EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 7
Issue: 9
390-395
Year: 2020

# FORMULATION AND EVALUATION OF MUCCOADHESIVE BUCCAL TABLET OF ONDANSETRON HYDROCHLORIDE (ANTI-EMETIC AGENT)

**Shaikh Shakil Shaikh Khalil* and V. P. Wankhade**

Vidyabharati College of Pharmacy, C. K. Naydu Road, Camp, Amravati 444602 Maharashtra [INDIA].

***Corresponding Author: Shaikh Shakil Shaikh Khalil**
Vidyabharati College of Pharmacy, C. K. Naydu Road, Camp, Amravati 444602 Maharashtra [INDIA].

**Article Received on 10/07/2020** **Article Revised on 20/07/2020** **Article Accepted on 01/09/2020**

## ABSTRACT
Mucoadhesive buccal tablets containing ondansetron hydrochloride (ODH) were prepared using polymers like gelatin, chitosan, xanthan gum in varying concentration of 5, 10, 15% w/w and HPMC K4M 40% w/w by direct compression technique. Precompressional studies revealed good micromeritic properties of powder blend for compression and were found as per literature limits. The prepared tablets were evaluated for thickness, hardness, uniformity of weight, drug content, friability, swelling index, mucoadhesion strength, *in vitro* disintegration, dissolution time. The formulations containing xanthan gum gave better mucoadhesion, release characteristics compared to those containing gelatin and chitosan and the rank order of mucoadhesion. The tablets apart from fulfilling all the official specifications, exhibited higher rate of release, *in vitro* release from all ODH buccal tablets followed Super case II transport due to polymer chain disentanglement and relaxation. The results revealed that mucoadhesive buccal tablets containing ODH were successfully formulated by direct compression technique as an alternative to conventional tablets for therapy of nausea condition in patients.

**KEYWORDS:** Buccoadhesive tablet, Ondansetron HCl, direct compression.

## INTRODUCTION
For many decades, treatment of an acute disease or a chronic illness has been mostly accomplished by delivering drugs using various pharmaceutical dosage forms, including tablets, capsules, pills, suppositories, creams, ointments, liquids, aerosols and injectables as carriers. Amongst various routes of drug delivery oral route is perhaps the most preferred to the patient and the clinician alike. However this route presents some problems for a few drugs. The enzymes in the GI fluids, GIT-pH conditions and the enzymes bound to GIT membranes are a few factors responsible for the bioavailability problems. The blood that drains the GIT carries the drug directly to the liver leading to first-pass metabolism resulting in poor bioavailability. The inherent problems associated with the drug in some cases can be solved by modifying the formulation or by changing the routes of administration. Parenteral, mucosal and transdermal routes circumvent hepatic first-pass metabolism and offer alternative routes for the systemic delivery of drugs.[1]

In recent years, the interest in novel routes of drug administration occurs from their ability to enhance the bioavailability of drugs. Drug delivery via the buccal route using bioadhesive dosage forms offers such a novel route of drug administration. Extensive first-pass metabolism and drug degradation in the harsh gastrointestinal environment can be circumvented by administering the drug via buccal route.[2] Buccal delivery involves administration of desired drug through the buccal mucosal membrane lining of oral cavity. The mucosal lining of oral cavity offers some distinct advantages. It is richly vascularized and more accessible for the administration and removal of a dosage form. Additionally, buccal drug delivery has high patient acceptability compared to other non-oral routes of drug administration.[3] Drug absorption through buccal mucosa is mainly by passive diffusion into the lipoidal membrane. After absorption the drug is transported through facial vein which then drains into the general circulation via jugular vein bypassing the liver and thereby sparing the drug from first-pass metabolism.[4] Buccal route provides one of the potential routes for typically large, hydrophilic and unstable proteins, oligonucleotides and polysaccharides as well as conventional small drug molecules. The oral cavity can be used for local and systemic therapy. Examples of local therapy would be the treatment of oral infections, dental caries, mouth ulcers and stomatitis. The buccal route is of particular interest with regard to the systemic delivery of small molecules that are subjected to first pass metabolism or for the administration of proteins and peptides.[5]

## MATERIALS AND METHODS

ODH was obtained as a complimentary sample from Swami Samarth Pharm, Jalgaon. Spray dried lactose was obtained as Complimentary Sample from S.D Fine Chem. Mumbai. Chitosan was obtained as Complimentary Sample from Ozone Pharmaceutical Pvt.Ltd.Mumbai. Xanthan gum from s.d. fine chem. limited. Mumbai and gelatin from Epson chemicals Enterprises. Mumbai.

