CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.5160104

Online at: http://www.iajps.com *Review Article*

A REVIEW ON: MUCOADHESIVE BUCCAL PATCHES AN ADVANCE TECHNOLOGY FOR ORAL DRUG DELIVERY

[1]PoojaVijay Dhakarao*,[2]Dr. Sanjay B. Patil, [3] Shubhangi Purushottam Khode

[1]M.Pharm., SNJB'S SSDJ College of Pharmacy, Department of Pharmaceutics, Chandwad, Dist- Nashik.Email-id :poojadhakr@gmail.com

[2]M.Pharm Ph.D, Email-id : sbpatil_99@rediffmail.com

[3]B.Pharm, Email-id : khodeshubhangi.gmail.com

Article Received: July 2021 **Accepted:** July 2021 **Published:** August 2021

Abstract:

Now-a-days mucoadhesive buccal patches are widely used in drug delivery system.It is very effective mode of administration of drug into a human body.It is used for both systemic and local application. It is a most easy and convenient route of administration. hence widely selected in drug delivery system.Mucous membrane is relatively permeable having a rich blood supply hence absorption of the drug takes place rapidly. To increase bioavailability of the drug mucoadhesive buccal patches are widely selected in drug delivery system. Film casting technique is the common technique for manufacture of buccal film. It is proven and accepted technology for the delivery of personal care products.

Keywords:*Buccal patches,Film casting, Mucoadhesive patches, Recent advancements*

Corresponding author:

PoojaVijayDhakarao *,

M.Pharm., SNJB'S SSDJ College of Pharmacy,
Department of Pharmaceutics, Chandwad,
Dist- Nashik. Email-id : poojadhakr@gmail.com

QR code

Please cite this article in press Pooja Vijay Dhakarao al., ***A Review On: Mucoadhesive Buccal Patches An Advance Technology For Oral Drug Delivery****.., Indo Am. J. P. Sci, 2021; 08(08).*

INTRODUCTION:

There are many routes of administration of drug. Some of them are Oral, transdermal, parenteral and local applications. But in all the most preferred route and convenient route of administration is oral. Oral route of drug delivery system is very traditional, convenient and most accepted route.

In Recent time the most accepted route of drug delivery system is Transmucosal route. It includes various regions of mucosal liningof nasal,oral,rectal, vaginal cavity.But the novel site is Oral cavity which includes sublingual,buccal,and local drug delivery sites. Mostly buccal region offers a attractive route for systemic drug delivery system for longer period of time. "BIOADHESIVE" formulations have become a most wanted route for drug administration for both systemic and local effects of the drug. "MUCOADHESIVE" is defined as state in which two materials are held together for extended period of time,of which one is in contact with mucous membrane. The mucous membrane is the region of relatively permeable with rich blood supply.

Mucoadhesive drug delivery system is mostly used as it avoids pre-systemic elimination in gastrointestinal tract. Hence Buccal patches are prioritypreferred rather than adhesive tablets in terms of their flexibility and comfort. The oral gels mostly get washed off or removed by saliva hence to protect the wound surface,to increase drug bioavailability buccal patches are widely used.

MUCOADHESION

'Mucoadhesion' can be use when the bond with a mucosal surface is formed. Mucoadhesion define as a state in which two components, one from biological source, are joined together for prolonged periods of time by the aid of interfacial forces. the mucoadhesive ability of dosage form is dependent upon a variety of factors, including nature of the mucosal tissue and the physicochemical properties of polymeric formulation.

MECHANISM OF MUCOADHESION

The mucoadhesive dosage form must proliferate over the substrate to induct a close contact and hike the surface contact assisting the diffusion of mucus chains. The mechanism of mucoadhesion is generally divided into two steps:

A)Contact stage

B)Consolidation stage

- The first stage is characterized by the contact between the mucoadhesive and the mucus membrane, with spreading and swelling of the formulation, initiating its deep contact with the mucus layer.
- In the consolidation step, the mucoadhesive materials are activated by the presence of moisture. Moisture plasticizes the system, allowing the mucoadhesive molecules to break free and to link up by weak van der waals and hydrogen bonds. Essentially, there are two theories explaining the consolidation step: the diffusion theory and the dehydration theory. According to the diffusion theory, the mucoadhesive molecules and the glycoproteins of the mucus mutually interact by means of interpenetration of their chains and building of secondary bonds. For this to take place, the mucoadhesive device has features favoring both chemical and mechanical interactions.

