The solvent is kept to evaporate before being spread on the lubricated surface. The surface is collected using prepared film.

2.6. Intra-Pocket/Periodontal route for controlled Medicament Delivery Systems

Modern drug administration methods like intra-pocket systems provide benefits such as fewer side effects, higher value, and better patient compliance. [20] The main benefit of treating periodontal diseases with local delivery systems is the direct placement of the active ingredient into the periodontal cavity, which allows for greater accessibility and concentration at a level that has a long-lasting bacteriostatic or bactericidal effect on the affected area. [20] The periodontal cavity provides a natural reservoir that is advantageous for the installation of a drug-containing device because it causes a 40-fold increase in the flow rate of gingival crevicular fluid (GCF) compared to normal. [19] A suitable medium for both medication release from the dosage form and drug distribution throughout the pocket is provided by the GCF. [20] These characteristics make the periodontal pocket a natural location for treatment using local delivery systems since periodontal disorders are limited to the area immediately surrounding the pocket. [20] To satisfy pharmacological and biological requirements, intrapacket medication delivery devices are developed using biodegradable and biocompatible polymers of natural, synthetic, or semi-synthetic origin. [20] Many active components, including antiseptics, antimicrobials, and host response modifiers like anti-inflammatory drugs, growth factors, and enamel derivative matrices, have been explored for local delivery direct in the periodontal cavity. Compared to conventional methods, local controlled delivery systems offer focused distribution of active ingredients and require a lower dose. Reduce dose frequency while maintaining sustained release and patient compatibility.

2.7 Intra-Pocket/Periodontal Device for Controlled Medicament Delivery Systems

The most popular intra-pocket medication administration method films. Films are a form of matrix drug delivery system where the drug is dispersed throughout the matrix and released through erosion, matrix dissolution, or drug diffusion. Comparing this technology to previous intra-pocket medication delivery systems reveals several advantages. While films that release the medication via diffusion and matrix erosion or dissolution are made with water-soluble or biodegradable polymers, those that release the medication by diffusion alone use non-degradable, water-insoluble polymers. Using ethyl cellulose and a solvent evaporation technique, several nonbiodegradable periodontal films of chlorhexidine diacetate, metronidazole, tetracycline, and minocycline have been created. Films made of ethylene cellulose exhibited prolonged drug release; when compared to ethanol as a casting solvent, the use of chloroform considerably slowed the medication's rate of release. However, the films' addition of polyethylene glycol increased the medication's rate of release, and the amount of medication and the casting solvent both affected the rate of release.

Fig: V Various devices for controlled medicament delivery [50]

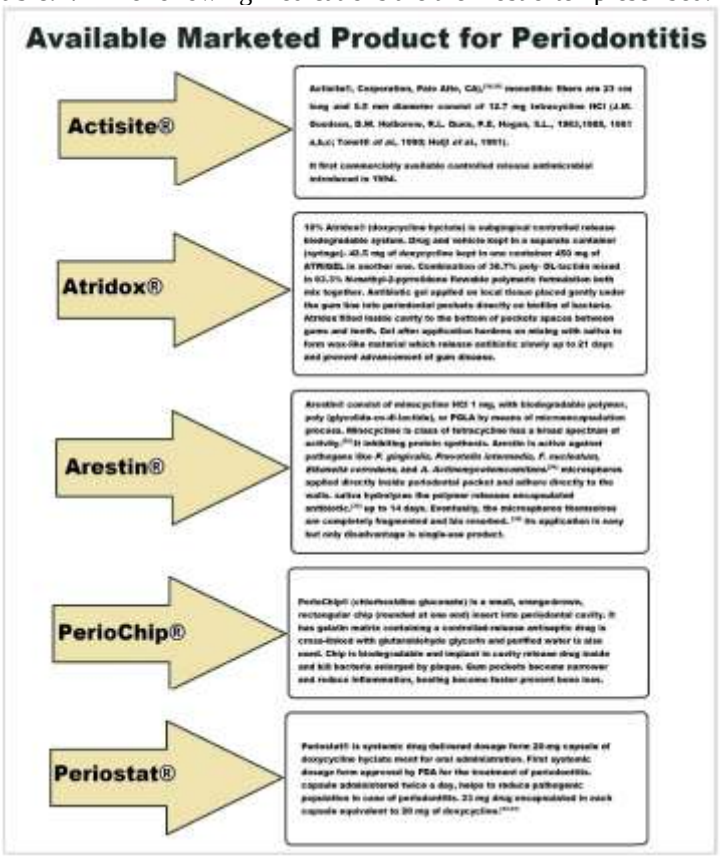
2.7.1. Advantage of periodontal controlled Medicament Delivery system [40]

• It ought to be very patient-compatible.
• The therapeutic concentration should be present at the site of action.
• It needs to be economical.
• It should prevent the digestive issues that are typically present with systemic administration.
• Due to the high number of blood arteries, drugs are absorbed quickly compared to when they are applied systemically.
• First-pass metabolism can limit medication loss through the liver.
• Improve medication efficacy.
• The action lasts a long time.
• It is easy and painless to apply.

