ISSN: 0975-766X
Research Article

Available Online through
www.ijptonline.com

DESIGN AND DEVELOPMENT OF MUCOADHESIVE DRUG DELIVERY SYSTEM OF ZOLMITRIPTAN

N. G. Raghavendra Rao*, M. R. Munde, Mohd Abdul Hadi, Shrishail M. Ghurghure
PG Department of Pharmaceutics, Luqman College of Pharmacy, Gulbarga - 585 102, Karnataka, India.
Email:ngraghu@rediffmail.com

Received on 03-02-2011 *Accepted on 15-02-2011*

ABSTRACT:

The zolmitriptan is a serotonin (5-HT_1) agonist used for the treatment of migraine with or without aura. The half-life of zolmitriptan is 2.5 to 3 hrs and it undergoes hepatic metabolism, the absolute oral bioavailability is about 40 to 50%. So, in order to improve the bioavailability and efficacy, we have prepared buccal films of zolmitriptan. In the present research work, buccal films were prepared using different mucoadhesive polymers by Solvent Casting Technique. Buccal films were characterized for number of parameters like physical appearance and surface texture, weight uniformity, thickness, folding endurance, swelling index, surface pH, drug content uniformity, *in-vitro* residence time, tensile strength, drug-excipients interaction study, and *in-vitro* drug release study. All the prepared films were smooth surface and elegant texture. All the prepared films are weighing in between 20.66 to 26.66 mg. The thickness of the films was in the range of 0.220 to 0.306 mm. Folding endurance was in the range of 265 to 295. Swelling index in the range of 29.93 to 40.15 %. Surface pH was in the range of 6.50 to 6.83 pH. Drug content uniformity study showed uniform dispersion of the drug throughout the formulation in the range of 95.66 to 98.54 %. The *in-vitro* residence time for all the films is in between 4.36 to 8.23 hrs. The tensile strength of films is in the range of 6.233 to 4.533 Kg/cm^2**.** FT-IR studies revealed that, there was no incompatibility of the drug with the excipients used. *In-vitro* drug release studies in the range of 71.22 to 96.55 in 10 hrs. Formulations like ZBF1 and ZBF3 shows highest drug release at 10^{th} hrs 96.55%, 83.60% respectively. Release of Zolmitriptan from all films followed zero order and mechanism was diffusion rate limited. Hence these formulations of

Zolmitriptan mucoadhesive buccal films promising one as the controlled drug delivery, shows moderate swelling, convenient resident time will lead to improve the bioavailability and greater therapeutic efficacy.

Keywords: Zolmitriptan, buccal films, mucoadhesion / Bioadhesion, i*n-vitro* drug release.

INTRODUCTION:

The extensive efforts have recently been focused on targeting a drug or drug delivery system in a particular region of the body for extended period of time to get the desire benefit, not only for local targeting of drugs but also for the better control of systemic drug delivery[1]**.** Buccal delivery of dugs provides an attractive alternate to the oral route of drug administration. The mucoadhesive drug delivery system is delivery system which become adhesive on hydration and hence can be used for targeting a drug to particular region of the body for extended period of time. Buccal cavity has wide variety of functions and it acts as an excellent site for the absorption of the drugs. It provides direct entry of drug molecules into the systemic circulation, and avoids hepatic first pass metabolism and gastrointestinal drug degradation[2]. Various mucoadhesive formulations were suggested for buccal delivery that includes buccal patches [3,4], adhesive tablets[5,6] and adhesive gels[7] . Buccal films over come some of the drawbacks of other dosage forms. They have unique characteristics including flexibility, relatively rapid onset of drug delivery, sustained drug release and rapid decline in the serum drug concentration when the patch is removed. The film is confined to the buccal area over which it is attached and therefore the absorption profile may have less inter and intra-individual variability.

The zolmitriptan is a serotonin (5-HT_1) agonist used for the treatment of migraine with or without aura. The absolute oral bioavailability is about 40to 50%. The half-life of zolmitriptan is 2.5-3 hrs and it undergoes hepatic metabolism[8-10]. In order to overcome such hepatic metabolism and poor bioavailability the drug is selected as suitable candidate for bioadhesive buccal drug delivery. The objective of present work to develop the mucoadhesive films of zolmitriptan using solvent casting technique by using different polymers like sodium carboxy methyl cellulose (NaCMC), hydroxy ethyl cellulose (HEC), hydroxy propyl methyl cellulose (HPMC), Chitosan and evaluated for different parameters.

MATERIALS AND METHODS:

Zolmitriptan was obtained as gift sample from Cipla Pvt. Ltd., Mumbai. NaCMC, HPMC, HEC were purchased from Loba chemical Pvt. Ltd., Mumbai. Chitosan was purchased from Sangam Lab. Pvt. Ltd., Mumbai. Propylene glycol was purchased from S.D. Fine Chem. Lab., Mumbai.