### Formulation of Mucoadhesive Buccal tablets containing ODH

Mucoadhesive tablets containing ODH were prepared by direct compression technique. The drug and the bioadhesive polymers, Xanthan Gum, Chitosan, Gelatin, HPMC K4M and Spray dried lactose as diluent as given in table 1 was taken; weighed individually and blended to fineness in a ball mill. Each powder was separately passed through sieve 100/120 and the undersized particles were used for further mixing. The powder beds were all taken into a cube mixer and mixed for 10 min. After adequate mixing of drug as well as other components talc and magnesium stearate were added and further mixed for additional 3-5mins. The powder bed was studied for pre compressional parameters and then compressed into tablets on a 10 station rotary tablet press using 6 mm diameter, flat faced punches at a pressure of approximately 4- 6 kgs /$cm^2$.

### Evaluation of ODH buccal tablets

Ten tablets were selected at random and weighed individually. The individual weights were compared with the average weight for determination of weight variation. Hardness and friability of the tablets were determined by using Pfizer hardness tester and Roche friabilator respectively. From each batch three randomly selected tablets were weighed accurately and powdered in a clean and dry glass mortar with pestle. Powder equivalent to 100 mg of drug was transferred into 100 mL volumetric flask containing methanol; the remaining volume was made up to 100 mL with methanol. Shaken intermittently for 24 h and the solution was filtered, make up desired dilutions and analyzed for drug content at $\lambda_{max}$ 212.5 nm, using a methanol as a blank. Triplicate readings were taken and average was computed. Disintegration test was performed for the prepared tablets in 900 mL, pH 6.8 at 37±2 $^{o}$C by using USP disintegration apparatus. Time was noted with a digital chronometer. Triplicate readings were taken and average was computed. The various post compression characteristics evaluated for Mucoadhesive buccal tablets are illustrated in table no. 3 and 4.

### Determination of swelling index

The swelling properties of the tablets were evaluated by determination of percent of swelling. Each tablet was weighed (W1) and immersed in a simulated saliva fluid at pH6.8 for predetermined times. After immersing the formulation for specified time, the tablets were wiped off to remove excess of surface water by using filter paper and weighed (W2) The %Swelling = (W2) – (W1)/ (W1)x100. Where, W 1 is the initial weight of the tablet and W2 is the weight of the tablet after the particular swelling time interval.[6]

### Mucoadhesion strength

The equipment was fabricated by us in the laboratory. A double beam physical balance was taken, both the pans were removed. The left pan was replaced with a brass wire to which was hanged a polypropylene disc (A), also locally fabricated include an expanded cap another propylene disc was placed right below the suspended disc upon the base of the balance. The right pan (C) was replaced with a lighter pan so that the left pan weighs 9.5gm more than the right pan. The lower polypropylene block was intended to hold the mucosal tissue (D) of bovine buccal mucosa and placed in a beaker containing pH 6.8(E). Fresh bovine buccal mucosa obtained from local slaughterhouse was cut into pieces, washed with distilled water followed by phosphate buffer pH 6.8. This buccal mucosa was placed over the surface of lower polypropylene cylinder (B) and secured this assembly was placed in a beaker containing pH 6.8 buffer at 37±2$^{0}$c.

From each batch one tablet at a time was taken and stuck to the lower surface of upper polypropylene cylinder with a standard cyanoacrilate adhesive. The beaker containing mucosal tissue secured upon the lower cylinder (B) was manipulated over the base of the balance so that the mucosal tissue is exactly below the upper cylinder (A). The exposed part of the disc was wetted with a drop of buffer, then a weight of 15gms was placed was placed above the expanded cap, left for 15 minutes. After which the tablet binds with mucin, weight was removed.

Then slowly and gradually weights were added on the right side pan till the disc separates from mucosal surface/membrane. The weight required for complete detachment is noted ($W_1$gms). ($W_1$–9.5gms) gives force required for detachment, expressed weight in grams. Procedure was repeated for two more tablets and average was computed and recorded.

