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# BUCCAL PATCHES: THE GATEWAY OF MUCOADHESIVE DRUG DELIVERY – A REVIEW

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## ABSTRACT

Over the past 20 years, there has been a lot of scientific interest in the delivery of medications through the buccal mucosa. Various conventional and complicated techniques have been developed in an effort to transport a variety of pharmaceutical substances via the buccal route. Mucoadhesive buccal patches are a type of dosage form that uses controlled release to distribute drugs over a longer period of time. These patches often assist drugs in bypassing the liver's first pass processing and entering the systemic circulation directly. This kind of drug administration technique is thought to improve a medicine's bioavailability. The nature of the mucosal tissue and the physicochemical characteristics of the polymeric formulation are just two examples of the many variables that affect a dosage form's capacity to adhere to mucous membranes. This article provides an information on buccal patches advantages, disadvantages, ideal characteristics and basic components of mucoadhesive buccal patches.

**KEYWORDS:** Structure of buccal cavity, theories of bioadhesive, mechanism of bioadhesive and methods to increase drug delivery via buccal route.

## INTRODUCTION

In order to address shortcomings with the latter route of administration, the buccal region of the mouth cavity is a desirable target for medication delivery. By giving the medication via the buccal route, issues such high first-pass metabolism and drug degradation in the gastrointestinal environment can be avoided. Therefore, it was discovered that the buccal cavity was the most accessible region for local and systemic medication delivery. The use of mucoadhesive polymers is necessary for a bioadhesive dosage form to stick to mucosa and

endure prolonged swallowing, tongue movement, and salivation.[1] In the last few decades, new medication formulations and administration methods have been developed, and at the same time, our knowledge of how drugs move through tissues has grown. The polymer composition used to prepare buccal patches affects how effective mucoadhesive preparation is.[2] Buccal patches have the advantages of easy exclusion, low enzymatic activity, straightforward patch delivery, and the capacity to include permeability enhancers, enzyme inhibitors, or pH changers.[3]

**Mucoadhesive drug delivery system**

The attachment of synthetic or biological macromolecules to biological tissue is known as mucoadhesion or bioadhesion. Mucoadhesion is the term for the bioadhesive interaction that mostly happens with the mucus layer when it is applied to the mucosal epithelium. A medicine can be targeted to a specific area of the body for an extended period of time using mucoadhesive drug delivery systems, which leverage the bioadhesion of certain polymers, which become adhesive upon hydration.[4] The mucoadhesive drug delivery system covers buccal, sublingual, rectal, vaginal, ocular, and nasal drug delivery systems. It also includes vaginal, ocular, and nasal drug delivery systems.

Numerous drug delivery systems designed for buccal administration have been developed over the years, up to the present. Tablets and patches are the most popular buccal dose forms. Even after being hydrated in the oral cavity, such a form must be of a modest size and have a proper geometry in order to not obstruct mouth physiological function. Either the buccal or sublingual routes can be used to absorb medications from the oral cavity through the oral mucosa.[5]