Preparation of Zolmitriptan buccal films[11]: Buccal films of zolmitriptan were prepared by solvent casting technique. Composition of circular cast films of various formulations is mentioned in **Table 1.** The mucoadhesive films were prepared using polymers like NaCMC, HPMC, HEC, and Chitosan; Propylene glycol was used as plasticizer. The calculated amount of polymer was dispersed in three fourth volume of water with continuous stirring using magnetic stirrer and the final volume was adjusted with distilled Water. In case of chitosan the polymeric solution was prepared by using 1.5% (v/v) acetic acid in distilled water with continuous stirring for 48 hrs. The resultant viscous Chitosan solution was filtered through gauze. The calculated amount of zolmitriptan was incorporated in the polymeric solutions after levigation with 30% propylene glycol of polymer weight. The solution was casted onto mercury substrate then kept in hot air oven at 40° C for 24 hrs (or at room temperature in case of chitosan). The film was punched into size 10 mm films containing 2.5 mg of zolmitriptan.

Table-1: Composition of zolmitriptan mucoadhesive buccal films.

FC	Polymer Concentration (%w/v)				Plasticizer* conc.(%w/v) Propylene Glycol
	Na CMC	HEC	HPMC	Chitosan	
ZBF1	3	--	--	--	30
ZBF 2	--	3	--	--	30
ZBF 3		--	8	--	30
ZBF 4	--	--	--	1.5	30

Percentage of polymer weight.
FC= Formulation code
Each 10 mm film contains 2.5 mg of zolmitriptan

Evaluation of zolmitriptan mucoadhesive buccal films: The prepared Zolmitriptan buccal films were evaluated for following properties like weight uniformity, thickness, folding endurance, swelling index, surface pH, drug content estimation, *in-vitro* residence time, tensile strength, *in-vitro* release study, and drug polymer interaction.

Weight uniformity and film thickness[12]: Three films of size 10mm diameter were weighed individually using digital balance and average weights were calculated. Thickness of films was measured by using screw gauge at different spots of films and average was taken.

Folding endurance[13]: The test for folding endurance ensures the tensile strength of the films. Folding endurance of the film was determined by repeatedly folding a small strip of film at the same place till it breaks. The number of times the film could be folded at same place without breaking gives the value of folding endurance.

Swelling Index[14]: The swelling index of the films determined by immersing pre-weighed film of size 2 cm^2 in 50 ml water. The strip were taken out carefully at 5, 10 upto 30 min intervals, blotted with filter paper and weighed accurately.

The swelling index calculated by

$$\% \text{ Swelling Index} = \frac{Xt - Xo}{Xo} x100$$

Where,

Xo is the initial film weight at zero time.

Xt is the weight of the swollen film after time‘t’.

Surface pH study[15]: Surface pH was determined by the films were allowed in contact with 1ml of distilled water. The surface pH was noted by bringing a combined glass electrode or pH paper near the surface of films and allowing equilibrate for 1 min.

Tensile strength of the films[16]: Tensile strength of the film was determined with Digital Tensile Tester Tinius olsen (model HT 400 Pneumatic Grip Controller force). The sensitivity range of the machine is 1 to 10 Newtons. It consisted of two load cell grips. The lower one was fixed and upper one was movable. The test patch of size (1×4 cm^2) was fixed between these cell grips and force was gradually applied till the film broke. The tensile strength of the patch was taken directly from the dial reading in Newtons, which was converted into kilograms.

***In-vitro* residence time[17]:** The *in-vitro* residence time was determined using IP disintegration apparatus. The disintegration medium was 800 ml of pH 6.8 phosphate buffer maintained at 37 ± 2^0 C. The segments of rat intestinal mucosa, each of 3 cm length, were glued to the surface of a glass slab, which was then vertically attached to the apparatus. Three mucoadhesive films were hydrated from one surface using pH 6.8 phosphate buffer solutions and then 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 immersed in the pH6.8 phosphate buffer solution at the lowest point and was out at the highest point. The time required for complete erosion or detachment of the film from the mucosal surface was recorded. A test for measuring the resistance of a film to tensile strength and reported in Kg/cm^2. The bursting strength of all the films was evaluated by using standard bursting strength tester.

Drug content uniformity[18]: The films were tested for drug content. Films of 10mm diameter were cut from three different places from casted films. Each film was placed in separate 100 ml volumetric flask and dissolved in pH 6.8 phosphate buffer and continuous stirred for 24 hrs. The solutions were filtered, and diluted and analyzed at 222 nm using UV/visible spectrophotometer (Shimadzu UV-1700). The average of drug content of three films was taken. The percentage drug content was determined using the standard graph.

***In-vitro* release studies[19]:** *In-vitro* release studies were carried out by attaching sigma dialysis membrane to one end of the open cylinder which acts as donor compartment. The prepared buccal films containing drug was placed inside donor compartment which is agitated continuously using magnetic stirrer and then

temperature was maintained at 37 ± 1^0 C. Receptor compartment consists of 100 ml of pH6.8 phosphate buffer solution, sample of 2 ml were withdrawn at periodic intervals from receptor compartment and replaced with fresh 2 ml of pH6.8 phosphate buffer solution immediately and the drug release was analyzed spectrophotometrically at 222 nm.

Characterization of zolmitriptan films:

FTIR Studies: IR spectra for drug zolmitriptan, excipients and formulations ZBF1, ZBF2, ZBF3 and ZBF4 were recorded in a Fourier transform infrared (FTIR) spectrophotometer (FTIR 410, Jasco) with KBr pellets.

RESULTS AND DISCUSTION:

In the present study mucoadhesive buccal films for zolmitriptan were developed to improve the bioavailability and half life of the drug. At the outset method, as a preformulation study for drug polymer compatibility by FTIR gave conformation about their purity and showed no interaction between drug and selected polymers. Mucoadhesive films of zolmitriptan were prepared using mucoadhesive polymers NaCMC, HEC, HPMC, and Chitosan. The drug delivery system was designed as a matrix.

