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# A review: Treatment of gingivitis by buccal patches

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**Abstract**
Most of the population are affected by prevalent diseases which affect the oral cavity mostly inflamed gums every now and then. Several diseases can affect the mouth, such as oral cancer, dental caries, Lichen Planus and, of course, periodontal disease with its variants. This review discusses gingivitis, a gum inflammation usually doesn't cause any major problems at first but when left untreated it may lead to tooth damage. Later it may spread to other parts of the oral cavity, the term periodontitis is nothing but the inflammation in the periodontium the soft tissue and bone which is responsible to keep our tooth firm. As the time precedes, this periodontitis. May lead to loosen the teeth. This article also discusses the usage of buccal patches a novel delivery route for the treatment of red, swollen and bleeding gums of gingivitis.

**Keywords:** Gingivitis, periodontitis, buccal patches, bleeding gums, oral cancer, lichen planus, dental caries

## Introduction

### Definition [1, 2]

Gingivitis explains the inflammation of the gingivae, which is a reversible form of periodontal disease characterized by inflammation of the gingivae in response to a mature dental plaque biofilm. Which includes swelling, redness, influx of inflammatory cells, edema in the tissue, change of normal contours, and bleeding. Gingival pockets from tissue swelling and loss of attachment not involving bone are usually present.

### Pathophysiology [3, 4]

- The most common type of gingivitis involves the marginal gingiva and is brought on by the accumulation of microbial plaques in persons with inadequate oral hygiene.
- The inflammation proceeds through an initial stage to produce early lesions, which then progress to advanced disease.
- The initial stage which begins within 4 or 5 days of plaque accumulation is acute exudative inflammatory response which in turn increases gingival fluid and transmigration of neutrophils. Due to this deposition of fibrin and destruction of collagen can be seen priorly.
- At approximately 1 week, transition to early lesions is marked by the change to predominately lymphocytic infiltrates. Monocytes and plasma cells also may be present. Within the time, lesions become chronic and are characterized by the presence of plasma cells and B lymphocytes. As chronic local inflammation progresses, pockets develop where the gingiva separates from the tooth.
- Further the pockets may bleed during tooth brushing, flossing, and even normal chewing which gets deepen. As this inflammation continues, there may be break down of periodontal ligaments and destruction of the local alveolar bone is seen. Finally the Tooth loosen and falls out eventually.

Acute necrotizing ulcerative gingivitis (ANUG) is a completely different syndrome caused organisms such as Prevotella intermedia, alpha-hemolytic streptococci, Actinomyces species, or any of a number of different oral spirochetes which is an acute infection of the gingival. ANUG may result in accelerated destruction of affected tissues, as well as local or systemic spread of infection.

Noma (Cancrumoris) is a syndrome in which ANUG spreads beyond the gingiva. The infection invades local tissues of the mouth and face.

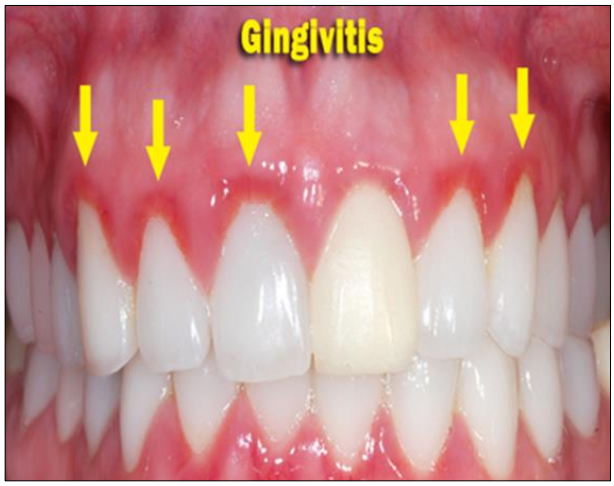



**Fig 1:** Inflammation of Gingiva

**Causes** [4]

Gingivitis is a bacterial infection of the gums. Several theories exist but the exact reason why gingivitis develops has not been known.