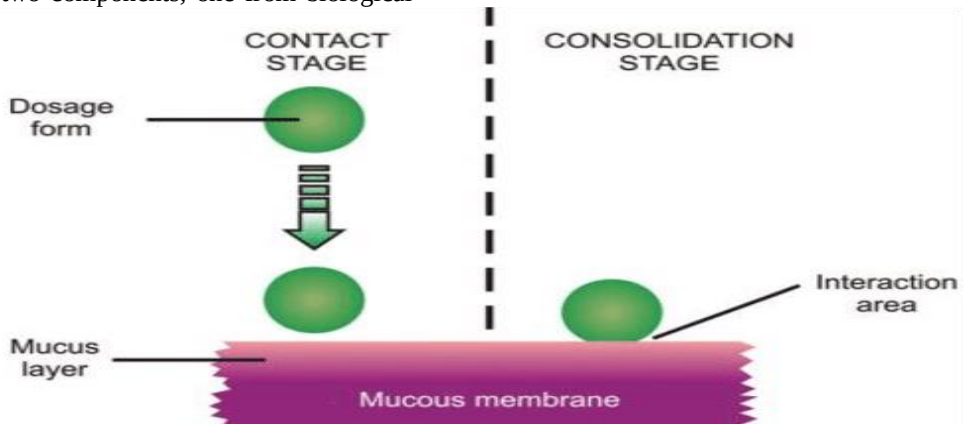

FIGURE NO.1.MECHANISM OF MUCOADHESION.

Benefitsof buccal drug delivery system

- It avoid first pass effect because drug directly absorbed from oral mucosa.
- Buccal drug delivery benefits by more blood supply towards oral cavity.
- Bypass exposure of the drugs to the gastrointestinal fluids.
- It shows lower side effect as compare to tablet and improved patient compliance.
- The use of buccal dosage forms is easier than others. They can be discontinued if toxic effects are appeared.
- The peptide molecules that not suitable for delivering through oral route can easily administered by buccal mucosa.
- buccal delivery system has capacity to withstand environmental conditions and sustained delivery of drugs possible.
- Non-invasive method of drug administration.
- Facility to include permeation enhancer or enzyme inhibitor or pH modifier in the formulation. An expanse of
- smooth muscle and relatively immobile mucosa, suitable for administration of retentive dosage forms.
- More rapid cellular recovery and achievement of a localized site on smooth surface of buccal mucosa.
- Low enzyme activity, suitability for drugs/ excipients that mildly and reversibly damages or irritates the mucosa.

Drawbacks:

- The unintentional removal of dosage form happens by incessant swallowing of saliva probable loss of medication.
- Drug which are unstable at buccal pH cannot be administered.
- The dilution of the drug takes place by uninterrupted excretion of the saliva.
- Lesser area of the oral cavity available for drug absorption.
- Drugs with large potency dosage are problematic to be given by buccal route.
- Drugs which have an acrimonious flavor are not appropriate for oral route.
- Only those drugs, which are absorbed by passive diffusion, can be administered by this route.
- Eating and drinking may become restricted.
- There is an ever-present possibility of the patient swallowing the tablet

Transmucosal drug delivery system:

Delivery of drugs through the absorptive mucosa in various easily accessible body cavities, like the Buccal, ocular, nasal, rectal, and vaginal mucosae, has the advantage of bypassing the hepatic-gastrointestinal first pass elimination associated with oral administration. Furthermore, because of the dual biophysical and biochemical nature of these mucosal membranes, drugs with hydrophilic and/or hydrophobic characteristics can be readily absorbed. Different types of transmucosal drug delivery systems are:

- Buccal Drug Delivery System.
- Ocular Drug Delivery System.
- Vaginal Drug Delivery System.
- Rectal Drug Delivery System.
- Nasal Drug Delivery System.
- Gastro Intestinal Drug Delivery System.

Polymer selection criteria for buccal Patches:

- It has to compatible with oral mucosal membrane**.**
- They have narrow delivery through tissues and polymer should have higher molecular weight.

Characteristics of ideal polymer:

- It has optimum molecular weight
- Degradation product should be non-toxic and non-absorbable from gastrointestinal tract.
- It hasGood spreadibility, wetting, swelling and biodegradable properties.
- It should not irritant to mucous membrane.
- Form a strong non-covalent bond with mucin epithelial cell surface.
- Rapid adherence to mucosa.
- Show bioadhesive properties in both dry and liquid state.

