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Mucoadhesive Buccal Drug Delivery System - An Overview

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ABSTRACT

Bioadhesive drug delivery system as a novel route of drug administration. It extends the residence time of the dosage form at the site of administration. It bypasses the hepatic first-pass metabolism by enhancing directly draining high blood supply into the jugular vein. These delivery systems close contact with the absorption tissue and the mucous membrane, hence it contributes to improves both therapeutic performances of the drug and local or systemic effects. The mucoadhesive buccal drug delivery system facilitates ease of drug delivery even in unconscious patients who are not swallowing by mouth. This system is an alternative route for various therapeutic classes like peptides, vaccines, and nanoparticles. The present review article covers a brief description of periodontitis disease, advantages, and disadvantages of buccal drug delivery, stages of mucoadhesion, various methods and excipients used in the preparation of buccal drug delivery (patches/films), and characterizations of buccal drug delivery system.

INTRODUCTION

Periodontitis is an inflammatory disease of the gums that rupture the soft tissues and bones that support the teeth. These are the oral route for the treatment of a variety of local and systemic diseases. The treatment of periodontitis includes the crushing and eradication of subgingival periodontal pathogens, which require sustained delivery of antibacterial agents. the oral controlled delivery can be achieved by using some drug delivery systems, including strips, gels, films, and implants.[1]the classes of drug-like peptides and proteins cannot be administered.[2] Biofilm (deposition of plaque) affect the gingival coating and provide an ideal environment for the growth of anaerobic bacteria. The progression of such a destructive process leads to tooth loss.[3]Buccal films normally made up of different components such as a polymer, plasticizer, drug, sweetener, and necessary additives.[4] these are the buccal mucoadhesive dosage form has shown a lot of potential as a drug delivery system and it has originated a lot of interest both in industry and in academics. The system is explored for various reasons such as prolonging the drug action, targeting the drug to a localized site, avoidance of degradation of drug in gastrointestinal tract, to deliver high molecular weight proteins and peptides systemically and to avoid first-pass metabolism.[5] these are the Conservative therapy, which is based on scaling, surgery and the use of antibiotics or antimicrobials has been proposed. But due to bacterial resistance and toxic side effects of the administered antibiotics local delivery system are designed to maintain the antibiotic, in the gingival crevicular fluid at a concentration higher than that achieved by systemic administration.[6]

Mucoadhesive drugs delivery can be categorized into three classes: 7

1. Buccal delivery

2. Sublingual delivery

3. Local delivery

- **Buccal delivery**: Buccal delivery is drug administration over the mucosal membranes lining the cheeks (buccal mucosa).

- **Sublingual delivery**: Sublingual delivery is systemic delivery of drugs through the mucosal membranes lining the surface of the mouth.

- **Local delivery**: Local delivery is drug delivery among the oral cavity.

Classification of Buccal Bioadhesive Dosage Forms:[8]

1. Buccal Bioadhesive Tablets.

2. Buccal Bioadhesive semisolids.

3. Buccal Bioadhesive patch and films.

4. Buccal Bioadhesive Powders

Advantages of Buccal Drug Delivery System:[9]

- Available in various sizes and shapes.
- Taste masking.
- Increased stability.
- Hydrate and dissolves in the buccal cavity within a fraction of seconds.
- Fast disintegration or dissolution.
- Small size for improved patient compliance.
- Ease of handling and transportation

Disadvantages:[10]

- High doses cannot be incorporated into oral films.
- Eating and drinking may become restricted.
- It is hygroscopic so it must be kept in dry places.
- Buccal films are moisture sensitive.
- The packaging of films requires special equipment's and it is difficult to pack.