When a bacterium from dental plaque invades adjacent tissues, plaque deposition at the gingival border causes an inflammatory response. As a result, pockets form between the gingiva and the tooth, causing gingival margin retraction and the development of an excellent environment for the disease-causing anaerobic bacterial growth. This, in turn, can lead to gingival tissue damage which can advance to periodontal attachment apparatus destruction.

These are the general causes for gingivitis:

- Blood dyscrasias
- Allergic reactions
- Endocrine disturbances, such as diabetes mellitus, drugs such as diphenylhydantoin or the heavy metals
- Chronic debilitating disease or local factors such as dental calculus or plaque
- Food impaction or
- Faulty dental restorations and dental hygiene.

In vulnerable people, persistent gingivitis can progress to chronic periodontitis. This results in irreparable periodontal tissue damage.

**Gingivitis Associated Factors** [5]

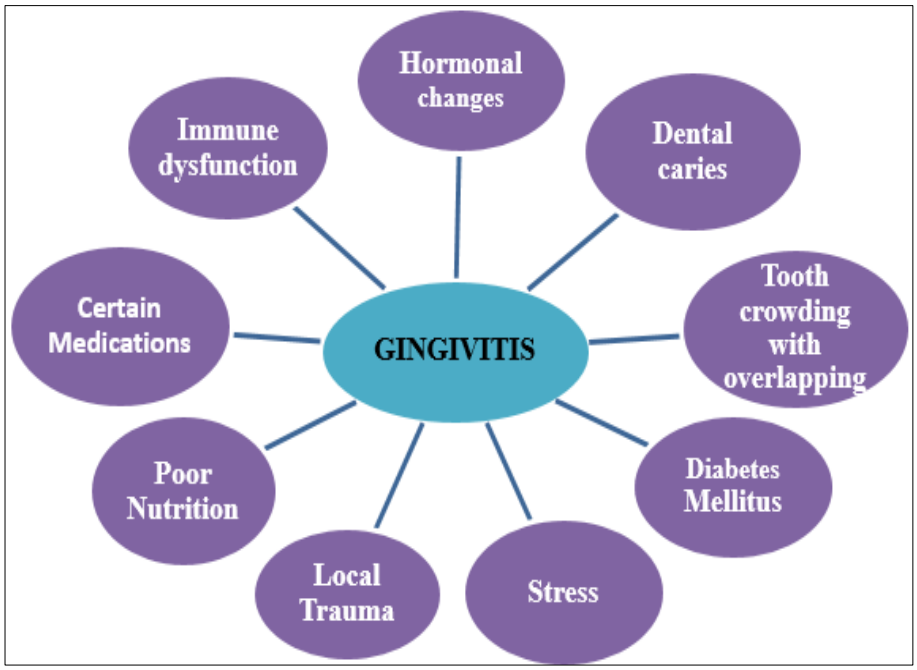



**Fig 2:** Factors Influencing Gingivitis

**Classification of gingivitis**

This inflammation of the gingiva is classified according to severity. It can range from mild to severe gingivitis, which are as follows-

a) According to duration
b) According to clinical appearance
c) According to etiology