Film Forming Polymers:

TABLE NO.1.FILM FORMING POLYMERS.

Synthetic polymer	**Natural polymer**
Hydroxy propyl methyl cellulose (HPMC)	Chitosan
Poly (acrylic acid) polymer	Sodium alginate
Polyvinyl pyrrolidone (PVP)	Pectin
Polyvinyl alcohol (PVA)	Locust bean gum
Poly hydroxyethyl methacrylate	Guar gum
Polyethylene oxide	Xanthan gum
Sodium carboxymethyl cellulose (Na CMC)	Karaya gum
Hydroxy ethyl cellulose (HEC)	Gelatin
Hydroxrpropyl cellulose (HPC)	Tragacanth
Ethyl cellulose (EC)	Soluble starch

Factors Affecting Mucoadhesion:

TABLE NO.2. SHOWING FACTORS AFFECTING MUCOADHESION

- Molecular weight of the polymer
- Mucin turn over rate
- Flexibility of polymer chains
- pH at polymersubstrate interact
- Swelling factor, stereochemistry of polymer
- Concentration of polymer used

Theories of Mucoadhesion

Mucoadhesion is recently described by six different theories.These theories helps to manufactured a ideal type of mucoadhesive patches.These various theories are listed below as-

Electronic theory,Adsorption theory,Wetability theory,Diffusion theory,Fracture theory,& Mechanical theory.These theories were adapated by studying on the performance of several material and polymer-polymer adhesion which explains the phenomenon.

1] Electronic Theory

This theory is based on electronic differences in structure.In mucoadhesive patches different surfaces have different structural properties & electronic structure. These surfaces have opposing electrical charges.when these both material come into contact they transfer electrons leading to formation of double layer at the interface while the attractive forces within this electronic double layer determines the mucoadhesive strength.

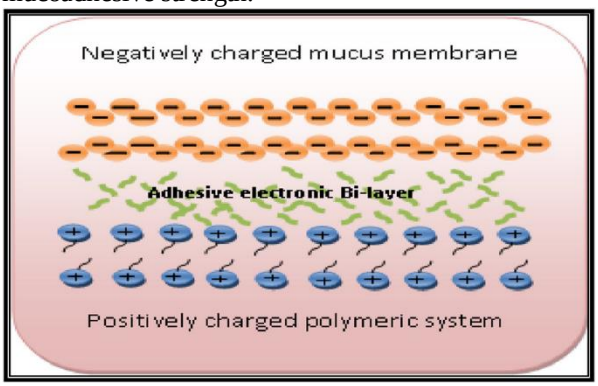

FIGURE NO.2.SHOWINGELECTRONICTHEORY OF MUCOADHESION.

2] Adsorption theory

Adsorption theory described the attachment of two surfaces on the basis of hydrogen bonding & van der waal's forces.It has known that these two forces are main contributor to adhesive interaction.this theory assumes an interaction across the interface occurs as a result of strong covalent bonding.

3]Wetability theory

This theory mostly accepted in liquid system. This theory presents the affinity to the surface in order to spread over it. This affinity is measured using a contact angle. Lower the contact angle more is the affinity. The contact angle should be equal or close to zero to provide adequate spreadability. Hence this spreadability is measured using mathematical equation as-

$S_{AB} = \gamma_B - \gamma_A - \gamma_{AB}$

where, S_{AB}=Spreadability coefficient

$\gamma_B - \gamma_A$ = difference in surface tension of two liquids A&B

γ_{AB}= Interfacial energy.

This energy should be positive to spread spontaneous on the membreane.