Evaluation of physicochemical parameters of developed zolmitriptan films:

All the films were shows smooth surface and elegant texture. The physical characteristics of various films are given in **Table 2.** The weight of 10 mm film was in the range of 20.66 to 26.66 mg and film thickness in the range of 0.220 to 0.306 mm. The surface pH was determined in order to investigate the possibility of any side effects, in the oral cavity. Acidic or alkaline pH is bound to cause irritation to the buccal mucosa. Attempt was made to keep the surface pH close to the neutral pH. The surface pH of all the formulations was found to be within ±1.5 units of neutral pH. Hence it is assumed that these formulations cause no irritation in the oral cavity. Surface pH of film was in the range of 6.50 to 6.833 pH.

Table-2: Physical evaluation of mucoadhesive buccal films of Zolmitriptan.

FC	Weight uniformity (mg) ±SD, (n=3)	Thickness (mm) ±SD, (n=3)	Surface pH ±SD, (n=3)	Folding Endurance ±SD, (n=3)	% Swelling Index ±SD, (n=3)
ZBF1	20.66 ± 1.833	0.2633 ± 0.015	6.63 ± 0.057	265 ± 3.605	40.15 ± 1.537
ZBF 2	23.66 ± 1.032	0.220 ± 0.020	6.70 ± 0.173	285 ± 3.605	32.65 ± 1.358
ZBF 3	23.00 ± 2.316	0.243 ± 0.020	6.83 ± 0.057	274 ± 2.000	38.01 ± 1.746
ZBF 4	26.66 ± 1.527	0.306 ± 0.015	6.50 ± 0.200	295 ± 2.645	29.93 ± 1.100

F.C - Formulation code

Note: Values in parenthesis are standard deviation (±SD)

The folding endurance gives the idea of flexible nature of films. The folding endurance was measured manually, films were folded repeatedly till it broke, and it was considered as the end point. The recorded folding endurance of all the prepared films was > 300 times, that can be consider as a sign of good flexibility. Folding endurance was found to be in the range of 265 to 295. ZBF1 showed minimum folding endurance. However, all the films showed satisfactory flexibility. The swelling behavior and *in-vitro* residence time of the mucoadhesive polymers are observed as given in **Table 2 and 3.** The percent swelling index and *in-vitro* residence time for the films is in between 29.93 to 40.15 % and 4.36 to 8.23 hrs respectively. The swelling behaviors of polymer in film were shown in **Fig 1.** The drug content results were shown in **Table 3** in all the formulations drug was uniformly distributed throughout the films in the range of 95.66 to 98.54 %.

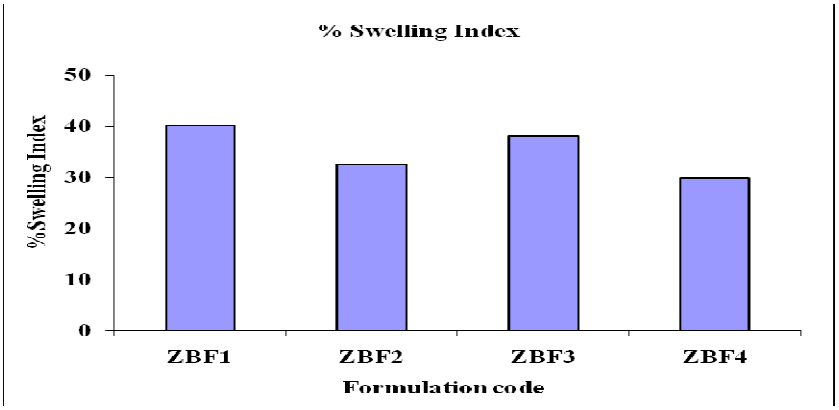

Fig1: Comparative swelling index of formulations ZBF1to ZBF4

Table-3: Physical Evaluation of Mucoadhesive Buccal films of Zolmitriptan.

FC	*In-vitro* residence time(Hrs) ±SD, (n=3)	%Drug Content ± SD, (n=3)	Tensile Strength ±SD, (n=3)	Drug released in 5 hrs. ±SD, (n=3)	Drug released in 10 hrs. ±SD, (n=3)
ZBF1	4.36 ± 0.152	98.54 ± 1.732	4.53 ±0.251	56.54 ± 0.385	96.55 ± 0.385
ZBF 2	6.23 ± 0.152	96.52 ± 1.732	5.533 ± 0.208	48.10 ± 1.920	78.67 ± 1.405
ZBF 3	5.23 ± 0.152	95.66 ± 1.154	4.866 ± 0.251	50.42 ± 0.715	83.60 ± 0.975
ZBF 4	8.23 ± 0.0577	97.24 ± 1.000	6.233 ± 0.152	37.51 ± 0..997	71.22 ± 0.728

F.C - Formulation code
Note: Values in parenthesis are standard deviation (±SD)

The tensile strengths of drug-loaded films were in the range of 6.233 to 4.533 Kg/cm^2. The results are given in **(Table 3).** This is justified because dissolved zolmitriptan strengthened the bonding of polymer chains. The tensile strengths of films were in the order of ZBF1 > ZBF3 > ZBF2 > ZBF4. Among all the patches studied film ZBF4 showed highest tensile strength and film ZBF1 showed lowest tensile strength. This must be due to the hydrogen bonding between alcohol groups of drug and polymer. However, film ZBF4 in presence of chitosan along with drug showed increased tensile strength.