### Surface pH study

The buccal tablet was allowed to swell by keeping it in contact with 1ml of distilled water for 2hr at room temperature. The pH was measured by bringing the pH-meter electrode, in contact with the surface of the tablet and allowing it to equilibrate for 1 min. The mean of three readings was recorded.[7]

### *In vitro* Dissolution studies

*In vitro* dissolution of mucoadhesive buccal tablets of ODH was studied in USP XXII type-II dissolution apparatus (Electro lab Mumbai.) employing a paddle stirrer at 50 rpm using 900 ml of pH 6.8 buffer at 37 ± 0.5º C as dissolution medium. Aliquots of dissolution medium (1 ml) were withdrawn at specified intervals of

time and analyzed for drug content by measuring the absorbance at 212.5 nm. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. Cumulative percent of ODH released was calculated and plotted against time.[6]

**Drug release kinetics**

The *in vitro* drug release profiles were subjected for regression analysis and for kinetic study by zero order, first order and higuchi square root kinetics.[8]

**Table No. 1: Formulation Of Mucoadhesive Buccal Tablet.**

| Ingredients (mg) | Formulation Code | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
| Ondanstron HCL (mg) | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 |
| Gelatin (5% 10% 15% w/w) | 5 | 10 | 15 | -- | -- | -- | -- | -- | -- |
| Chitosan (5% 10% 15% w/w) | -- | -- | -- | 5 | 10 | 15 | -- | -- | -- |
| Xanthan Gum (5% 10% 15% w/w) | -- | -- | -- | -- | -- | -- | 5 | 10 | 15 |
| HPMC K4M (40%) | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 |
| Spray Dried Lactos (Diluent) | 45 | 40 | 35 | 45 | 40 | 35 | 45 | 40 | 35 |
| Talc & Magnesium Stearate | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Total | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |

Note: All ingredients taken in mg.

**Table No.2: Pre-compression Parameters of mucoadhesive Buccal tablet.**

| Formulation Code | Compressibility index % | Bulk density gm/ml | Tapped density gm/ml | Angle of repose ( ° θ) | |
|---|---|---|---|---|---|
| | | | | Before adding glidants | After adding glidants |
| **F1** | 13.6 | 0.454 | 0.526 | 30.96 | 23.96 |
| **F2** | 12.2 | 0.457 | 0.517 | 30.01 | 24.62 |
| **F3** | 12.8 | 0.457 | 0.521 | 30.65 | 28.61 |
| **F4** | 12.30 | 0.500 | 0.569 | 21.80 | 18.43 |
| **F5** | 14.2 | 0.489 | 0.576 | 29.24 | 26.56 |
| **F6** | 13.0 | 0.483 | 0.555 | 32.61 | 29.05 |
| **F7** | 12.5 | 0.491 | 0.561 | 34.9 | 29.87 |
| **F8** | 12.9 | 0.487 | 0.568 | 28.61 | 25.08 |
| **F9** | 13.4 | 0.459 | 0.530 | 26.05 | 19.79 |

**Table No. 3 Post-compression parameter of Formulation Batches (n=3).**

| Parameters | Formulation Batches | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
| Weight (mg ±SD) | 105.4 ± 6.32 | 104.6 ± 3.83 | 102.2 ± 2.25 | 101.3 ± 4.96 | 104.9 ± 6.24 | 103.6 ± 3.71 | 101.8 ± 2.09 | 101.1 ± 1.28 | 100.8 ± 1.54 |
| Hardness (kg/cm ± SD) | 5.7 ± 0.115 | 5.8 ± 0.100 | 5.83 ± 0.152 | 5.16 ± 0.208 | 3.02 ± 0.004 | 3.06 ± 0.004 | 3.17 ± 0.005 | 3.13 ± 0.005 | 3.18 ± 0.005 |
| Thickness (mm ± SD) | 3.15 ± 0.002 | 3.16 ± 0.004 | 3.14 ± 0.004 | 3.02 ± 0.004 | 3.06 ± 0.004 | 3.06 ± 0.004 | 3.17 ± 0.005 | 3.13 ± 0.005 | 3.18 ± 0.005 |
| Drug content (mg ± SD) | 7.804 ± 0.001 | 7.929 ± 0.011 | 7.612 ± 0.017 | 7.754 ± 0.003 | 7.75 ± 0.002 | 7.945 ± 0.006 | 7.741 ± 0.001 | 7.925 ± 0.006 | 7.916 ± 0.005 |
| Friability % | 0.16 | 0.60 | 0.49 | 0.70 | 0.65 | 0.80 | 0.81 | 0.49 | 0.49 |
| Disintegration time (sec) | 248 | 278 | 336 | 210 | 217 | 220 | 514 | 636 | 750 |
| Bioadhesion strength ± SD | 9.667 ± 0.115 | 12.133 ± 0.208 | 14.267 ± 0.157 | 15.200 ± 0.450 | 17.567 ± 0.115 | 21.500 ± 0.500 | 20.933 ± 0.404 | 23.000 ± 0.500 | 26.833 ± 0.288 |
| Surface Ph ± SD | 6.24 ± 0.02 | 6.60 ± 0.09 | 6.47 ± 0.05 | 6.60 ± 0.03 | 6.23 ± 0.05 | 6.52 ± 0.01 | 6.64 ± 0.08 | 6.57 ± 0.04 | 6.93 ± 0.09 |