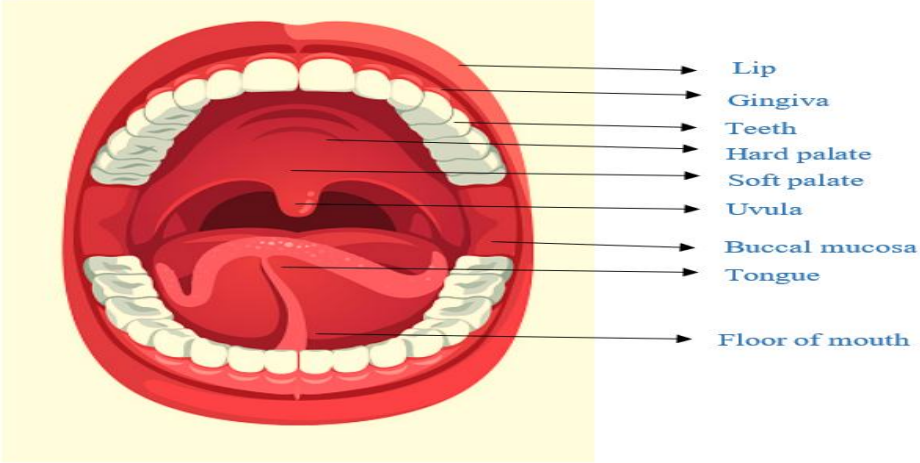


**Figure 1: Structure of buccal cavity.**

**Structure of buccal mucosa**

An epithelium with many layers that is mucus-sealed makes up the oral mucosal tissues. According to the needs of the tissue's functional requirements, the epithelium of the human oral mucosa exhibits a variety of unique patterns of development. The epithelium is joined to a layer of connective tissue by the basal lamina.[6] the submucosal region, which is home to numerous blood arteries and CNS neurons. Drug delivery methods for the buccal mucosa are divided into three categories. Local delivery, buccal delivery, and sublingual delivery are the three types. Treatment of oral cavity diseases, primarily periodontal disease, fungus, and ulcers, is done locally. These oral mucosal locations are quite different from one another in terms of their anatomical make-up, permeability to drugs, and capacity to hold a delivery system in place for the necessary amount of time.[7,8] The administration of medication through the buccal mucosa is known as buccal delivery. Drug administration through the sublingual mucosa is known as sublingual delivery. The structure of buccal mucosa in figure 2.

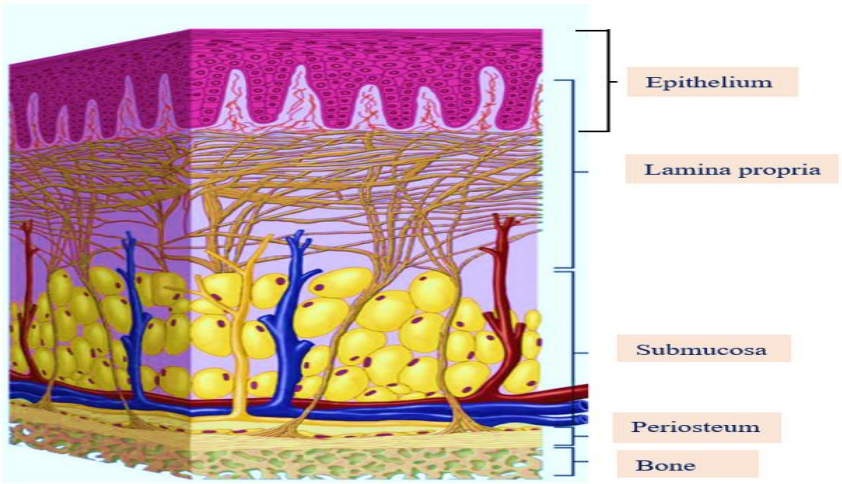


**Figure 2: Structure of buccal mucosa.**

**Advantages of mucoadhesive drug delivery systems**

Buccal dose forms are simpler to use than other types. Drug administration is simple, and it is possible to expedite the termination of therapy in an emergency.[9] Drugs can be given to unconscious and injured patients. Therapy can be stopped at any time. Rapid systemic absorption. It is possible to obtain a large dose decrease, which will lessen adverse effects that are related to dose. Buccal mucosa is an effective way to provide peptide molecules that are not suited for delivery through the oral route. Buccal delivery systems can give medications continuously and can tolerate environmental conditions.[10,11] Due to the

avoidance of first pass metabolism, medication bioavailability has increased. allows for long-term localisation of the medication in the oral cavity. Due to improved control over plasma levels, high strength medicines have developed a safety margin. Vomiting and nausea are strongly discouraged. improved patient compliance as a result of the absence of injection-related pain. The mouth cavity's vast contact surface increases the rate and extent of medication absorption. Drugs are guarded against deterioration in the GIT's acidic environment.

**Disadvantages of mucoadhesive drug delivery systems**

Only medications with low dose requirements can be taken. Drugs may be ingested with saliva but lose the benefits of the buccal route. It is forbidden to administer medications with a bitter or unpleasant taste, a repulsive odour, or that irritate the mucosa.[12] Only medications that are absorbed through passive diffusion can be given this way. The buccal membrane has a low permeability, especially when compared to the sublingual membrane. Only deliver the tiny dose of medication that is necessary. Only through this route may medications that are absorbed passively be given. Food and liquid intake might be limited.[13] The natural bacteria in the buccal cavity are impacted if the formulation contains antimicrobial drugs. The buccal membrane has a low permeability, especially when compared to the sublingual membrane. This method cannot be used to give medications that are unstable at buccal Ph.[14,15,16]

**Ideal characteristics of mucoadhesive buccal patches**

It is ideal for polymers and the breakdown products they produce to be non-toxic, non-irritating, and impurity-free. Polymer needs to be readily available and reasonably priced. It should have bioadhesion characteristics in both the dry and liquid states. It should have qualities that increase penetration and inhibit local enzymes. The shelf life should be appropriate. It must not encourage the growth of secondary infections such dental caries. The molecular weight needs to be ideal. It must have groups that are capable of adhesion. Good spreadability, wetting, swelling, solubility, and biodegradability qualities are required. It ought to have demanded spatial conformity. It should be sufficiently cross-linked, but not to the point where bond forming groups are completely suppressed.