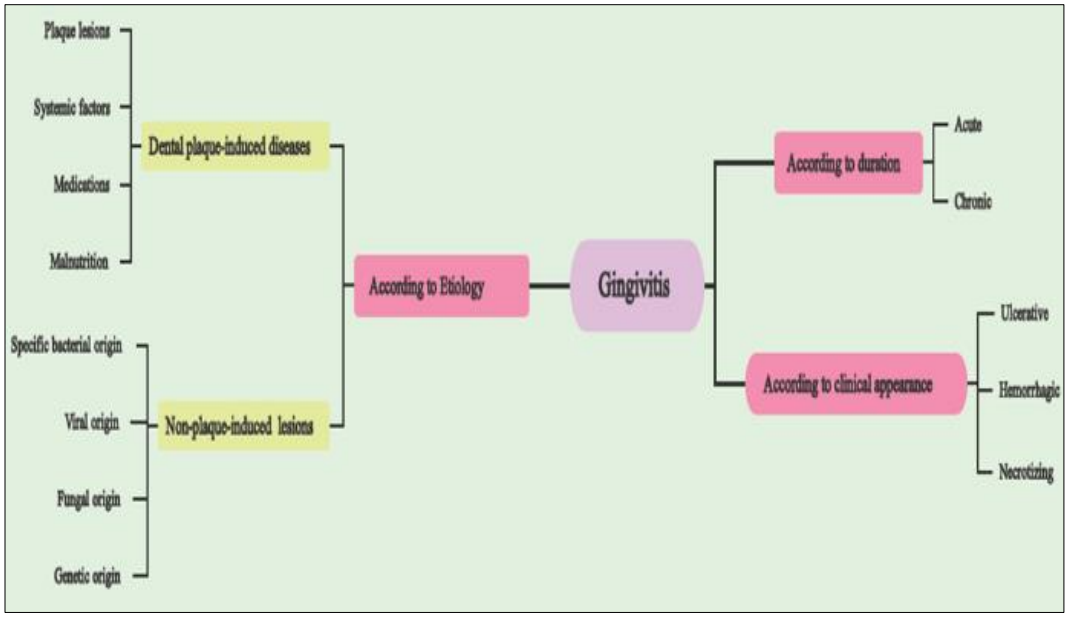



**Fig 3:** Classification of Gingivitis

**Signs and symptoms** [6, 7]

The typical indicators of inflammation that appear in the gum tissue as a result of gingivitis include:

- Swollen gums,
- Bright red or purple gums,
- Gums that are tender or painful to the touch,
- Bleeding gums or bleeding after brushing and/or flossing Bad breath (halitosis)

Additionally, when the gum tissue swells and stretches over the inflammatory underlying connective tissue, the stippling that some people's gum tissue normally has may disappear and the gums may appear shiny which may emit an unpleasant odour. The epithelial lining of the gingiva becomes ulcerated when the gingiva are swollen, and even light brushing and flossing will cause the gums to bleed more readily.

**Diagnosis of Gingiva**

A clinical diagnosis of gingivitis exists. This means that the doctor or dentist can make a diagnosis by asking about the patient's dental and medical history and doing an oral examination. Blood work, X-rays, and tissue samples may be indicated for people not responding to initial therapy. The person should, however, be evaluated for underlying disease that may cause gingivitis.

**Management or Prevention**

Gingivitis can be prevented through regular oral hygiene that includes daily brushing and flossing [8]. Hydrogen peroxide, saline, alcohol, or Chlorhexidine mouthwashes may also be employed. In a 2004 clinical study, the beneficial effect of hydrogen peroxide on gingivitis has been highlighted [9]. The use of oscillation-type brushes might reduce the risk of gingivitis compared to manual brushing [10]. Rigorous plaque control programs along with periodontal scaling and curettage also have proved to be helpful, although according to the American Dental Association, periodontal scaling and root planning are considered as a treatment for periodontal disease, not as a preventive treatment for periodontal disease. [11] In a 1997 review of effectiveness data, the U.S. Food and Drug Administration (FDA) found clear evidence showing that toothpaste containing Triclosan was effective in preventing gingivitis [12].

**Oral mucosal sites**

Three categories are used to categorize medication distribution within the oral mucosa.

1. Sublingual delivery system
2. Local delivery system
3. Buccal delivery system

**1. Sublingual delivery**

It is the introduction of medication to the systemic circulation through the sublingual mucosa, which is the membrane covering the ventral surface of the tongue and the oral cavity.

**2. Local delivery**

For the treatment of oral cavity disorders, primarily periodontal disease, fungal infections, and ulcers.

**3. Buccal delivery**

Is the process of delivering medication to the bloodstream through the buccal mucosa, which lines the cheek?

These oral mucosal locations are quite different from one another in terms of their anatomy, permeability to drugs, and capacity to hold a delivery system for the necessary amount of time [13,14].

**Introduction of Buccal Patches**

The placement of a drug delivery system in a specific area of the body has recently been the subject of intensive investigation in an effort to maximize biological drug availability and reduce dose-dependent side effects. So improving bioavailability through buccal medication administration is a highly effective method. The buccal mucosa has a rich blood supply, which allows the direct entry of drug molecules into the systemic circulation, making buccal drug delivery an appealing alternative to more traditional routes of systemic drug administration which acts as an excellent site for the absorption of drugs [15, 16].