**Table 4: Swelling studies of Mucoadhesive Buccal tablets of Ondansetron Hydrochloride.**

| | Swelling Index% | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Time (h)** | **0.25** | **0.50** | **0.75** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | 8 |
| **F1** | 3.96 | 5.50 | 10.87 | 12.48 | 20.03 | 31.25 | 40.82 | 42.14 | 44.78 | - | - |
| **F2** | 2.614 | 5.55 | 10.45 | 13.07 | 23.53 | 29.41 | 34.31 | 39.86 | 46.40 | 49.67 | 55.22 |
| **F3** | 4.90 | 8.49 | 10.13 | 14.70 | 31.37 | 42.15 | 47.71 | 54.57 | 54.90 | 57.18 | 59.80 |
| **F4** | 2.26 | 3.55 | 5.17 | 6.79 | 12.79 | 26.86 | 31.71 | 37.21 | 39.48 | - | - |
| **F5** | 2.61 | 5.22 | 8.23 | 10.78 | 23.20 | 34.31 | 44.44 | 56.86 | 57.36 | - | - |
| **F6** | 4.33 | 6.66 | 10.66 | 15.33 | 24.33 | 32.00 | 41.66 | 44.66 | 51.33 | 58.33 | 66.30 |
| **F7** | 5.0 | 8.0 | 13.00 | 18.00 | 26.66 | 33.0 | 37.0 | 40.33 | 45.33 | 49.34 | 59.66 |
| **F8** | 5.28 | 7.92 | 13.86 | 18.48 | 29.70 | 37.62 | 50.825 | 55.44 | 61.71 | 67.65 | 72.77 |
| **F9** | 4.33 | 9.66 | 16.33 | 26.00 | 39.00 | 52.66 | 63.00 | 70.66 | 75.66 | 81.33 | 87.33 |

**Table.No.5: Various kinetic parameters derived from *invitro* study of mucoadhesive buccal tablets.**

| Formulation | *In-Vitro* dissolution Study | | | |
|---|---|---|---|---|
| | Zero Order | | Peppas | |
| | n | r | n | r |
| **F1** | 0.866 | 0.997 | 1.709 | 0.926 |
| **F2** | 0.820 | 0.993 | 1.557 | 0.909 |
| **F3** | 0.753 | 0.975 | 1.737 | 0.931 |
| **F4** | 0.809 | 0.975 | 1.601 | 0.929 |
| **F5** | 0.791 | 0.992 | 1.328 | 0.867 |
| **F6** | 0.780 | 0.993 | 1.424 | 0.892 |
| **F7** | 0.979 | 0.997 | 1.652 | 0.913 |
| **F8** | 0.865 | 0.987 | 1.794 | 0.922 |
| **F9** | 0.842 | 0.982 | 1.818 | 0.983 |

## RESULTS AND DISCUSSION

Mucoadhesive Buccal Tablets of ODH were prepared by direct compression technique using gelatin, chitosan and xanthan gum as mucoadhesive polymers and Spray Dried Lactose as diluent along with 40 % w/w HPMC K4M as binder. A total of nine formulations (F1 to F9) were designed and evaluated for various parameters. The tablet powder beds showed uniform and reproducible precompressional parameters indicated their free flowing and ease for compression as indicated in table 2. The average weight of the prepared tablets was in between 100.8 ± 1.54 mg to 105.4 ± 6.32 mg for a 100 mg tablet (n=10). The average thickness was found to be 3.02±0.004 mm to 3.17±0.005 (n=3).