4]Diffusion theory

This theory explains the interdiffusion of polymer chains across an adhesive interface. This process is performed by concentration gradients and is affected by the available molecular chain lengths. The compatability of two polymers & their mobilities. The adhesion forces increase with degree of penetration. Hence the penetration depends on diffusion coefficients-

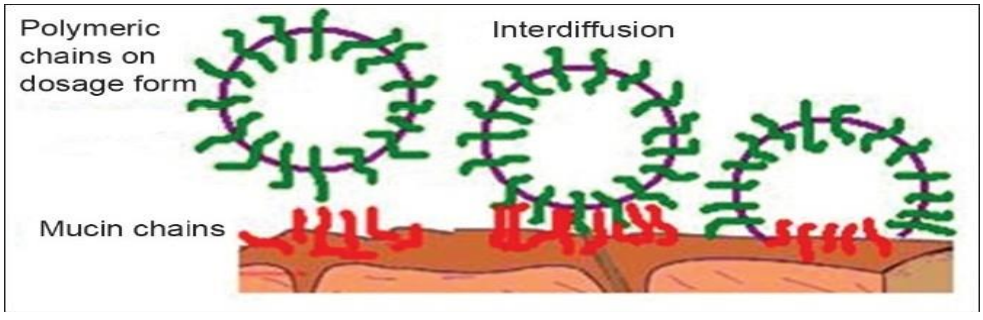

FIGURE NO.3.SHOWING DIFFUSION THEORY OF MUCOADHESION.

5] Fracture theory

This theory is an important theory in studying the mechanical strength of mucoadhesion.It finds the force required to break the two surfaces after adhesion is established. Mathematically it is expressed as –

$$S_m = F_m/A_0$$

Where, Sm is force calculated in tests of resistance to rupture.
Fm is maximal detachment force,A0 is total surface area involved in adhesive interaction.

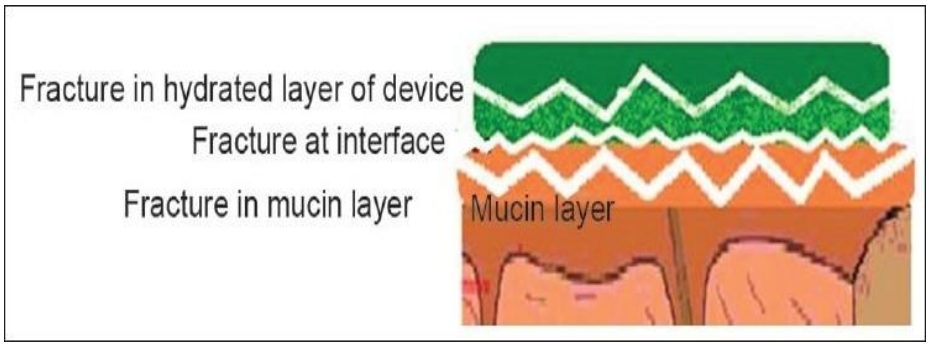

FIGURE NO.4.SHOWING FRACTURE THEORY OF MUCOADHESION.

6] Mechanical theory-

This theory assumes that adhesion arises from an interaction of liquid adhesive into irregularities on a rough surface also provides an increased surface area available for interaction which enhanced viscoelastic & plastic dissipation of energy.

- **Following charts summarizes the theories of mucoadhesion.**

TABLE NO.3.SHOWING SUMMARIZED THEORIES OF MUCOADHESION.

Electronic theory	• Attractive electrostatic forces between glycoprotein mucin network and the bioadhesive material.
Wetting theory	• Ability of bioadhesive polymers to spread and develop intimate contact with the mucous membrane.
Adsorption theory	• Surface forces (covalent bond, hydrogen nbond and van der waals forces) resulting in chemical bonding.
Diffusion theory	• Physical entanglement of mucin strands and flexible polymer chains.

Method of preparation:
Following methods are use for preparation of mucoadhesive buccal patches/films:

- Solvent casting method
- Hot melt extrusion method
- Direct milling method
- Semisolid casting method
- Rolling method

From above methods solvent casting is the most preferable because of its ease of method of preparation:

- In solvent casting method mucoadhesive polymers in required quantity is treated with solvent and polymer swell after vertexing.
- The measured quantity of plasticizer added in polymer mixture again vortexed.
- The quantity of drug that needed liquified in small volume of solvent system and added to the polymer solution and mixed well.
- Then entrapped air is removed and blend is transferred into a cleaned petri plate for drying.
- The drying temperature was kept at 40-50^{0}C till the flexible patches was formed.
- Lastly the patches were packed into an aluminum foil and stored in desiccators to maintain the integrity and elasticity of the patches.

Evaluation of Mucoadhesive buccal Patches:
There are various evaluation parameters to perform on prepared mucoadhesive patches. These parameters help to prepare proper dosage form and release a accurate dose into a body. Various evaluation parameters performed are as follows:

1]Film weight and Thickness:
It is the very first evaluation parameters of prepared patches for these 3 patches of every formulation were taken and weighed individually on digital balance. The average weights are calculated, and the weight variation is observed.
While, from the formulation 3patches were used for measuring the thickness using digital vernier caliper at six different places and the mean value was recorded.