Ideal Properties of Mucoadhesive Polymers: [11]

It must assure the following properties:

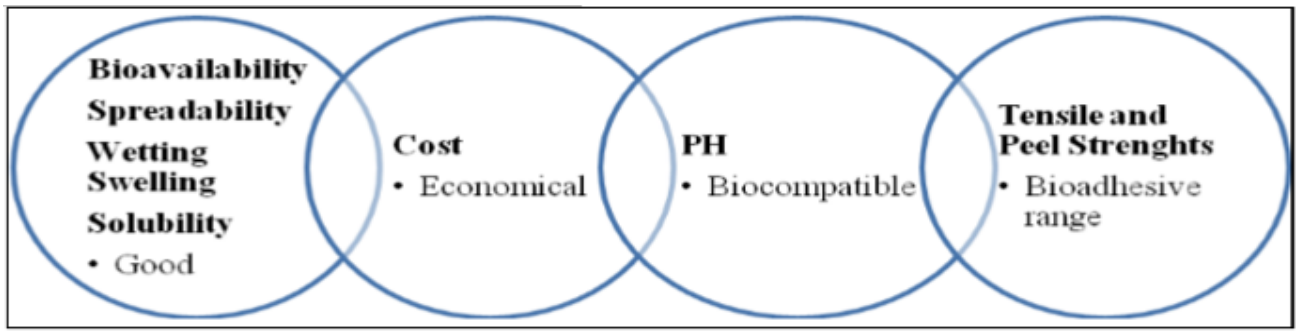

Figure No. 1: Representation of Model Properties of mucoadhesive polymers

Mechanism of mucoadhesion:

Contact between a pressure-sensitive adhesive material and a surface is called adhesion, which can be defined as the state in which two surfaces are attached due to valence interfacial forces or interlocking action or both.

Mucoadhesion is two stages:[12]

Stage-I (Contact Stage):

Wetting, spreading and expanded of the bioadhesive surface makes close contact between a bioadhesive and a layer. At times extra powers like a mechanical framework in vaginal delivery, streamlined features in nasal delivery and peristaltic movements in an intestinal conveyance of measurement structure.

Stage II (Consolidation Stage):

Humidity breaks particles and inter dispersion or prevailing appealing contact between two surfaces starts due to Vander walls powers, electrostatic attractions, hydrogen holding, and hydrophobic communications. For complete Bio attachment, appealing powers must beat horrendous powers. union advance is clarified by two theories:

Diffusion theory: bodily fluid glycol proteins communicate with the mucoadhesive atoms by interpenetrating their chains and shaping optional securities. This is a concoction just as a mechanical connection.

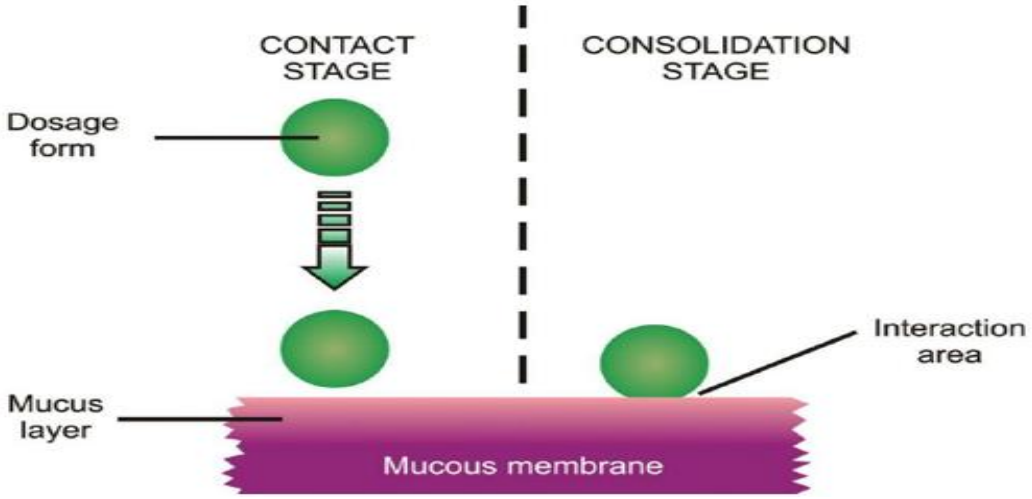

Figure No. 2: Mucoadhesion is two stages

Dehydration theory:[13]