**Structure and Design for buccal dosage forms**

Types of buccal dosage forms are categorised based on their structure and design. They are of the reservoir and matric type. When a buccal patch is of the matrix kind, the medicine, adhesive, and additives are all blended together. The reservoir type is a buccal patch with a

cavity for the medication and any additives separate from the adhesive. To manage the direction of drug delivery, lessen patch deformation and disintegration while in the mouth, and avoid drug loss, an impermeable backing is used.

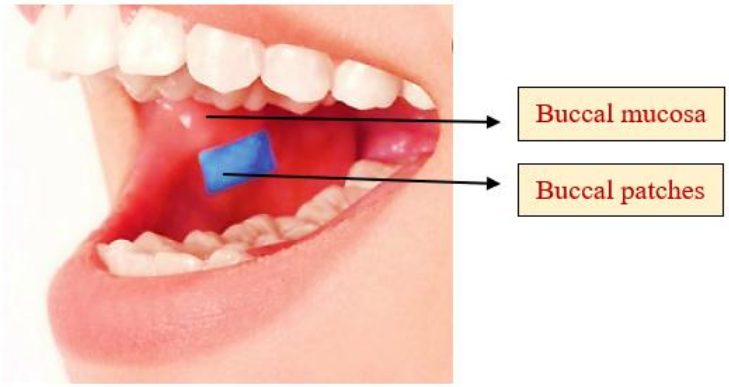


**Figure 3: Buccal patches.**

**Mucoadhesion or bioadhesion**[17,18,19,20]

A chemical that may interact with biological material and be maintained on them or hold them together for an extended amount of time is referred to as a bioadhesive or mucoadhesive. Three types of bioadhesives are categorised. They are mentioned in figure: 4.

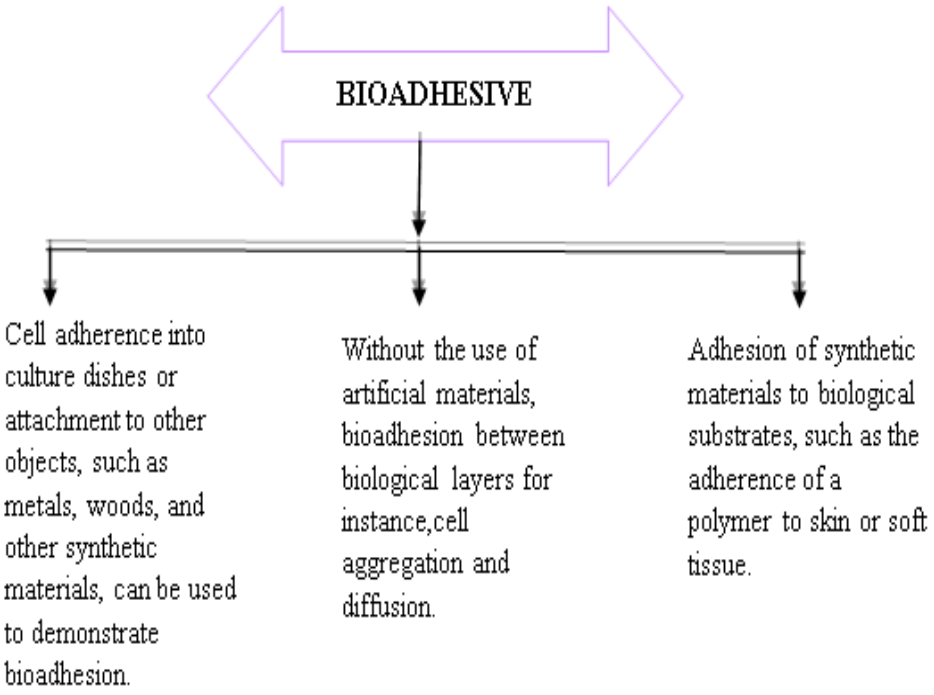


**Figure 4: Bioadhesion categories.**

**Mechanism of bioadhesion**[21,22,23]

A good wetting of the bioadhesive and the membrane or the bioadhesive swelling will result in intimate contact between the two. The bio-adhesive enters the tissue and adheres there. Mucous penetrates the bioadhesive's chain on multiple occasions. Then, low chemical bonds may settle. The expansion of the sticky material and chemical connections caused by electrostatic contact, hydrophobic interaction, hydrogen bonding, and dispersion forces are the main causes of the bonding between mucus and the biological substance.