The data obtained from *in-vitro* drug release study performed upto 8 hrs gives a clear indication that prepared films shows necessary control release profile desire for bucco adhesive drug delivery. The *in-vitro* release studies of various formulations were performed in pH 6.8 phosphate buffer solutions at 222 nm. The drug release profiles of zolmitriptan films were shown in **Fig 2.** Amongst them, Formulations like ZBF1 and ZBF3 shows highest drug release at 10th hrs 96.55%, 83.60% respectively. On the other side ZBF4 formulation shows lowest release profile 71.22% at end of 10th hrs among all. Again all the formulation shows more than 70 % of drug release at 10th hrs. The differences of release profile may be due to differences in characteristics and presence of different functional groups of introduced polymers. Again it has been found that increase solid content of polymer has a negative effect on drug release.

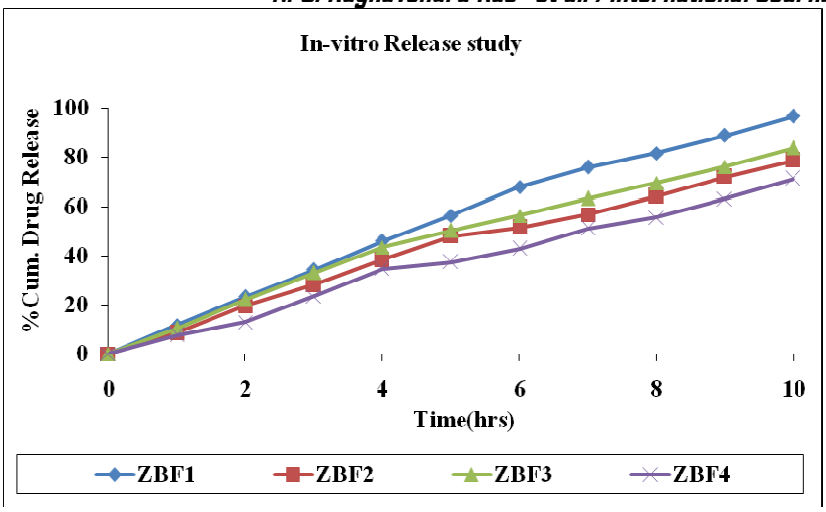

Fig 2: Comparative release profile of zolmitriptan buccal film formulations ZBF1to ZBF4.

Kinetics drug release result shown in **Table 4** reveals that all formulations follows zero-order kinetics as correlation coefficient (r^2) values are higher than that of first-order release kinetics. Mechanism of drug release pattern i.e. diffusion and swelling was confirmed by Higuchi plots. The Higuchi plots represent of cumulative percentage drug release versus square root of time. The Higuchi plots were found to be linear with correlation coefficient values shown in **Table 4 and Figs 3-5**. It was concluded that the release of drug from the films followed the diffusion controlled mechanism in all the formulations. The plots of log cumulative percentage drug release versus log time were found to be linear to the all formulations. On the basis of plots it is concluded that the release of zolmitriptan from films have obeyed Super Case- II transport.

Table 4: Kinetic parameters of zolmitriptan buccal films.

FC	Zero-order (r^2)	First- order (r^2)	Highuchi plot (r^2)	Peppas plot (r^2)
ZBF1	0.9887	0.8884	0.9506	0.9962
ZBF 2	0.9875	0.9769	0.9515	0.9888
ZBF 3	0.9833	0.9757	0.9628	0.9896
ZBF 4	0.9917	0.9748	0.9315	0.9883

F.C - Formulation code

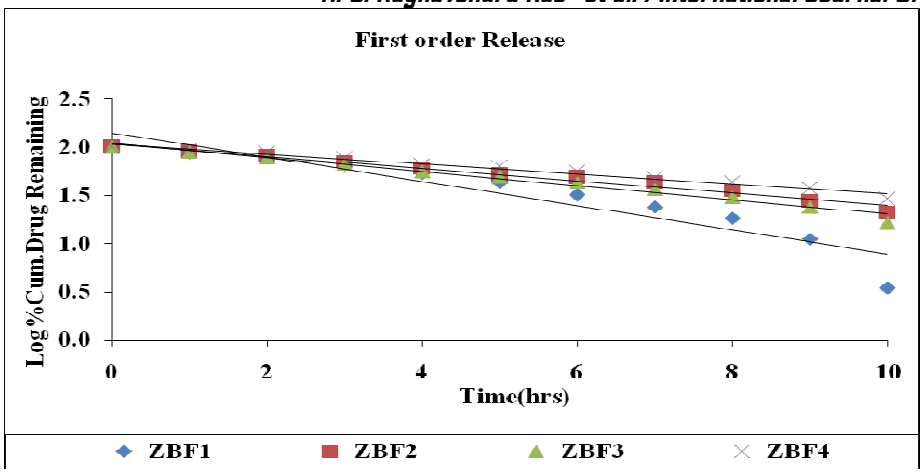

Fig 3: First order release plots of zolmitriptan buccal film formulations ZBF1to ZBF4.