Biological fluid in the wet condition. The drawing of water into the detailing because of the focus inclination until the osmotic equalization is come to. This procedure expands the contact time of the mucous layer with a blend of definition and bodily fluid. So it isn't the interpenetration of macromolecules chains, it is the water movement that prompts the union of the adhesive bond. The drying out hypothesis does not have any significant bearing to exceptionally hydrated structures or strong plans.

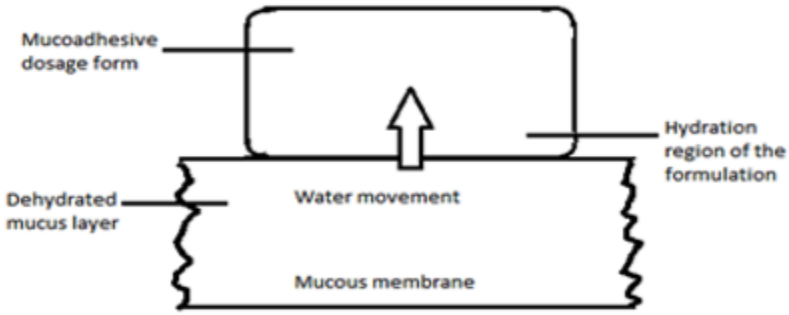

Figure No. 3: Dehydration theory

Theory of mucoadhesion [14]

1. Wetting theory:

This hypothesis applies to the fluid framework .it clarifies the capacity of the spreadability of polymer is having a tendency to the surface to spread over it. The inclination can be controlled by utilizing various methods, for example, the contact point. Partiality is indirectly corresponding to the contact point it implies, bring down the contact edge more prominent the liking.

2. Electronic theory:

In this hypothesis the electron move among mucoadhesive and Biological film prompting the detailing of a double electrical layer at the Interface of the mucoadhesive and layer because of contrasts in their electronic Structure. This outcome is appealing powers within the double layer and decides the quality of mucoadhesive.

3. Adsorption theory:

In this mucoadhesive device, different, types of chemicals bonding play an important role in the adhesion interaction i.e Hydrogen bonds. Van der walls and electronic attraction.

4. Fracture theory: [15]

This fracture theory is important to clarify. Power required separating obligations of a bond between two surfaces. at that point, crack quality can be dictated by utilizing the accompanying condition.

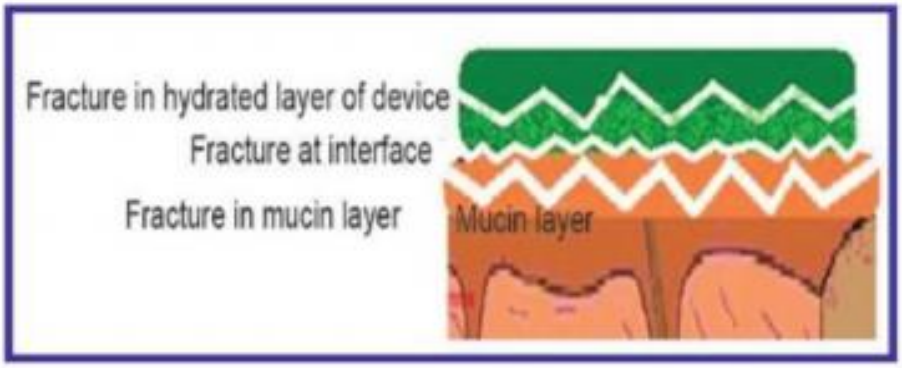

Figure No. 4: Fractures occurring for mucoadhesion

5. Diffusion interlocking theory:

This hypothesis clarifies the mucoadhesive polymer chain diffuses into the mucous layer because of the breaking of the glycoproteins chain organize. This diffuses is relying upon dispersion co-effective and time-ward and time-subordinate additionally focus subordinate.