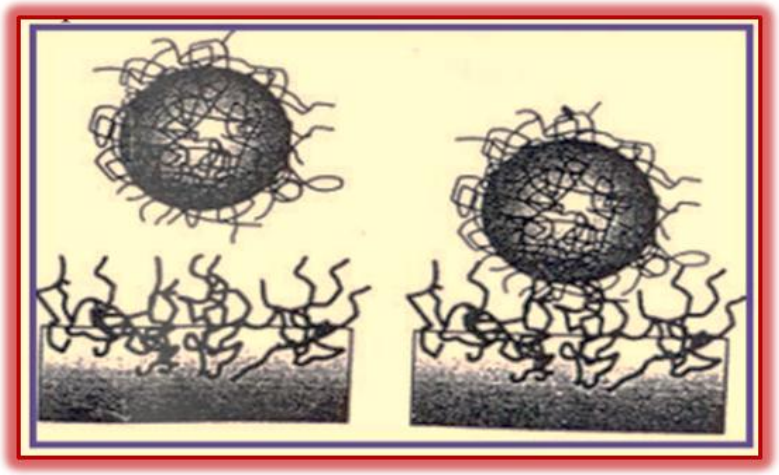

**Figure 5: Inter penetration of Bioadhesive and Mucus polymer chain.**

**Theories of bioadhesion or mucoadhesion**[24,25]

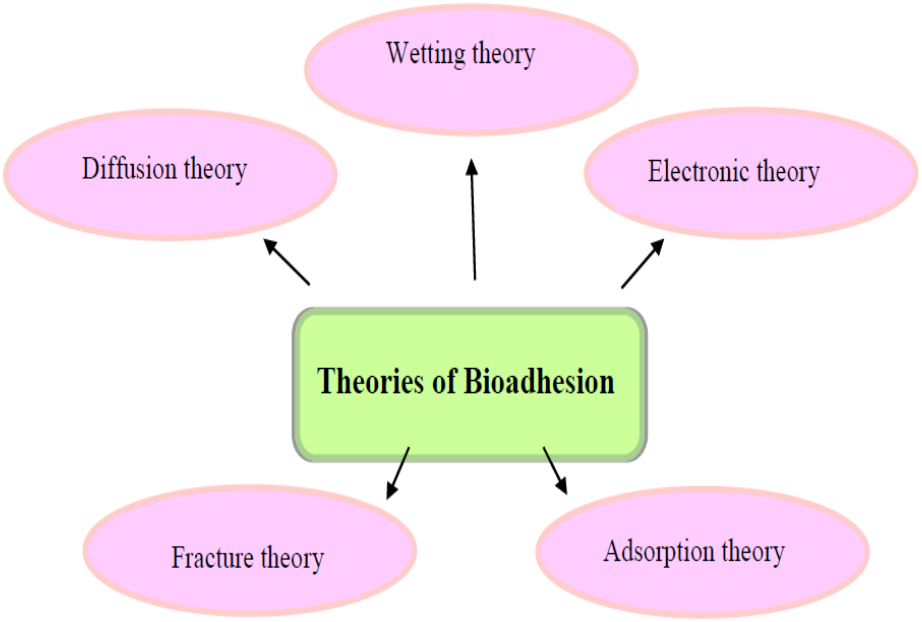


**Figure 6: Thoeries of bioadhesive.**

**Buccal patches composition**

**Table 7: Buccal patches composition.**

| S. no. | Ingredients | Examples |
|---|---|---|
| 1. | Active ingredients | Glipizide, terbutaline sulphate, lisinopril nifedipine, diltiazem, nicotine, clarithromycin, & nisoldipine , etc,…….. |
| 2. | Polymers | Hec, hpc, polyvinyl pyrrolidone(pvp), polyvinyl alcohol (pva), carbopol and other mucoadhesive polymers. |
| 3. | Diluents | Lactose dc is selected as diluents for its high aqueous solubility, its flavoring characteristics, and its physico-mechanical properties, which make it suitable for direct compression. Other example: microcrystalline starch and starch. |
| 4. | Flavouring agents | Menthol, vanillin, clove oil, etc. |
| 5. | Sweetening agents | Sucralose, aspartame, mannitol, etc |
| 6. | Backing layer | Ec etc. |
| 7. | Plasticizers | Peg-100, 400, propylene glycol, etc |
| 8. | Penetration enhancer | Cyano acrylate, etc |

**Basic components in buccal patches**[26]

There are four main basic components in buccal patches, They are drug substance, bio adhesive polymers, backing membrane and Permeation enhancers.

**Drug substance:** One must choose whether the intended action is for rapid release or extended release and for local or systemic effect before developing mucoadhesive drug delivery systems. Pharmacokinetic parameters should be used to choose the best drug for the design of buccoadhesive drug delivery systems.

**Bio adhesive polymers:**[27] (Polymers to prepare backing membrane, polymers to control rate of release, and mucoadhesive polymers) - More focus is currently placed on the use of mucoadhesive polymers in the formulation of buccal drug delivery systems since contact between the formulation and the buccal mucosa is one of the crucial elements in successful buccal delivery.

**Table 8: Bioadhesive polymers.**

| Criteria | Categories | Examples |
|---|---|---|
| Source | Semi natural/ Natural Synthetic | Agarose, chitosan, gelatin, Hyaluronic acid, Various gums (guar gum, xanthan, gellan, carrageenan, pectin and sodium alginate). |