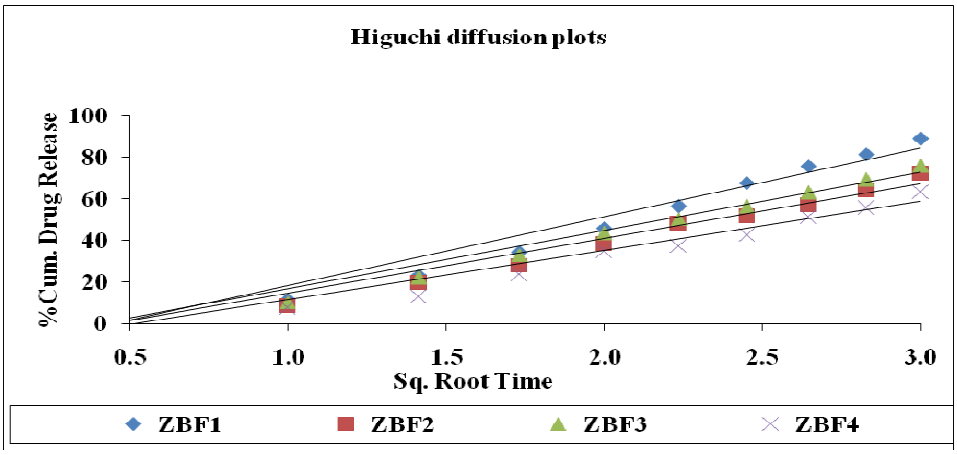

Fig 4: Higuchi Diffusion plots of zolmitriptan buccal film formulations ZBF1to ZBF4.

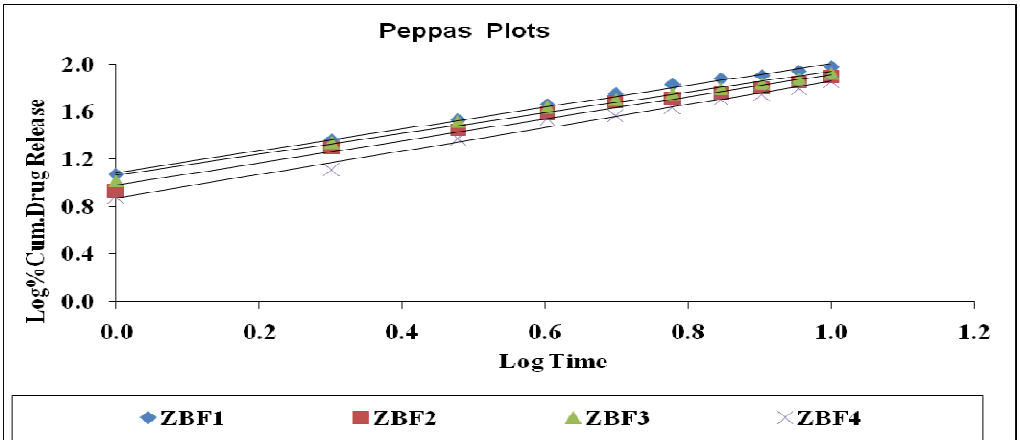

Fig 5: Peppas log-log plots of zolmitriptan buccal film formulations ZBF1to ZBF4.

In [Figs 6-10] shows IR spectrum of the pure drug zolmitriptan and ZBF1 to ZBF4 formulations. The zolmitriptan has indicating presence of absorption peak due to presence of N-H of the lactam, as well as secondary amine absorption, suggesting that these functionalities are present in the drug molecule.

The aromatic and aliphatic C-H absorption are noticed from 2850 cm^{-1} to 3100 cm^{-1}.The characteristics C=O-O of the drug exhibited a absorption peak at 1750 cm^{-1} which is in cyclic form. These are the characteristics of the zolmitriptan.

The zolmitriptan used in the formulations, with various excipients. In the ZBF1 formulation sodium salt of CMC and drug are used. In this case characteristics absorption peaks of sodium salt of CMC have been remained in the formulated product; hence formulation is a mixture but not a reaction product. The IR spectrum of the formulation ZBF2 in it the HEC and drug are used and observed that, it gives broad absorption peak of O-H present in molecule and C-H absorption peak at 2900 cm^{-1}, suggesting that aromatic nucleus is not present in molecule. The HEC used in preparation of formulation it is found that all the characteristics absorption peak of the drug and excipients supporting idea like, formulation is a mixture of both drug and excipients but not reaction product.

The IR spectrum of formulation ZBF3 in it HPMC and drug is used. In this formulation IR spectrum the strong hydroxyl peak is observed at 3400 cm^{-1}, suggesting that primary hydroxyl group is present. C-H aliphatic nature are found to present in molecule giving absorption peak from2833 cm^{-1} to 2974 cm^{-1} so, in this molecule these characteristics are observed in spectra. When this is along with drug presenting formulation taken for IR spectra. In this IR all the characteristics absorption peak of the drug and HPMC are observed and found that no chemical reaction taken place. Hence drug present in free state not in the form of reaction product.

In IR spectrum of formulation ZBF4 the chitosan is used in this formulation. The chitosan which is a polymer of carbohydrates. In this IR spectrum –OH/ NH peaks are observed around 3500 as a broad hump, suggesting that chitosan, characteristics peaks present. When chitosan are used in formulations, the

formulated product remains the entire characteristics absorption peak. Suggesting that during formulation drug has remained in an unaffected form.