Factors important to Mucoadhesion:[16]

1. Polymer-Related Factors:

a. The molecular weight of the polymer:

The most extreme bio adhesion relies upon the kind of polymers. The powers of bioadhesive build the atomic load of the polymer.

b. Polymer chain length:

The active polymer molecule should have adequate chain length.

C. Concentration of polymer:

Polymer concentration is directly proportional to the bio adhesion. The higher concentration of polymer leads to mucoadhesive strength significantly enhanced.

d. Molecular flexibility:

It is significant for increase and interpenetration. The versatility of the individual dynamic polymer binds decreases. Due to the cross-connecting of the water-dissolvable polymer. It encourages the cross-connecting thickness increments. They result in the entrance intensity of the dynamic polymer into the bodily fluid layer diminishes and bio adhesion mucoadhesion quality is diminished.

2. Environment Related Factors[17]

1. Applied Strength:

To put a strong bioadhesive framework, it is important to apply a characterized quality the bond quality expanded with the connected quality or with the length of its application up to an ideal. On the off chance that high weight is connected for a more drawn out time,

polymers become mucoadhesive even though they don't have alluring collaboration with mucin.

2. Initial contact time:

The mucoadhesive quality expanded as the original contact time increments.

3. Selection of the model substrate surface:

It should be necessary for examining the properties like permeability, electrophysiology or histology.

4. Swelling:

Swelling depends both on polymer focus and on the nearness of water. When swelling is excessively incredible, a lessening in grip happens.

3. PHYSIOLOGICAL FACTORS:[18]

a) Disease state:

The physicochemical property of bodily fluid may adjust during some disease state, for example, normal cool, gastric ulcers, ulcerative colitis, bacterial and parasitic contaminations, and so on. Along with these lines modification in the physiological state may influence the bioadhesive property.

b) Concomitant diseases:

Associative illnesses can adjust the physicochemical properties of mucous or its amount (for instance, hypo and hypersecretion of gastric juice), increments in body temperature, ulcer malady, colitis, tissue fibrosis, hypersensitive rhinitis, bacterial or contagious contamination, and irritation.

c) Mucin turnover:

High mucin turnover isn't valuable for the mucoadhesive property in light of the accompanying reasons:

• The high mucin turns over limits the habitation time of bioadhesive polymer as it disengages from the mucin layer, even though it has a decent bioadhesive property.

• High mucin turns over may create dissolvable mucin atom, along these lines particle associated with the polymer, before they cooperate with the mucin layer. Thus there won't be adequate mucoadhesion.

d) Rate of renewal of mucosal cells:

The rate of renewal of mucosal cells varies extensively from different types of mucosa. It limits the persistence of bioadhesive systems on mucosal surfaces.

The different components are used in the mucoadhesive buccal drug delivery system are follows: [19,20]

Table No. 1: Components of mucoadhesive buccal drug delivery system

Sl No.	Components	Example	Uses
1	**Polymers: (adhesive layer)**	Hydroxyethylcellulose Hydroxyl propyl cellulose Chitosan, Trimethyle chitosan	Polymer controls the rate of release of drug from the buccal mucoadhesive film
2	**Diluents:**	LactosDC, microcrystalline starch, and starch	To enhance aqueous solubility improves its flavoring characteristics,
3	**Backing layer:**	Ethylcellulose, etc,	The important role of the backing layer was an attachment of bioadhesive devices to the mucous membrane. This membrane was used to inert, and impermeable to the drug and penetration enhancer**.**
4	**Penetration enhancer:**	Cyano acrylate, dextrin	Substances that help to enhance drug permeation through a buccal epithelium and absorption
5	**Plasticizer:**	PEG100,400,Propyleneglycol, glycerol, castors oil etc**.**	A substance which is used to improves the softness and flexibility of the thin buccal film
6	**Sweetening agent:**	Sucralose, Aspartame, Mannitol, etc	They are used to reduce the bitter taste of the formulation and increase the palatability of the therapeutic agents
7	**Solvents:**	Methanol, dichloromethane**,**	Increases the solubility