Bypassing the first-pass metabolism and drug degradation in the gastrointestinal environment that are frequently associated with oral delivery, the buccal route promotes the direct entrance of drug molecules into the systemic circulation [17, 18, 19].

Therefore, many administration methods have been tested in novel drug delivery systems. Localized drug delivery to oral cavity tissues has been studied for the treatment of periodontal disease, bacterial and fungal infection; thus, localised drug delivery by retaining a dosage form at the site of action (e.g., within the GI tract) or systemic delivery by retaining the formulation in intimate contact with the absorption site (e.g. buccal cavity) [20].

Patients prefer buccal drug delivery because the buccal cavity is easily accessible for self-medication. Furthermore, buccal dosage forms allow drug absorption to be stopped quickly in the event of an adverse reaction. The use of mucoadhesive polymers in buccal drug delivery which includes adhesive tablets [21] gels and patches of which patches are preferable in terms of flexibility and comfort [22, 23].

**Components used in Buccal Patches [24, 25, 26, 27]**

a. **Active ingredient**.
b. **Polymers (adhesive layer):** Hydroxyethylcellulose, hydroxypropyl cellulose, polyvinyl pyrrolidone, polyvinyl alcohol, carbopol and other mucoadhesive polymers.
c. **Diluents:-** Lactose DC is selected as diluent for its high aqueous solubility, its flavouring characteristics, and its physico-mechanical properties, which make it suitable for direct compression. Other example: microcrystalline starch and starch.
d. **Sweetening agents:** aspartame, mannitol, etc.
e. **Flavouring agents:** Menthol, vanillin, clove oil, etc.
f. **Backing layer:** Ethyl cellulose, etc.
g. **Penetration enhancer:** Cyanoacrylate, etc.
h. **Plasticizers:** PEG-100, 400, propylene glycol, etc

**Method of Preparation of Mucoadhesive Patches**

Mucoadhesive buccal patches can be prepared by methods mentioned below:-

**1. Solvent Casting Method [28, 29]**

With this technique, each item was precisely weighed before being combined in a mortar and pestle. The mixture was then progressively introduced to a solvent system containing a magnetic stirrer. Up until a clear solution is obtained, keep stirring. The solution is then quantitatively transferred to petri dishes. The petri dish was covered with upside-down funnels to allow solvent evaporation. Depending on the solvent system utilised, these are stored at a temperature of 20-25ºC for 24–48 hours. The patches are carefully removed from the petri dish and measure 15 to 20 mm in diameter and 0.2 to 0.3 mm in thickness. In a desiccator, the created patches were kept for further evaluation tests.

**2. Semi solid casting**

Prepare a solution of a film-forming polymer that is water soluble before using the semisolid casting process. The resultant solution is mixed with an ammonium or sodium hydroxide-prepared solution of an acid-insoluble polymer (such as cellulose acetate phthalate or cellulose acetate butyrate). The correct amount of plasticizer is then added to create a gel mass. Finally, using heat control drums, the gel mass is cast into the films.

**3. Hot melt extrusion**

When compared to other pharmaceutical processing methods, the Hot-melt extrusion (HME) technology is a desirable replacement for conventional processing techniques. As polymers are still liquid during the extrusion process, they can serve as thermal binders, drug depots, or release inhibitors when they cool and solidify. There are fewer processing steps and time-consuming drying steps because solvents and water are not required. Independent of compression properties, a matrix can be massed into a larger unit. The rotating screw's intense mixing and agitation cause de-aggregation of suspended particles in the molten polymer, resulting in a more uniform dispersion, and the process is continuous and efficient. When a drug substance is solubilized or dispersed at the molecular level in HME dosage forms, its bioavailability may improve. Pharmaceutical Hot-Melt Extrusion processes are classified as either ram or screw extrusion.

**4. Solid dispersion extrusion**

Immiscible components are extruded with drug and then solid dispersions are prepared in this method. The solid dispersions are shaped into films by mean of dies finally.