2]Drug content uniformity:
A film was cut into three pieces of equal diameter were taken in separate 100 ml of pH 6.8 phosphate buffer was added and continuously stirred for 24 h. The solutions were filtered, suitably diluted and analyzed at 313 nm in a UV Spectro meter. The average of drug content of three films was taken as final reading. which gives the drug content and uniformity records.

3]Folding endurance:
This evaluation parameter helps to evaluate the patches for it's flexibility and breakability. It also ensures the folding ability of the patches. The 3 patches from the formulation were taken in this film is repeatedly folded at the same place of the patch till it breaks or folded manually which ensures the good film properties.Hence the number of times film gets folded at same place without breakage gives folding endurance value.

4]Surface pH: Buccal patches were left to swell for 2hr on the surface of an agar plate prepared by dissolving 2%(w/v) agar in warmed distilled water. Under continuous stirring and then pouring the solution into a petri-plate till gelling at room temperature then pH was measured by means of pH paper places on the surface of the swollen patch.

5]Stability of patches: In this parameter the two films were taken and kept for two different measured temperatures (4^0,25^0& 40^0) for continuous two months. Then samples were withdrawn for observing physical appearance, weight variation, thickness and drug content.

6]**Percentage moisture absorption (PMA):**
For the percentage moisture absorption parameter 10 test was carried out to check the physical stability of the buccal films at high humid conditions. In this evaluation parameter the moisture absorption capacity of the patches were determined as follows. Three 1cm diameter films were cut out and weighed accurately then the films were placed in desiccator containing saturated solution of aluminum chloride, keeping the humidity inside the desiccator at 79.5 %. After 3 days the films were removed, weighed and percentage moisture absorption was calculated. Average percentage moisture absorption of three films was found.

$$\text{Percentage moisture absorption} = \frac{Final\ weight - initial\ weight}{Initial\ weight} \times 100$$

7]**Percentage moisture loss (PML):**
Percentage moisture loss was performed to check the integrity of patches at dry condition. For this three 1cm diameter patches was cut out and weighed accurately and kept in desiccator's containing fused anhydrous calcium chloride. After 72 hours the films were removed, weighed. Average percentage moisture loss of three patches was observed using a mathematical expression.
Percentage moisture loss

$$= \frac{Initial\ weight - Final\ weight}{Initial\ weight} \times 100$$

8)Swelling Percentage (% S):
A drug loaded patches were placed in a thoroughly cleaned petri-dish and a graph paper was placed below the petri-dish, to measure the increase in area

due to swelling of the film. 50ml of pH 6.8 phosphate buffer was poured into the petri-dish. An increase in the weight of the patch was noted in 15 min intervals for 60 min and the weight was calculated. The swelling percentage11,12 was calculated by using the following formula,

$$\% S = \frac{X_t - X_0}{X_0} \times 100$$

Where,

% S - swelling percentage,

X_t - the weight of swollen film after time t,

X_0 -weight of film at zero time zero.

CONCLUSION:

The mucosa is well supplied with both vascular and lymphatic drainage and evading first pass metabolism. Buccal drug delivery is an encouraging area for continued research with the purpose of systemic delivery of orally inefficient drugs. The usage of buccal drug delivery is safe in patients because drug usage stopped if adverse effect appears. So in forthcoming years, it is predictable that buccal patches are one of the vital dosage forms in pharmaceutical and healthcare sector. Hence, the final conclusion of this review highlights the increase in percent of bioavailability and prevent first pass metabolism of buccal patches.

ACKNOWLEDGEMENT:

Author would like to thanks to professor Dr. S.B. Patil for his great guidance. She would also like to thanks for her colleagues Miss.Shubhangi khode for their contribution in preparing the article.