Methods of manufacture of mucoadhesive buccal films:

1. **Solvent casting :**

2. **Hot-melt extraction** :

3. **Rolling method**:

1. Solvent casting technique: (21,22,23)

The Solvent casting method is an antibiotic drug used to prepare the mucoadhesive buccal films because of the simplicity and low-priced operation.[6] chitosan and peg 400 were used as mucoadhesive polymers. The amount of polymer was dissolved in 20ml distilled water, and 250 mg antibiotic drug was added to this solution with continuous stirring until a homogeneous solution formed. The excess quantity (2 % w/v) of methanol was added to the homogenized drug-polymer solution as a plasticizer. Then, the polymer solution was transferred to previously made glass molds and kept at room temperature for drying [3]. The dried film was cut into pieces of (7mm×2mm), wrapped in an aluminum foil and stored in a desiccator at room temperature in a dark place for further evaluation studies.[21]

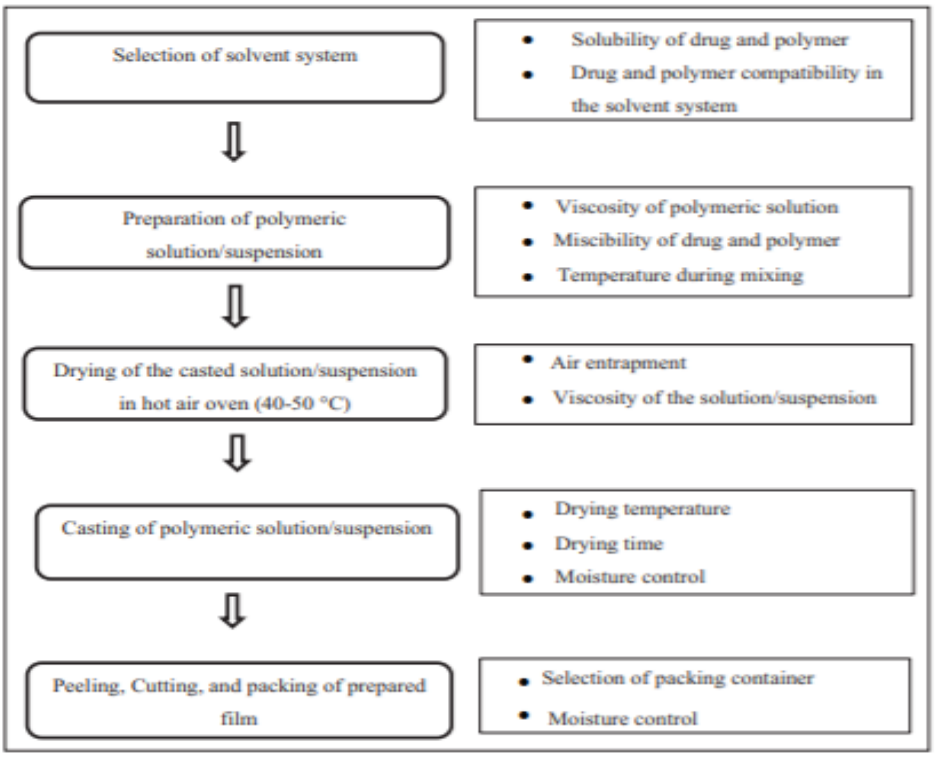

Figure No. 5: Steps involved in the film casting process and the critical parameters

2. Hot-Melt Extrusion:[24]

In hot liquefy expulsion strategy, initially; the medication is blended with transporters in strong structure. At that point, the extruder containing radiators are utilized to soften the blend. At last, the liquefy is given the state of movies with the assistance of passes on. Hot dissolve expulsion has merit as patches arranged through this strategy have better content consistency.