3. MARKETED ANTIMICROBIAL PRODUCTS FOR CONTROLLED MEDICAMENT DELIVERY

Degradable and non-degradable intra-pocket devices are the two primary categories. The main benefit of non-degradable devices is that we can manage their application and removal, giving us significant control over the cavity's exposure time. The use of degradable devices decreases patient non-compliance by requiring only one visit from the patient to the therapist for device insertion. [27]

Table: VI The following medications are the most often prescribed.[28]



4. MUCOADHESIVE GEL FOR PERIODONTAL CAVITY

4.1. PATHOPHYSIOLOGY OF ORAL MUCOSA:

This idea states that after adhesion, two surfaces must be driven apart. The fracture strength is transformed into an equivalent adhesive strength using the following equation. This idea is useful for the tensile apparatus research of bioadhesion.
Based on function and histology, there are three basic kinds of oral mucosa:
Lining mucosa the majority of the oral cavity's nonkeratinized stratified squamous epithelium, including the:

Alveolar mucosa between the buccal and labial mucosa lining. It is a brighter red, smooth, shiny structure with numerous blood arteries, and there are no rete pegs holding it to the surrounding tissue. [6]

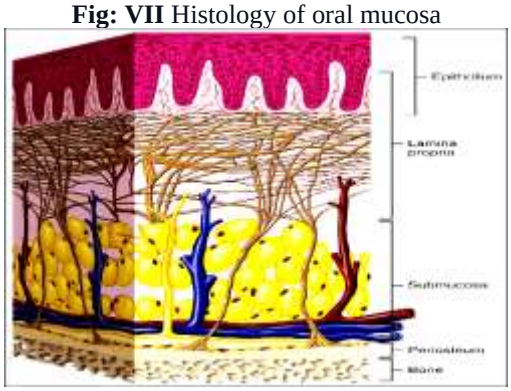
The buccal mucosa is the mucosa that lines the interior of the cheeks.

Labial mucosa the mucosa that lines the inside of the lips;[7]

Masticatory mucosa squamous epithelium that is stratified and keratinized; it is present on the connected gingiva, hard palate, and dorsum of the tongue.

Specialized mucosa there are nerve endings for both general sensory reception and taste perception on the tongue's dorsal surface, more especially in the areas of the taste buds on the lingual papillae. [8]
The surface stratified squamous epithelium, and the deeper lamina propria make up the two layers that make up the oral mucosa. The epithelium in keratinized oral mucosa has four layers:
· Stratum Basale (basal layer)
· Stratum spinosum (prickle layer)
· Stratum granulosum (granular layer)
· Stratum corneum (keratinized layer)

Fig: VII Histology of oral mucosa



1. Gingiva

The lamina propria, an underlying connective tissue, and the highly keratinized epithelium that surrounds the teeth make up the gingiva. The surface area for epithelial attachment to the connective tissue is increased by the considerable interdigitation with the lamina propria. You can see the change from keratinized gingiva to nonkeratinized mucosa on one side of the slice.

2. Tooth

Since the tissue has been decalcified (enamel is approximately 95% mineral), the tooth in these pieces is missing its outer coating of enamel. However, the dentin matrix as well as the cementum and neighboring matrix of the mandibular alveolar bone, have been well preserved. Since this tooth has several roots, relatively few slides show the entire length of the root. However, the periodontal ligament should be visible in excellent areas. Linking the alveolar bone to the root cementum. Using a light microscope, you may see Sharpe's fibers insertion into the alveolar bone and root cementum if you close the iris diaphragm. Note the substantial vascular supply that goes in (an interconnected network of) loose connective tissue to the periodontal ligament.

4.2. THEORIES OF MUCOADHESION

4.2.1. Wetting Theory of Mucoadhesion

Perhaps the first accepted theory of adhesion is the wetting theory. It works best with liquid or bioadhesives with low viscosity. It describes adhesion as an embedding process in which adhesive chemicals enter the substrate's surface

imperfections and eventually harden, creating numerous sticky anchors. The adhesive must overcome any surface tension effects at the interface in order to travel freely across the substrate's surface.[46]
The work done is related to the surface tension of both the adhesive and the substrate, as given by Dupre's equation;
$\omega A = \gamma b + \gamma t - \gamma b$
where ωA is the specific thermodynamic work of adhesion and γb, γτ, and γbt represent, respectively, the surface tensions of the bioadhesive polymer, the substrate, and the interfacial tension. The adhesive work done is a sum of the surface tensions of the two adherent phases, less the interfacial tensions apparent between both phases.[7] Figure 1 shows a drop of liquid bioadhesive spreading over a soft-tissue surface.