**5. Rolling Method**

A drug-containing solution or suspension is rolled on a carrier in the rolling method. Solvents are primarily water or a mixture of water and alcohol. The film is dried on the rollers before being cut into the desired shapes and sizes.

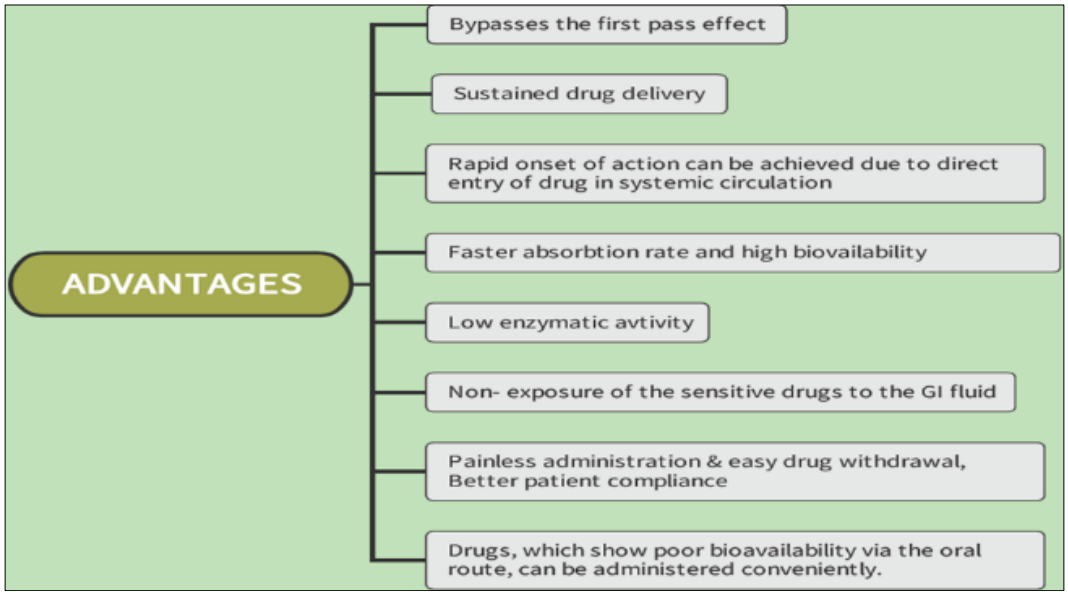
**6. Solvent evaporation method**

The required quantity of mucoadhesive polymer is treated with required volume of solvent system and heated on water bath to dissolve polymer properly than dissolve the drug in that solution by heating and add plasticizer in required quantity. Then resulting mixture was set aside for some time to remove any entrapped air and transferred into a previously cleaned petriplate. In a desiccator, the created patches were kept for the evaluation tests to be performed.