3. Rolling Method: [25]

In moving strategy, an answer or suspension of medication with film framing polymer is arranged and exposed to the roller. The arrangement or suspension ought to have explicit rheological thought. The dissolvable is for the most part water and blend of water and liquor. The film is dried on the rollers and cut into wanted shapes and sizes. Blend level surface to shape a film. The film is dried and cautiously evacuate.

Evaluation test for mucoadhesive buccal films:

1. Film thickness:[26]

As the Weight variation test was done by weighing five films individually on a weighing balance. The average weight of the film was taken as the mass.[27]

2. Weight variation[27]

Three samples of films with an area of four-centimeter square were separated from a casted film by cutting. The weight of each film was taken and weight variation was calculated.

3. Folding endurance:[28]

Folding endurance was measured by repeatedly folding the specified area of each film (3×2cm2) at the same point until breaking occurs. Several times a film was folded without breaking was informed as folding endurance value.

4. Surface pH of films:[29]

For surface pH, three films of each preparation were allowed to swell for 2h on the surface of the agar plate. The surface pH was measured by using a ph paper placed on the surface of the swollen patch. A mean of three readings was recorded.

5. Tensile strength:[30]

The Tensile strength of the films was determined by the Universal strength testing machine. It consists of two load cell grips, the lower one is fixed and the upper one is movable. The test films of a specific size (2 × 2 cm) were fixed between these cell grips and force was gradually applied till the film breaks. The tensile strength of the films was taken directly from the dial reading in kilograms Measurements were run in triplicate for each film.

6. Drug content uniformity[31]

To determine the drug content uniformity, three film units of each formulation were taken in separate 100 ml volumetric flasks, 100 ml of pH 6.6 phosphate buffer was added and continuously stirred for 24 hrs. The solutions were filtered, diluted suitably and analyzed at 217 nm in a UV spectrophotometer (Lambda 25, Perkin Elmer). The average drug content of the three films was taken as a final reading.

7. *In-vitro* residence time:[32]

The *in-vitro* residence time was determined using an IP disintegration apparatus. The disintegration medium was composed of 800 ml pH 6.6 phosphate buffer (PB) maintained at 37 + 27℃. The segment of the porcine intestinal mucosa, 3 cm length, was glued to the surface of a glass slab, vertically attached to the apparatus. Three mucoadhesive films of each formulation were hydrated from one surface using pH 6.6 PB and then the hydrated surface was brought into contact with the mucosal membrane. The glass slab was vertically fixed to the apparatus and allowed to move up and down. The film was completely submerging in the buffer solution at the lowest point and was out at the highest point. The time required for complete abrasion or detachment of the film from the mucosal surface recorded.

8. Stability study:[33]

Stability study was carried out at two different storage conditions, one was normal room conditions and the other was 400C/75% RH for 4 weeks. Each piece of the films of formulation F1 and F2 was packed in butter paper followed by aluminum foil and plastic tape. After 4 weeks, the films were evaluated for the physical appearance, surface pH, drug content and in vitro drug release.

9. Scanning Electron Microscopy (SEM):[34]

Scanning electron microscopy is an important tool to study the surface characteristics of the oral film. Excipients added in formulation affect the surface morphology of film differently which affects various parameters of the film. A film sample is taken and placed in the sample holder of SEM and various photomicrographs are taken.

CONCLUSION

Nowadays, drug delivery systems are developed to improve patient compliance and convenience. The buccal drug delivery system is a novel and used for the controlled drug delivery of various classes of drugs along with extended periods. Mucoadhesive polymers may improve the bioavailability of the active agent by avoiding pre-systemic metabolism in the GIT and first-pass metabolism. Also, buccal adhesive dosage forms have been used to treat local disorders at the mucosal surface e.g. periodontitis, mouth ulcers. This system is majorly used to reduce the quantity of dose and minimize the side effects that may be caused by local or systemic administration of drugs. Overall mucoadhesive buccal delivery system provides satisfactory treatment than other drug delivery systems.