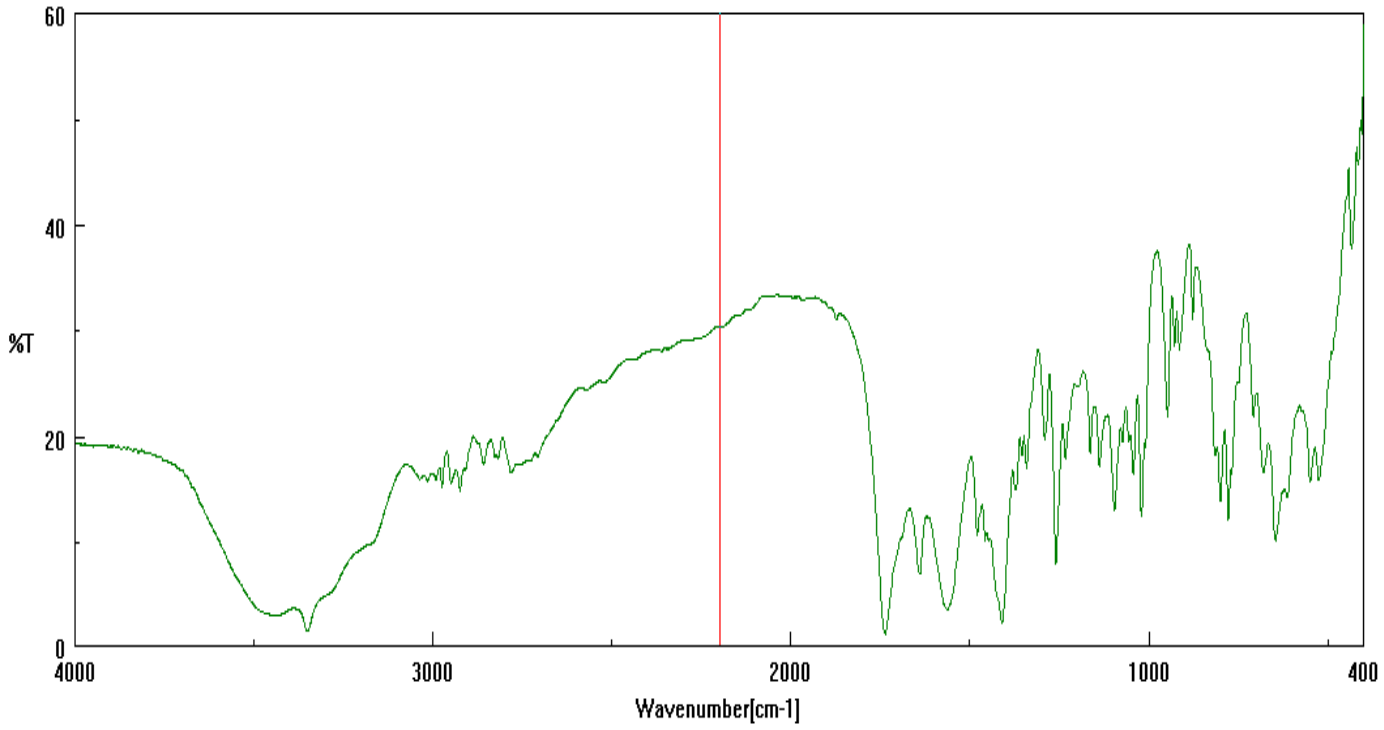

Fig 6: FTIR spectra of zolmitriptan pure drug.