| | | |
|---|---|---|
| | | Cellulose derivatives: [CMC, thiolated CMC, NaCMC, HEC, HPC, HPMC, MC.] Poly (acrylic acid)-based polymers: [CP, PC, PAA, polyacrylates, poly (methyl vinyl ether-co-methacrylic acid), poly (2- hydroxy ethyl methacrylate), poly (acrylic acidcoethyl hexyl acrylate), poly (methacrylate), poly (isobutylcyanoacrylate), copolymer of acrylic acid and PEG]. Others: polyoxyethylene, PVA, PVP, thiolated Polymers. |
| Charge | Cationic<br>Anionic<br>Non-ionic | Aminodextran, Chitosan, (DEAE)- dextran, TMC<br>Chitosan-EDTA, CP, CMC, pectin, PAA, PC, sodium alginate, NaCMC, xanthan gum.<br>Hydroxy ethyl starch, HPC, poly(ethylene oxide) |
| Aqueous solubility | Water soluble | CP, HEC, HPC, HPMC (cold water), PAA, NaCMC, sodium alginate. |
| Bioadhesive forces | Electrostatic interaction | Acrylates [hydroxylatedmethacrylate, poly (methacrylic acid)], CP, PC, PVA, Chitosan |
| Potential | Covalent<br>Hydrogen bond | PVP, scleroglucan<br>Cyanoacrylate |

**Backing membrane**

The backing membrane for patches can be prepared using a polymer whose solution can be cast into a uniform, thin, poreless film that is water impermeable. It should have low water permeation, strong tensile strength, and good flexibility. On long-term storage, they ought to remain stable and retain their original physical characteristics. When 2.4% w/v cellulose acetate in acetone and 10% plasticizer (PEG 4000 or glycerol) of the total polymer weight are air dried, the result is a thin film that is ideal for backing membranes. Similar to this, film can be cast from a 2-4% w/v solution of ethyl cellulose in a 1:4 mixture of alcohol, toluene, and a suitable plasticizer.

**Penetration enhancer[28]**

Penetration enhancers, permeation promoters, or absorption enhancers are terms used to describe substances that aid in promoting drug permeation through the buccal epithelium. Chemicals used as penetration enhancers should ideally be secure, nontoxic, chemically and pharmacologically inert, without irritants, and without allergens. Additionally, upon removal of the chemical, surfactants, anions like sodium laurate and sodium lauryl sulphate, and cations like cetylpyridium chloride, the tissue should return to its usual integrity and barrier qualities.