REFERENCES:

1. Michael j. Rathbone, Ian W. Kellaway, Gilles Pochel, and D.Duchene, Modified released drug delivery, Copyright by Marcel Dekker, pp.no 350-60.
2. Raymond C Rowe, Paul J Sheskey, Hand book of Pharmaceutical Excipients, Fifth Edition, pp. no. 336, 346,592, 624.
3. Brahmankar, D.M. and Jaiswal, S.B., Biopharmaceutics and pharmacokinetics a treatise, second edition., Vallabh prakashan publications, Delhi, 2009, pp. no. 397-470.
4. Lachman, L., Lieberman, H.A., The theory and practice of industrial pharmacy, third edition., Varghese Publishing House, Bombay, 1990. pp. no. 197- 243.
5. Indian Pharmacopoeia 2007, Vol. I, II & II
6. European pharmacopoeia 5.0, pp.no. 1444.
7. www.drugbank.com
8. www.wikipedia.com.
9. M Alagusundaram, C Madhusudhana Chetty, K Umasankari, P Anitha, K Gnanprakash and D Dhachinamoorthi. Buccal Drug Delivery System – An Overview. Research J. Pharm. and Tech. 2 (4): 653-663; (2009).
10. Navneet verma, pronobesh chattopadhyay, Polymeric platform for mucoadhesive buccal drug delivery system: a review, International journal of current pharmaceutical research vol 3(3), 3-8; (2011).
11. Yajaman Sudhakar, Ketousetuo Kuotsu, A.K.Bandyopadhyay. Buccal bioadhesive drug delivery -A promising option for orally less efficient drugs. Journal of Controlled Release. Vol. 114: 15–40; (2006).
12. B. K. Satishbabu* and B. P. Srinivasan, Preparation and Evaluation of Buccoadhesive Films of Atenolol, Indian J Pharm Sci; Vol. 70(2): 175– 179;(2008).
13. Soad A. Yehia, Omaima N. El-Gazayerly and Emad B. Basalious, Fluconazole Muco adhesive Buccal Films: In Vitro/In Vivo Performance, Current Drug Delivery, Vol.6, 17-27; (2009).
14. Rohit Chaudhary, Md. Shamim Qureshi, Jitendra Patel, Uttam Prasad Panigrahi, I.C.Giri. Formulation, Development and In-Vitro Evaluation of Mucoadhesive Buccal patches Of Methotrexate. International Journal of Pharma Sciences and Research, Vol.1 (9), 357-365; (2010).
15. J. Sahni, S. Raj, F. J. Ahmad,* and R. K. Khar. Design and In Vitro Characterization of Buccoadhesive Drug Delivery System of Insulin. Indian J Pharm Sci; 70(1): 61–65, (2008).
16. L. Perioli, V. Ambrogi, F. Angelici, M. Ricci, S. Giovagnoli, M. Capuccella, and C. Rossi. Development of mucoahesive patches for buccal administration of ibuprofen. J. Control. Release. Vol. 99; 73–82; (2004).
17. Soad A. Yehia, Omaima N. E. Gazayerly, and Emad B. Basalious. Design and In Vitro/In Vivo Evaluation of Novel Mucoadhesive Buccal Discsof an Antifungal Drug: Relationship between Swelling, and Erosion. Drug Release AAPS Pharm SciTech, Vol. 9, No. 4, 1207-1217; (2008).
18. Sonia Pandey, Arti Gupta, Jitendra Singh Yadav and D. R. Shah. Formulation and In-vitro evaluation of bilayered buccal tablets of carvedilol. Indian J.Pharm. Educ. Vol. 44(3): 1-8; (2010).
19. M. Alagusundaram, B. Chengaiah, S. Ramkanth, S. Angala Parameswari, C. Madhu Sudhana Chetty and D. Dhachinamoorthi. formulation and evaluation of mucoadhesive buccal films of