4.2.2. Electrostatic Theory of Mucoadhesion

According to electrostatic theory, electrons are transferred between the adhering surface and adhesive interface. Due to a number of attraction factors, the electrical double layer is created at the interface and is responsible for sustaining contact between the two layers. [48]

4.2.3. Diffusion Theory of Mucoadhesion

According to diffusion theory, polymeric chains from the bioadhesive interpenetrate into glycoprotein mucin chains and enter the opposing matrix deeply enough to permit the creation of a semi-permanent connection. [49] The procedure can be seen starting at the first point of contact. Until an equilibrium penetration depth is reached, concentration gradients will force the bioadhesive's polymer chains into the mucus network and the glycoprotein mucin chains into the bioadhesive matrix.

4.2.4. Adsorption Theory of Mucoadhesion

The surface forces between the chemical structures at the two surfaces, according to the adsorption theory, lead materials to adhere after initial contact between two surfaces. [52] Polar molecules or groups reorient at the connection when they are present. [48] Adhesion can lead to chemisorption if it is very strong. According to the hypothesis, one or more secondary forces—van der Waal's forces, hydrogen bonds, and hydrophobic bonds—are what ultimately cause adherence to tissue. [53–55]

4.2.5. Fracture Theory of Adhesion

According to this hypothesis, two surfaces must be forced apart following adhesion. The following equation converts the fracture strength to an equivalent adhesive strength. For the study of bioadhesion by tensile apparatus, this theory is helpful.
$\sigma = (E \times \varepsilon/L)1/2$
where σ is the fracture strength, e fracture energy, E young modulus of elasticity, and L the critical crack length.

4.3. Kinetics of Topical Permeation[51-53]

To successfully create topical systems, it is essential to have a solid understanding of skin penetration kinetics.
The following procedures are involved in topical medication permeation:
a. The stratum corneum's sorption
b. Drug penetration through healthy epidermis
c. Drug absorption by the dermal papillary layer's capillary network
If the medicine contains particular Physico-chemical properties, this penetration may be conceivable.
The formula for the rate of permeation across the skin (dQ/dt) is

$$\mathbf{dQ / dt = P_s (C_d - C_r)} \qquad \textbf{Eq. 1}$$

Where,
Cd stands for the skin penetrant concentration in the donor compartment (e.g., on the surface of the stratum corneum)
Cr stands for the concentration in the receptor compartment, such as the body.
Ps = Skin tissue's overall permeability constant to penetrant

$$\mathbf{P_s = (K_s D_{ss}) / h_s} \qquad \textbf{Eq. 2}$$

Where Ks is the partition coefficient for the penetrant molecule's interfacial partitioning from a solution medium.
hs is the total thickness of skin tissues, and Dss is the apparent diffusivity for the steady state diffusion of the penetrant molecule through that thickness.
A skin penetrant's permeability coefficient (Ps) can be thought of as constant since Ks, Dss, and hs are constant under the circumstances.
It is obvious from Eq. 1 that a constant rate of drug permeation can only be achieved when Cd>>Cr, i.e., the drug concentration at the stratum corneum's surface is constantly and significantly higher than the drug concentration inside the body.:

$$\mathbf{dQ / dt = P_s C_s} \qquad \textbf{Eq. 3}$$

Permeability coefficient = (KsDss) / hs = 1 / resistance

4.4. POSITIVE ASPECTS:

Due to a number of benefits, topical drug administration has recently become more popular in order to ensure optimal cutaneous and percutaneous drug delivery:

i. To prevent drug interactions with food and drink and problems with gastrointestinal drug absorption brought on by gut pH, enzymatic activity, and drug.

ii. To prevent the first pass effect, which is when a pharmacological material passes through the systemic and portal circulation for the first time after being absorbed through the gastrointestinal tract, potentially preventing the drug's deactivation by digestive and liver enzymes.

iii. Non-invasive, with patient cooperation.

iv. Less oily and simple to wash off the skin.

v. Economical and easy to prepare.

vi. Lower dosages when compared to oral administration types.

vii. Localized impact with few adverse consequences.

4.5. NEGATIVE ASPECTS

I. The wide range of solubility in the vehicle component and the large range of cutaneous fluxes make the entire drug unsuitable for such a delivery method.

ii. The small number of drugs that can be delivered by this route due to the skin's barrier qualities and dose size.

iii. A number of skin-related factors, including age and health, can impair the system's dependability in delivering medication.

5. CONCLUSION:

To address several significant issues associated with current systems, such as the active ingredient not reaching target areas in the requisite concentration, controlled devices for drug administration need to be investigated. Controlled drug delivery systems are more accurate and efficient and lower dosage and side effects while also ensuring patient compliance. This device can overcome numerous drawbacks associated with oral administration of the active ingredient. The ideal alternative to conventional dosage forms for dental formulations that target the periodontal cavity is controlled delivery systems, and their potential for clinical application in this rapidly expanding area is high. [36] The research will be useful to develop more physiologically suitable and commercially viable delivery systems as an alternative to the surgical and non-surgical treatments used in conventional systems, designing of controlled release, low dose, targeted medicament delivery devices. This is because systemic antibiotics can now be delivered with controlled medication using targeted devices. Compared to standard systemic administration, these devices are more efficient, practical, and simple to use. The future development of precise, appropriate, practicable, and promising targeted devices for controlled delivery systems is unquestionably paved by this progress.

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