**Table 9: Permeation enhancer.**

| Class of permeation enhancers | Examples |
|---|---|
| Surfactants | Sodium lauryl sulphate, polyoxyethylene, Polyoxythylene-20- cetylether, Benzalkonium chloride |
| Fatty acids | Oleic acid, capric acid, lauric acid, lauric acid/ propylene glycol, lyso phosphatidylcholine, phosphatidylcholine |
| Non-surfactants | Unsaturated cyclic ureas. |
| Inclusion complexes | Cyclodextrins. |
| Chelators | EDTA, citric acid, sodium salicylate, methoxy salicylates. |
| Bile salts | Sodium glycocholate, sodium deoxycholate, sodium taurocholate, sodium taurodeoxycholate. |

**Methods to increase drug delivery via buccal route**

**Prodrugs:** The opioid agonists and antagonists in bitter-less prodrug forms were studied, and it was discovered that the drug had a low prodrug bioavailability. When given to dogs through the buccal mucosa, the bitter medicines nalbuphine and naloxone resulted in excessive salivation and swallowing. The medication had a limited bioavailability as a result. Naloxone and nalbuphine were administered as prodrugs without causing any negative side effects, and their bioavailability ranged from 35 to 50%, a significant improvement over their oral bioavailability, which is typically 5% or less.

**Absorption enhancers:**[29] High molecular weight substances like peptides, which typically have low buccal absorption rates, have been successfully delivered via absorption enhancers. These may exert their effects through a variety of methods, including enhancing cell membrane fluidity, removing internal and extracellular lipids, changing cellular proteins, or changing surface mucin. The three substances that increase absorption the most frequently are fatty acids, bile salts, and surfactants like sodium dodecyl sulphate. Additionally, mannitol and fluorescently labelled dextrans were found to be transported more readily across chitosan solutions/gels in a tissue culture model of the buccal epithelium, whereas glyceryl monooleates were discovered to increase peptide absorption via a co-transport mechanism.

**pH:** Acyclovir's permeability between pH values of 3.3 and 8.8, as well as when sodium glycocholate, an absorption booster, is present. Numerous in vitro investigations on the kind and quantity of supporting materials and the drug release profile have been carried out, and it

has been demonstrated that both are connected. Additionally, single layered patches and multi-layered patches have variable drug release patterns.

## CONCLUSION

There are various benefits to using the buccal mucosa for prolonged controlled medication administration. First-pass metabolism in the liver and pre-systemic elimination in the digestive tract are prevented by the mucosa's adequate vascular and lymphatic drainage. Patients can safely employ buccal drug delivery because it can be stopped if side effects manifest. In the formulation of buccal patches, natural polymers are being used more and more. There is still a lot of research being done on mucoadhesive buccal patches made of different natural polymers all around the world. There are numerous prospective mucoadhesive systems being researched that might end up on the market soon.

## REFERENCE

1. Dr. Jasti B, Xiaoling Li and Gary Cleary, et al, “recent advances in Mucoadhesive drug delivery systems” Pharmatech, 2003; 194-196.
2. Pawar RR, Raut DB, Karde VK, Wadikar JC, Jadhav AS, Chintale AG. Mucoadhesive Buccal Drug Delivery System: A Review. Research Journal of Pharmacy and Technology, 2013; 1, 6(5): 4.
3. Lekshmi, A.M.R., Aniyan, N., Varghese, R., Lekshmi, L., Nair, MM., Nair, NM., Buccalmucoadhesive drug delivery system a novel drug delivery technique, EJPMR, 2016; 3(3): 129-137.
4. Shojaei AH. Buccal mucosa as a route for systemic drug delivery: a review. J Pharm Pharm Sci, 1998; 1, 1(1): 15-30.
5. Khanna R, Agarwal SP, Ahuja A. Mucoadhesive buccal drug delivery: a potential alternative to conventional therapy. Indian journal of pharmaceutical sciences, 1998; 60(1): 1.
6. Hoogstraate JA, Wertz PW. Drug delivery via the buccal mucosa. Pharmaceutical Science & Technology Today, 1998; 1, 1(7): 309-16.
7. Gandhi SD, Pandya PR, Umbarkar R, Tambawala T, Shah MA. Mucoadhesive drug delivery systems-An unusual maneuver for site specific drug delivery system. Int J Pharm Sci, 2011; 2(3): 132-52.
8. Patil SB, Murthy RS, Mahajan HS, Wagh RD, Gattani SG. Mucoadhesive polymers: Means of improving drug delivery. Pharma Times, 2006; 38(4): 25-8.