**Ideal characteristics of buccal patches [30, 31, 32]**

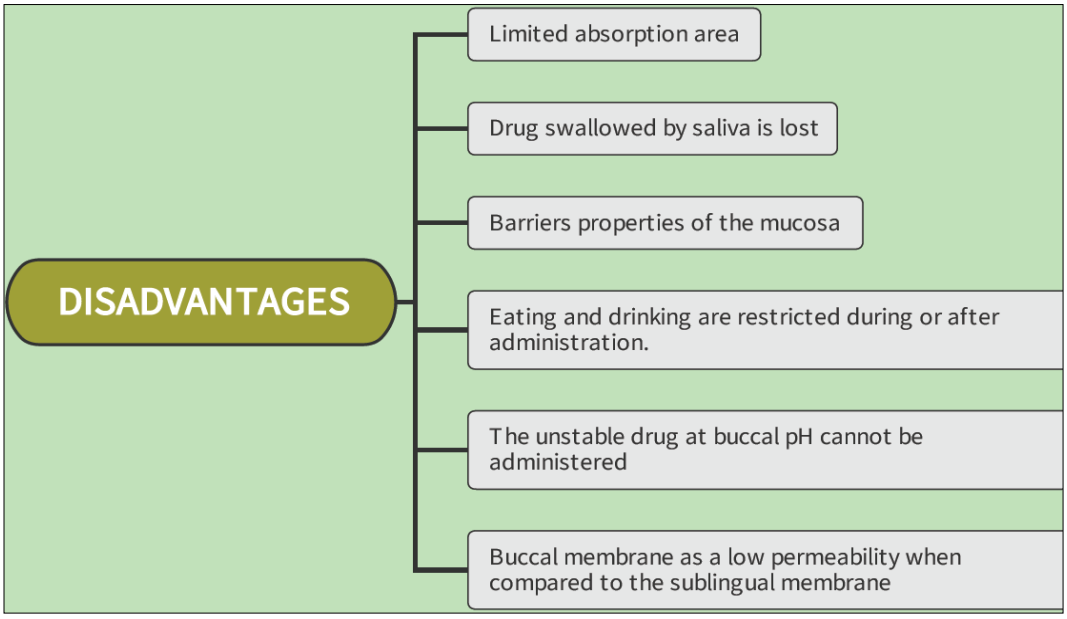
1. The Polymer and its degradation products should be non- toxic and non- irritant.
2. It should have quick adherence and sufficient mechanical strength to the buccal mucosa.
3. It should achieve unidirectional drug release towards the mucosa.
4. It must be resistant to the flushing action of saliva.
5. It should have good ability to easily removed after local treatment.
6. Should have good spreadability, wettability and solubility and biodegradable properties.
7. It should be patient compliance.
8. It facilitates the rate and extent of drug absorption.
9. It should not hinder normal functions such as talking, eating and drinking.
10. It should not aid in development of secondary infections such as dental caries.
11. It possess a wide margin of safety for both locally and systemically.

**Advantages of buccal drug delivery system** [33, 34, 35]




Other advantages includes excellent accessibility, Alternative route for hormones, narcotic analgesics, steroids, enzymes, cardiovascular agents, Delivery of therapeutic agents like peptides, proteins and ionized species can be given by this route, suitability for drugs or excipients that mildly and reversibly damage or irritate the mucosa, facility to include permeation enhancer/ enzyme inhibitor or pH modifier in the formulation, versatility in designing as multidirectional or unidirectional release system for local or systemic action [36].

**Disadvantages of Buccal Drug Delivery System**




Other disadvantages includes drug characteristics may limit the use of the oral cavity as a site for drug delivery.ie Taste, irritancy, allergy and adverse properties such as discoloration or erosion of the teeth may limit the drug candidate list for this route.

**Methodology**

**Evaluation of Buccal Patches**

**Thickness**

The patches were chosen from each formulation, and the thickness of the patches was determined using a digital vernier calliper and measured at three different locations on the patch. The average of the three values, namely mean thickness and standard deviation, was calculated [37].

**Weight Variation**

Five films from each batch having an area of 2×2cm were weighed individually in a digital balance and average weight and standard deviation was calculated [38].

**Folding Endurance**

The folding endurance of patches was determined by folding one patch repeatedly until it broke or by folding it up to 200 times without breaking. The experiments were carried out in triplicate, and the average and standard deviation values were reported [39].

**Drug content uniformity**

Drug content uniformity was determined by dissolving the patch by homogenization in 100 mL of IPB, (pH 6.8) for 10h under occasional shaking and the resulting solution was filtered through a 0.45 µm whatman filter paper. The drug content was then determined after dilution at 274 nm using a UV spectrophotometer. The experiments were performed in triplicate and average values were reported [40].

**Swelling study**

A digital balance was used to determine the initial weight of the patch (without the backing membrane) (Wo). The patches were then allowed to swell on the surface of an agar plate (as described under surface pH measurement) and kept in an incubator set to 37 °C. At predetermined time intervals for 60 min weight of the swollen patch was determined (Wt). The percentage of swelling (% S) was calculated using the following equation [41].

$$\%S = \frac{Wt - Wo}{Wo} \times 100$$

Where Wt is the weight of swollen patch after time t, Wo is the initial weight of patch at t=0.