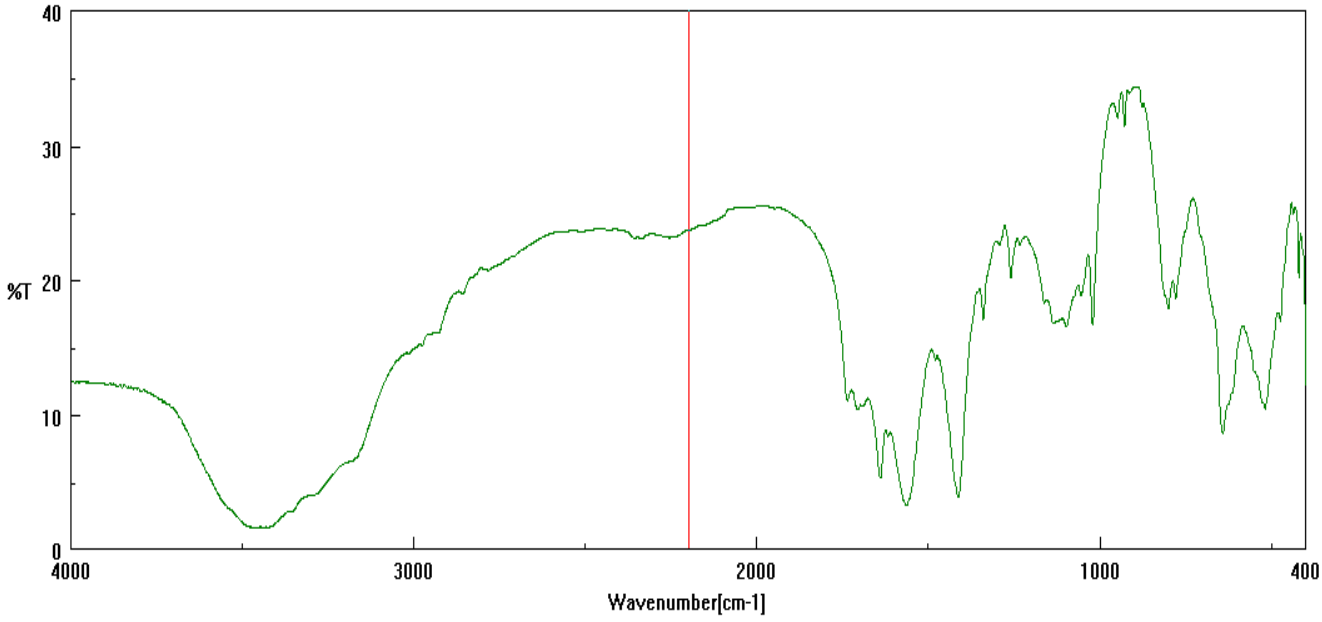

Fig 7: FTIR spectra of formulation ZBF1.

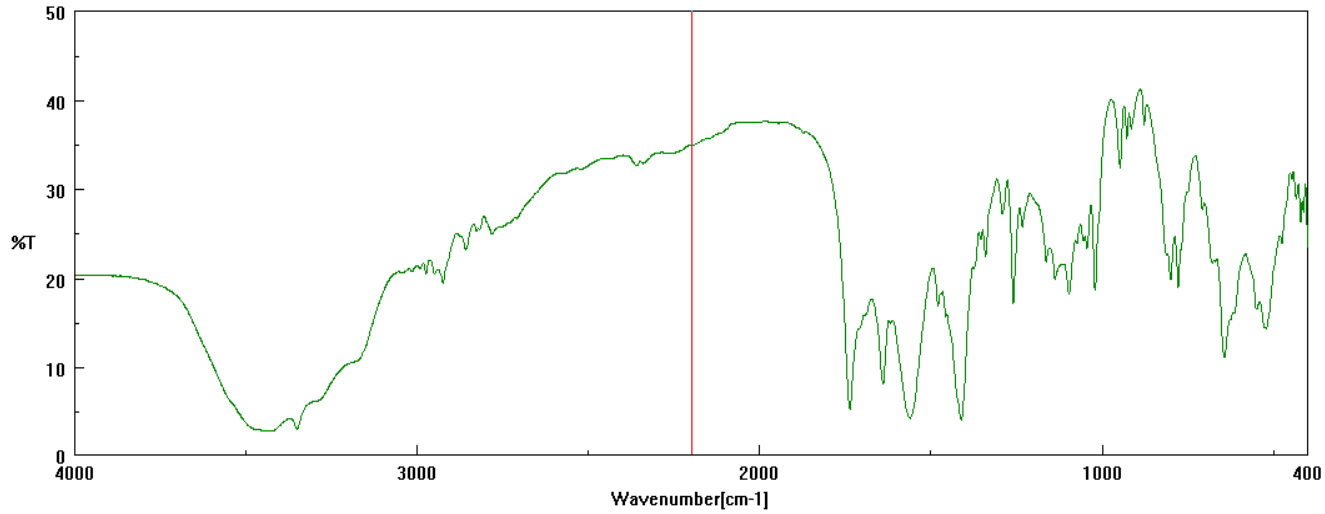

Fig 8: FTIR spectra of formulation ZBF2.

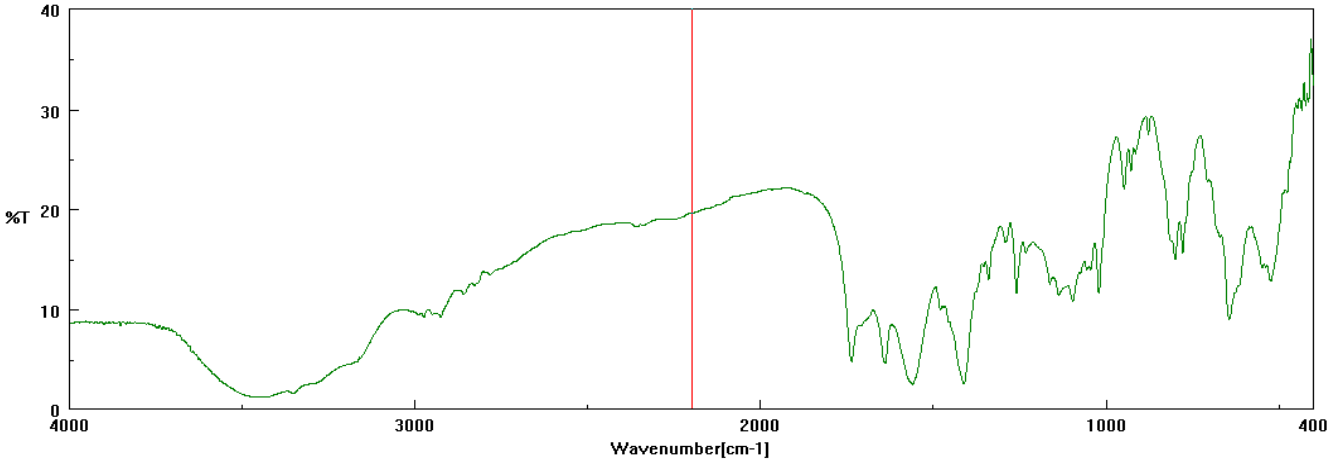

Fig 9: FTIR spectra of formulation ZBF3.