9. Satyabrata B, Ellaiah P, Choudhury R, Murthy KV, Bibhutibhusan P, Kumar MS. Design and evaluation of methotrexate buccal mucoadhesive patches. Int J Pharm Biomed Sci, 2010; 1(2): 31-6.
10. Bahuguna K, Ganarajan PK. Buccal Drug delivery: A Novel Approach. Indian Journal of Novel Drug Delivery, 2014; 6(3): 223-9.
11. Bobade NN, Atram SC, Wankhade VP, Pande DS, Tapar DK. A review on buccal drug delivery system. Int J Pharm Pharm Sci Res, 2013; 3(1): 35-40.
12. Jain N, Jain GK, Javed S, Iqbal Z, Talegaonkar S, Ahmad FJ, Khar RK. Recent approaches for the treatment of periodontitis. Drug discovery today, 2008; 1, 13(21-22): 932-43.
13. Patil BS, Tate SS, Kulkarni U, Hariprasanna RC, Wadageri GV. Development and in-vitro evaluation of mucoadhesive buccal tablets of Tizanidine hydrochloride using natural polymer xanthan gum. Int J Pharm Sci, 2011; 8(2): 140-6.
14. Miller N.S., Johnston T. P., The use of mucoadhesive polymers in buccal drug delivery, Adv. Drug Delivery Reviews, 2005; 57: 1666 – 1691.
15. Lalla JK, Gurnancy RA. Polymers for mucosal delivery-swelling and mucoadhesive evaluation. Indian drugs, 2002; 39(5): 270-6.
16. Johnston TP, Dias CS, Alur H, Mitra AK. Mucoadhesive polymers in ophthalmic drug delivery. InOphthalmic Drug Delivery Systems, 2003; 25: 430-457. CRC Press.
17. Rao NR, Shravani B, Reddy MS. Overview on buccal drug delivery systems. Journal of Pharmaceutical Sciences and Research, 2013; 1, 5(4): 80.
18. Koyi PK, Khan AB. Buccal patches: a review. International Journal of Pharmaceutical Sciences and Research, 2013; 1, 4(1): 83.
19. Gandhi RB, Robinson JR. Oral cavity as a site for bioadhesive drug delivery. Advanced drug delivery reviews, 1994; 1, 13(1-2): 43-74.
20. Boddupalli BM, Mohammed ZN, Nath RA, Banji D. Mucoadhesive drug delivery system: An overview. Journal of advanced pharmaceutical technology & research, 2010; 1(4): 381.
21. Srivastava N, Monga MG. Current status of buccal drug delivery system: a review. Journal of Drug Delivery and Therapeutics, 2015; 13, 5(1): 34-40.
22. Shakya AK, Madhav NS, Shakya P. Histological and mucoadhesion studies on transpalatal mucoadhesive disks of Rosiglitazone maleate. International Journal of Drug Delivery, 2011; 1, 3(3): 456.

23. Pharmaceutics the science of dosage form Design 2nd edition edited by M. E. Aulton. Published by Harcourt publishers Limited. 2002; 198-200.
24. Krishnarajan D, Jithin TG, Nikhil V, Nair AM, Sherin A, Thomas S, Purushothaman M. RECENT TREND AND APPROACHES OF BUCCAL DRUG DELIVERY SYSTEM: A REVIEW. Pharmacophore, 2016; 1, 7(5).
25. Madhav NS, Shakya AK, Shakya P, Singh K. Orotransmucosal drug delivery systems: a review. Journal of controlled release, 2009; 16, 140(1): 2-11.
26. Annigeri RG, Jadhav M, Juturu T. Clinical evaluation of transmucosal mucoadhesive meloxicam patch in dental pain reduction: A preliminary study. Indian journal of pain, 2015; 1, 29(2): 82.
27. Edgar WM. Saliva: its secretion, composition and functions. British dental journal, 1992; 172(8): 305-12.
28. Puratchikody A, Prasanth VV, Mathew ST, Kumar A. Buccal drug delivery: past, present and future-a review. International Journal of Drug Delivery, 2011; 1, 3(2): 171.
29. Paul AD, Samatha P, Manasa SL, Munemma R, Supriya D. Modeling the oral cavity with mucoadhesive drug delivery systems-a potential alternative to conventional therapy. Int J Pharm Sci Drug Res, 2017; 9(6): 299-307.