**Surface pH Study**

Each patch was allowed to swell for 2 hours at room temperature by being in contact with 5 mL of distilled water, and the pH was measured by bringing the electrode into contact with the patch's surface and allowing it to equilibrate for 1 minute. The experiments were carried out in triplicate, and the average values and standard deviation were computed [42].

***In vitro* Drug Release**

The USP Dissolution test apparatus (type 2) with slight modification (paddle over disc) method was used to study the *In vitro* drug release from buccal patches. The dissolution medium consisted of 300 mL of IPB, pH 6.8. The release was carried out at 37 °C and 50 rpm for the paddle rotation. With the help of instant adhesive, one side of the buccal patch was glued to the glass disc (cyanoacrylate). The patch was left on the top side of the disc, which was inserted into the bottom of the dissolving vessel. Five millilitre samples (5 ml) were taken out at predefined intervals, and the sample volume was replaced with fresh medium. The samples were examined using a UV spectrophotometer (Shimadzu (UV-1800), Japan) at 274 nm after being filtered through 0.45 m Whatman filter paper with the proper phosphate buffer pH 6.8 dilutions [43].

**Mucoadhesive Strength**

The patch's mucoadhesion strength was tested using a modified physical balance and a technique that used sheep buccal mucosa as a model mucosal membrane. A piece of sheep buccal mucosa cleaned in distilled water and connected to the opening of a glass vial that contained PBS pH 6.8. In order to maintain the buccal mucosa wet, the mucosa was securely knotted with the mucosal side facing up over the base of an inverted 50 ml glass beaker that was placed in a 500 ml beaker of phosphate buffer pH 6.8 that was kept at 37 ºC. Rubber stoppers lower side had patches glued to them using glue. For three minutes, the balance was held in this position. The right pan's weights were then raised until the patch had barely parted from the mucosal membrane. The excess weight on the right pan i.e. total weight minus 5 g was taken as a measure of the mucoadhesive strength and the mass (g) required to detach the patches from the mucosal surface was noted and taken as the mucoadhesive strength (shear stress) [16 44].

**Ex - vivo drug permeation**

A Franz type glass diffusion cell was used for the ex-vivo permeation research via the sheep buccal mucosa, which was carried out at 37±0.5 C. The donor and receptor compartments were covered in fresh goat buccal mucosa. The compartments were clamped together, and the patch was applied with the core towards the mucosa. Phosphate buffer with a pH of 6.8 was diluted to 1 ml and placed in the donor compartment. Phosphate buffer with a pH 6.8 was added to the receptor compartment, which has a 40ml capacity, and the hydrodynamics in the receptor compartment were maintained by stirring with a magnetic bead at 50 rpm. At predefined intervals, 1 ml of the sample was taken out and immediately refilled with an equivalent volume of PBS (pH 6.8) to be tested for drug content at 274 nm using a UV spectrophotometer [45].

**Stability Studies [46]**

The ability of a certain formulation, in a specific container, to maintain its physical, chemical, therapeutic, and toxicological requirements over the course of its shelf life is considered a drug's stability. Stability testing is done to demonstrate how a drug substance's or its product's quality changes over time under the effect of environmental conditions including temperature, humidity, and light. It is necessary to determine suggested storage conditions, retest intervals, and shelf lives.

**Conclusion**

Although gingivitis is always the first stage of periodontitis, only a tiny percentage of afflicted sites progress to the more serious condition. Regardless this condition, all clinicians and their patients should strive for optimal gingival health. Gingivitis can have a variety of causes and manifest as a symptom of a variety of systemic diseases. One of the most frequent lesions seen in a clinical environment is gingival tissue inflammation, which can also be the initial sign of many different diseases in the oral cavity. Therefore, gingivitis may have significant diagnostic importance, and it's essential for physicians to be familiar with its various causes to ensure accurate diagnosis and course of therapy.

The buccal mucosa is a promising delivery route for drugs that need to avoid the gastrointestinal tract due to degradation by the gastric pH, intestinal enzymes, or due to a substantial hepatic first pass effect. It can also be an alternative to skin, pulmonary, or nasal delivery. The physiology of the buccal mucosa allows for the penetration of active substances. As a result, the current work provides information on the use of buccal Patches for the treatment of gingivitis.

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