ranitidine. international J. pharmtech Vol.1, No.3, 557-563; (2009).
20. Smart JD, The basics and underlying mechanisms of mucoadhesion, Adv Drug Deliv Rev 2005; 57:1556- 68.
21. Nafee NA, Ismail FA, Boraie NA, Mortada LM, Mucoadhesive buccal patches of miconazole nitrate:in vitro/in vivo performance and effect of aging. Int J Pharm 2003; 264:1-14.
22. B.K. Satishbabu and B.P. Srinivasan, Preparation and evaluation of buccoadhesive films of atenolol, Indian. J. Pharm. Sci 2008; 70(2):175-179.
23. Noha AN, Nabila AB, Fatima A, Ismail and Lobna MM., Design and characterization of muco adhesive buccal patches containing cetyl pyridium chloride, Pharm. Acta Helvetiae 2003; 53: 199-212.
24. J Thimmasetty, GS Pandey and PR Sathesh Babu, Design and in vivo evaluation of carvedilol buccalmucoadhesive patches, Pak. J. Pharm. Sci 2008; 21(3), 241-248.
25. V.F. Patel, N.M. Patel and P.G. Yeole., Studies on formulation and evaluation of Ranitidine floating tablets, Indian J. Pharm. Sci 2005; 67(6):703-709.
26. Alka Lohani*, Neelima Prasad and Rajeshwer Kamal Kant Arya, formulation and characterization of mucoadhesive buccal films of ranitidine hydrochloride, international J. of Pharmaceutical sciences & research;2011; Vol. 2(9): 2457-2462.
27. Smart JD: The basics and underlying mechanisms of mucoadhesion. Advanced Drug Delivery Reviews 2005; 57:1556-68.
28. Amir H and Shojaei: Buccal mucosa as a route for systemic drug delivery: A Review. Journal of Pharmacy and Pharmaceutical Sciences 1998; 1:15-30.
29. Edith M, Donald EC and Claus ML: Bioadhesive Drug Delivery Systems, Marcel Dekker Inc New York 1999:541-562.
30. Pharmacopoeia of India. New Delhi: Ministry of Health and Family Welfare, Government of India, Controller of Publications 2007: Vol 1; 182-183., Vol 2; 889.
31. Michael J.R., Gilles P. and Firoz A.G.: Oral Mucosal Drug Delivery, Marcel Dekker Inc., New York, 1996:233-234.
32. Alfred Martin and James Swarbrick: Physical Pharmacy. Third edition 1994: 352-362.
33. Shubham Verma, Nitin Kumar and Pramod Kumar Sharma, Buccal Film: An Advance Technology for Oral Drug Delivery, Advances in Biological Research 8 (6): 260-267, 2014.
34. Hitanshi Kulinsinh Parmar, Kartik Kirit Pandya, Lalit Jitendrabhai Pardasani, Vibhuti Sanjeev Panchal and Hemal Thakorbhai Tandel, A systematic review on mucoadhesive drug delivery system, World Journal of Pharmaceutical Research, Volume 6,(9), 337-366.
35.www.researchgate.net
36.www.pharmainfo.net
37.www.pubchem.ncbi.nlm.nih.gov.
38. Chickering DE, III, Mathiowitz E. Fundamentals of bioadhesion. In: Lehr CM, editor. *Bioadhesive drug delivery systems-Fundamentals, Novel Approaches and Development*. New York: Marcel Dekker; 1999. pp. 1–85.
39. Ahuja A, Khar RK, Ali J. Mucoadhesive drug delivery systems. *Drug Dev Ind Pharm.* 1997;23:489–515.
40. Veuillez F, Kalia YN, Jacques Y, Deshusses J, Buri P. Factors and strategies for improving buccal absorption of peptides. *Eur J Pharm Biopharm.* 2001;51:93–109. [PubMed]
41. Punitha S, Girish Y. Polymers in mucoadhesive buccal drug delivery system: A review. *Int J Res Pharm Sci.* 2010;1:170–86.
42. Smart JD. The basics and underlying mechanisms of mucoadhesion. *Adv Drug Deliv Rev.* 2005;57:1556–68. [PubMed]
43. Hägerström H, Edsman K, Strømme M. Low-frequency dielectric spectroscopy as a tool for studying the compatibility between pharmaceutical gels and mucus tissue. *J Pharm Sci.* 2003;92:1869–81. [PubMed]
44. Dodou D, Breedveld P, Wieringa P. Mucoadhesives in the gastrointestinal tract: Revisiting the literature for novel applications. *Eur J Pharm Biopharm.* 2005;60:1–16. [PubMed]
45. Bindu M,Bodupalli,Zulkar N.K. Mohammed,Ravinder. A.Nath,David Banji, Mucoadhesive drug delivery system:an overview in Journal of Advanced Pharmaceutical Technology&Research, 2010 Oct-Dec; 1(4): 381–387.
46. Flávia Chiva Carvalho1, Marcos Luciano Bruschi2, Raul Cesar Evangelista1,3, Maria Palmira Daflon Gremião, "Mucoadhesive drug delivery system",by Brazilian journal of pharmaceutical sciences,vol.46.n.1,jan/march2010.
47. www.wikipedia.mucoadhesion.com