The hardness of prepared tablets was found to be fairly consistent and uniform, ranging between 5.06 ± 0.115Kg/cm$^2$ to 6.0±0 Kg/cm$^2$ (n=3). The friability of all the formulations was less than 1% indicating the ability of tablet to withstand abrasion in handling packaging and shipment. The drug content of all the formulations having dose of 8 mg were found to be fairly uniform, reproducible and consistent, ranging between of 7.612 ±0.004 mg to7.945±0.01 mg for a tablet weighing 100 mg. The surface pH of the tablets, were found to be 6.23 ±0.05 to 6.93 ± 0.09 as represented in table 3. It was found that, increase in mucoadhesive polymer content increases the swelling index; indicated in figure 1 and Mucoadhesion strength of the tablet formulations.

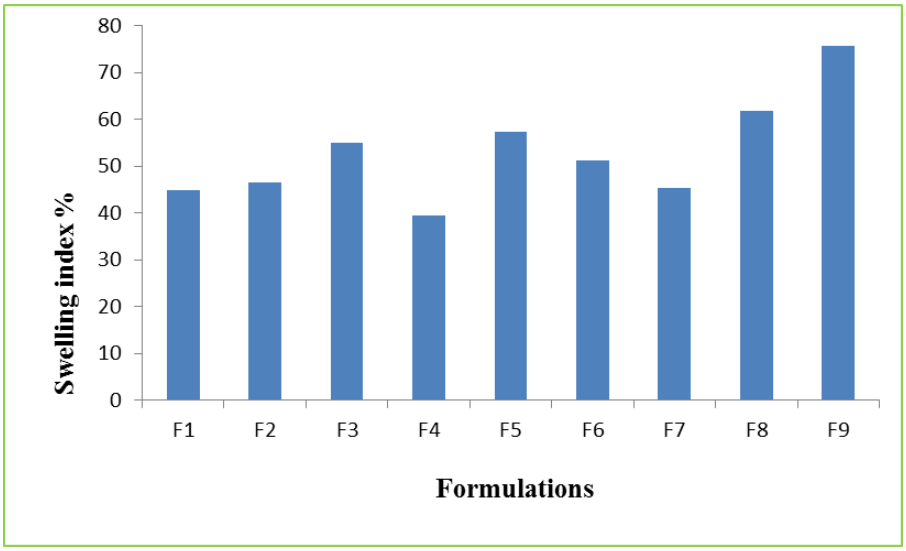


**Fig.1: percent swelling index of ODH mucoadhesive buccal tablet.**

The order of mucoadhesion strength was found to be F9> F8> F7 for tablets containing xanthan gum, F6> F5> F4 for tablets containing chitosan and F3>F2> F1 for tablets containing gelatin and the data was indicated in table 3.

As the content of mucoadhesive polymer in the tablet is

increased, the rate of release figure 2. To ascertain the mechanism of release the data was plotted according to korsemeyer peppa equation the obtained results of kinetic analysis were given in table 5. Later it was found that, the release from the tablet follows Super case II transport owing polymer chain disentanglement and relaxation.