REFERENCES

1. Wu W, Chen W, Jin Q. Oral mucoadhesive buccal film of ciprofloxacin for periodontitis: Preparation and characterization. Tropical Journal of Pharmaceutical Research. 2016;15(3):447-51.
2. Singh S, Jain S, Muthu MS, Tiwari S, Tilak R. Preparation and evaluation of buccal bioadhesive films containing clotrimazole. Aaps Pharmscitech. 2008 Jun 1;9(2):660-7.
3. Razzaq S, Hanif S, Syed MA, Iqbal J, Raza SA, Riaz H, Abid F. Development and evaluation of mucoadhesive buccal tablet containing metronidazole for the treatment of periodontitis and gingivitis. Pakistan journal of pharmaceutical sciences. 2018 Sep 1;31(5).
4. Salehi S, Boddohi S. New formulation and approach for the mucoadhesive buccal film of rizatriptan benzoate. Progress in biomaterials. 2017 Dec 1;6(4):175-87
5. Goudanavar PS, Bagali RS, Patil SM, Chandashkhara S. Formulation and in-vitro evaluation of mucoadhesive buccal films of Glibenclamide. Der Pharmacia Lettre. 2010;2(1):382-7
6. Chaudhary A, Nagaich U, Rastogi B, Partapur-Bypass M. Designing and evaluation of mucoadhesive buccal films of propranolol hydrochloride. Journal of Advanced Pharmacy Education & Research Oct-Dec. 2012;2(4).
7. Gawas SM, Dev A, Deshmukh G, Rathod S. Current approaches in buccal drug delivery system. Pharm Biol Eval. 2016;3(2):165-77.
8. Singh J, Deep P. A Review Article on Mucoadhesive Buccal Drug Delivery System. International journal of pharmaceutical sciences and research. 2013 Mar 1;4(3):916
9. Singh R, Sharma D, Garg R. Review on mucoadhesive drug delivery system with special emphasis on a buccal route: an important tool in designing of novel controlled drug delivery system for the effective delivery of pharmaceuticals. J. Dev. Drugs. 2017;6(1):1-2.
10. Roy S, Prabhakar B. Bioadhesive polymeric platforms for transmucosal drug delivery systems–a review. Tropical Journal of Pharmaceutical Research. 2010;9(1).