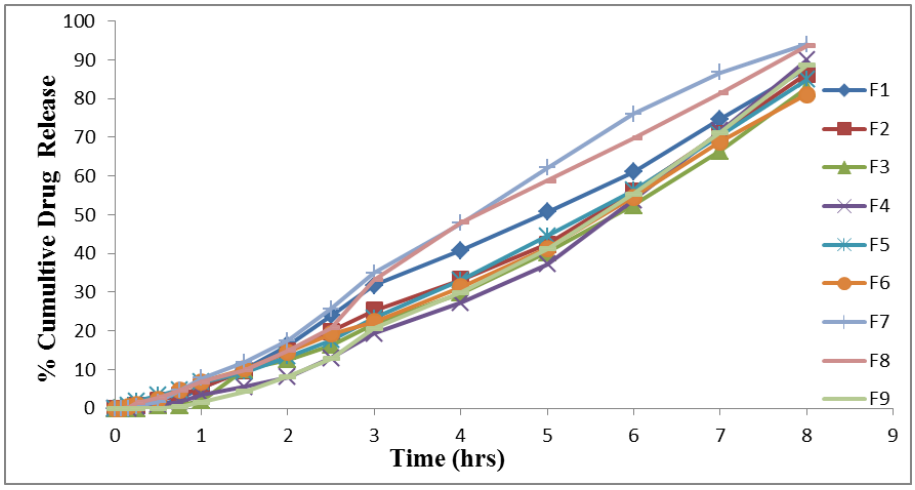


**Fig. 2: comparative in vitro drug release profile of ODH from mucoadhesive buccal tablet.**

## CONCLUSION

Buccal formulations of ODH in the form of mucoadhesive tablets were developed to a satisfactory level, in terms of drug release, bioadhesive strength, content uniformity, swelling index, surface pH, friability, hardness and weight variation. Development of mucoadhesive buccal drug delivery of ODH is one of the alternative routes of administration to avoid first pass hepatic metabolism, improve bioavailability and sustain release. In this present study a formulation comprises of xanthan gum (F8 and F9) showed optimum drug release and satisfactory mucoadhesive properties. Thus the study revealed that the ODH buccal tablets showed good mucoadhesion time with sustained release of drug for 8 hours. The optimized formulation also showed satisfactory surface pH and physical parameters, effective *in vitro* dissolution and comfort ability in the oral cavity. From the results of present investigation it can be concluded that ODH can certainly be administered through the oral mucosa and Xanthan gum is suitable for development of mucoadhesive system. Further work is recommended to support its efficacy claims by pharmacodynamic and pharmacokinetic studies in human beings. The results revealed that fast dissolving tablets containing ODH were successfully formulated by wet granulation technique as an alternative to conventional tablets.

## ACKNOWLEDGEMENT

The authors are thankful to Dr. V. P. Wankhde, Principal & management and staff of Vidyabharati College of Pharmacy for providing necessary facilities to carry out the present research and also to Swami Samarth Pharma, Jalgaon and S.D Fine Chem. Mumbai for providing complementary samples of active drug and excipients required for the study.

## REFERENCES

1. Jain NK. Controlled and novel drug delivery. 1st ed. New Delhi: CBS Publishers & Distributors, 1997; 52-81.
2. Patel VM, Prajapati BG, Patel MM. Formulation, evaluation and comparison of bilayered and multilayered mucoadhesive buccal devices of propranolol hydrochloride. AAPS Pharm Sci Tech., 2007; 8(1): 1-8.
3. Miller NS, Chittchang M, Johnston TP. The use of mucoadhesive polymers in buccal drug delivery. Adv Drug Deliv Rev., 2005; 57: 1666-1691.
4. Vyas SP, Khar RK. Controlled drug delivery-concepts and advances. 1st ed. New Delhi: Vallabh Prakashan, 2002.
5. Shojaei HA. Buccal mucosa as a route for systemic drug delivery: A Review. J Pharm Sci., 1998; 1(1): 15-30.
6. Balamurugan M, Saravanan VS, Ganesh P, Senthil SP, Hemalatha PV, Sudhir Pandya. Development and *in-vitro* evaluation of mucoadhesive buccal tablets of domperidone . Res. J. Pharm. and Tech., 2008; 1(4): 377-380.
7. Mahalaxmi D, Senthil A, Prasad V, Sudhakar B, Mohideen S.Formulation and evaluation of mucoadhesive buccal tablets of glipizide.Inter. J. Biopharm, 2010; 1: 100-107.
8. Korsmeyer RW, Peppas NA, Gurney R, Deckar B, Buri P. Mechanism of solute release from porous hydrophilic polymers. Indian j Pharm Sci., 1983; 15: 25-5.
9. Prasad Kadam B, Remeth Dias J, Kailas Malil K, Vijay Havaldarl D, Niranjan Mahajan S. Formulation and evaluation of buccoadhesive tablets of Atenolol, J. Pharm. Res., 2008; 1(2): 193-199.
10. Pulak Kumar Metia, Amal Kumar Bandyopadhyay, In-vitro Evaluation of Novel Mucoadhesive Buccal Tablets of Oxytocin prepared with Diospyros

Peregrine Fruits Mucilages, Yakugaku Zasshi. The pharmaceutical society of Japan, 2008; 128(4): 603-609.
11. Veuillez F, Kalia YN, Jaques Y, Deshusses J, Buri P. Factors and strategies for improving buccal absorption of peptides. Euro. J. Pharm. Biopharm, 2001; 51: 93-109.
12. Yajaman Sudhakar, Ketousetuo kuotsu and A K Bandyopadhyay. Buccal bioadhesive drug delivery-A promising option for orally less efficient drugs. J. Control. Rel., 2006; 114: 15-40.
13. Yamagar M, Kadam V, Hirlekar R. Design and evaluation of buccoadhesive drug delivery system of metoprolol tartrate. Inter. J. PharmTech Res., 2010; 2(1): 453-462.