11. Hamza M. DEVELOPMENT AND EVALUATION OF ORODISPERSIBLE FILMS OF LAMOTRIGINE: HYDROXYPROPYL B CYCLODEXTRIN INCLUSION COMPLEX. Al-Azhar Journal of Pharmaceutical Sciences. 2017 Sep 1;56(2):31-46.
12. Abha D, Sheeja K, Bhagyashri J. Design and evaluation of buccal film of diclofenac sodium. Int J pharm Bio sci. 2011;1(1):17-30.
13. Khan AB, Mahamana R, Pal E. Review on mucoadhesive drug delivery system: novel approaches in the modern era. Rajiv Gandhi Univ Heal Sci J Pharm Sci. 2015;4:128-41.
14. Verma S. Polymers in designing the mucoadhesive films: A comprehensive review. International Journal of Green Pharmacy (IJGP). 2018 Aug 3;12(02).
15. Khan AB, Mahamana R, Pal E. Review on mucoadhesive drug delivery system: novel approaches in modern era. Rajiv Gandhi Univ Heal Sci J Pharm Sci. 2015;4:128-41.
16. Arun P, Kumar SV, Kumar TA. DRUG DELIVERY VIA THE BUCCAL PATCH–A NOVEL APPROACH. Journal of Pharm Research. 2013;3(5).
17. Singh CL, Srivastava N, Monga MG, Singh A. A review: buccal mucoadhesive drug delivery system. World J Pharm Sci. 2014;2(12):1803-7.
18. Singh CL, Srivastava N, Monga MG, Singh A. A review: buccal mucoadhesive drug delivery system. World J Pharm Sci. 2014;2(12):1803-7.
19. Singh CL, Srivastava N, Monga MG, Singh A. A review: buccal mucoadhesive drug delivery system. World J Pharm Sci. 2014;2(12):1803-7.
20. Hamza M. DEVELOPMENT AND EVALUATION OF ORODISPERSIBLE FILMS OF LAMOTRIGINE: HYDROXYPROPYL B CYCLODEXTRIN INCLUSION COMPLEX. Al-Azhar Journal of Pharmaceutical Sciences. 2017 Sep 1;56(2):31-46.
21. Chaudhary A, Nagaich U, Rastogi B, Partapur-Bypass M. Designing and evaluation of mucoadhesive buccal films of propranolol hydrochloride. Journal of Advanced Pharmacy Education & Research Oct-Dec. 2012;2(4).
22. Razzaq S, Hanif S, Syed MA, Iqbal J, Raza SA, Riaz H, Abid F. Development and evaluation of mucoadhesive buccal tablet containing metronidazole for the treatment of periodontitis and gingivitis. Pakistan journal of pharmaceutical sciences. 2018 Sep 1;31(5).
23. Singh N, Malviya R, Bansal M, Sharma PK. Formulation and Evaluation of Different Polymer-based Periodontal Film of Ofloxacin. Der Pharmacia Letter. 2010;2:297-303
24. Mamatha Y, Selvi A, Prasanth VV, Sipai MA, Yadav V. Buccal Drug Delivery: A Technical Approach. Journal of Drug Delivery and Therapeutics. 2012 Mar 13;2(2).
25. Patil PB, Shrivastava SK. Fast dissolving oral films: An innovative drug delivery system. Structure. 2012;20(70):50-0.
26. Chaudhary A, Nagaich U, Rastogi B, Partapur-Bypass M. Designing and evaluation of mucoadhesive buccal films of propranolol hydrochloride. Journal of Advanced Pharmacy Education & Research Oct-Dec. 2012;2(4).
27. Bhyan B, Bhyan SJ, Chopra V, Berwal R. FORMULATION AND EVALUATION OF NOVEL ORODISPERSIBLE DRUG DELIVERY SYSTEM FOR THE ADMINISTRATION OF BROMHEXINE HYDROCHLORIDE.
28. Ahmed MG, Harish NM, Charyulu RN, Prabhu P. Formulation of chitosan-based ciprofloxacin and diclofenac film for periodontitis therapy. Tropical Journal of Pharmaceutical Research. 2009;8(1):33-41.
29. 29. Shridhar GS, Manohar SD, Bhanudas SR, Anjaneri N. Mucoadhesive buccal drug delivery: An Overview. Journal of Advanced Pharmacy Education & Research Oct-Dec. 2013;3(4).
30. Deepthi N, Velrajan G. Formulation and evaluation of moxifloxacin periodontal films. Int J Pharm Bio Sci. 2013 Apr;4:549-5.
31. Nautiyal U. Development and evaluation of buccal film.
32. Shridhar GS, Manohar SD, Bhanudas SR, Anjaneri N. Mucoadhesive buccal drug delivery: An Overview. Journal of Advanced Pharmacy Education & Research Oct-Dec. 2013;3(4).
33. Shivhare UD, Suruse PB, Varvandkar SS. Formulation and evaluation of buccal patch containing aceclofenac. Journal of Applied Pharmacy. 2014 Jan;6(1):65-76.

34. Joshua JM, Hari R, Jyothish FK, Surendran SA. Formulation of Propranolol Hydrochloride Oral thin films for Migraine Prophylaxis. Int J Pharm Sci Rev Res. 2017;42(1).