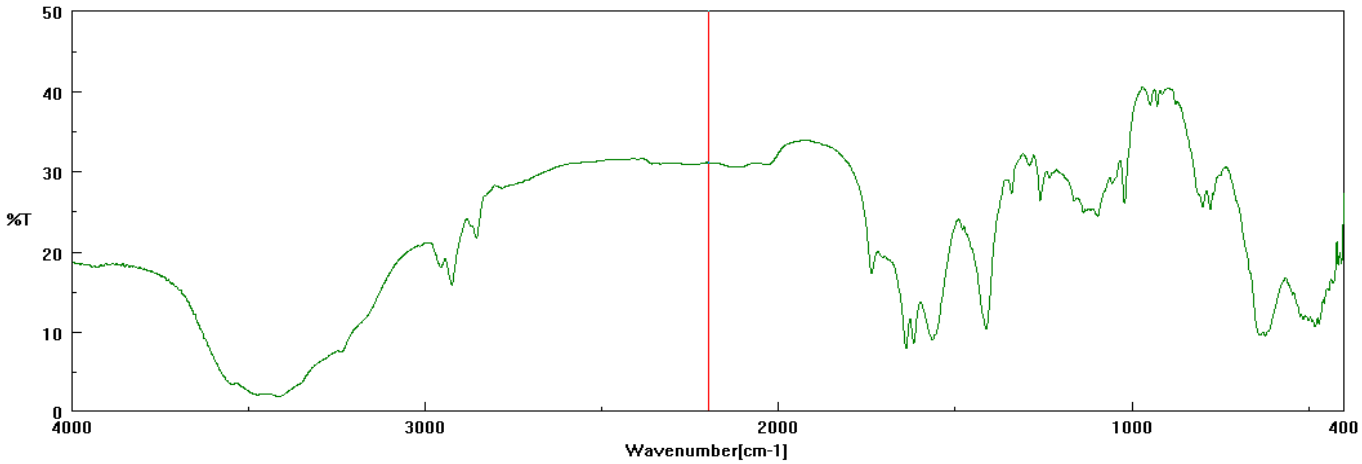

Fig 10: FTIR spectra of formulation ZBF4.

CONCLUSION:

Release of Zolmitriptan from all films followed zero order and mechanism was diffusion rate limited. Hence these formulations of Zolmitriptan mucoadhesive buccal films promising one as the controlled drug delivery, shows moderate swelling, convenient resident time will lead to may improve the bioavailability and greater therapeutic efficacy.

ACKNOWLEDGEMENTS:

Authors thank Cipla Pvt Ltd. Mumbai for providing a gift sample of Zolmitriptan. The authors are also thankful **to** Dr. M. G. Purohith, Emeritus Professor, Luqman College of Pharmacy, and Gulbarga for their valuable suggestions in carrying out this research work. The authors are also thankful to Dr. M. A. Mujeeb, Chairman, Luqman College of Pharmacy, Gulbarga, providing the facilities to carry out the research work.

REFERENCES:

1. Jain, N.K., Controlled and Novel Drug Delivery, 1st Edition, published by CBS publishers & Distributors, New Delhi; 1997: 52-81.
2. Parmar, V.J., Lumbhani, A.N., Vijaylakshmi, P, Sajal, Jha. (2010). Formulation development and evaluation of buccal films of carvedilol . International journal of pharmaceutical sciences and research, Vol.,1, issue 8 (Suppl.).
3. Anders, R., and Merkle H.P. (1989). Evaluation of laminated mucoadhesive patches for buccal drug delivery. Int. J. Pharm. **49:** 231-240.
4. Vamshi Vishnu, Y., Chandrasekhar, K., Ramesh, G., and Madhusudan Rao, Y. (2007) Development of mucoadhesive patches for buccal administration of carvedilol. Curr. Drug Del; **4:** 27-39.
5. Owens, T.S., Dansereau, R.J., and Sakr, A.,(2005). Development and evaluation of extended release bioadhesive sodium fluoride tablets. Int. J. Pharm. **288:** 109-122.
6. Jafar, A., Ali, N., Djavad, F., Massoud, A., Mohammad, R.S.S., and Majid, S. (2004). Development and evaluation of buccoadhesive Propranolol hydrochloride tablet formulations: effect of fillers. *IL Farmaco* **59:**155-161.

7. Ishida, M., Nambu, N., and Nagai, T. (1983). Highly viscous gel ointment containing carbopol for application to the oral mucosal. *Chem Pharm Bull*. **31:** 4561-4564.
8. S. C. Sweetman (Ed.), Martindale- the Complete Drug Reference Pharmaceutical Press, London (U. K.) 2002 33th edition, 458.
9. Moffat, A.C, Osselton, M.D., Widdop B. (2004) Clarke's Analysis of drugs and poisons. 3rd edition Vol (2); 1714.
10. http://www.drugs.com/cons/Zolmitriptan.
11. Nafee, N.A., Ismail, F.A., Boraiem, N.A., Mortada, L.M. (2005). Mucoadhesive buccal patches of miconazole nitrate*: in-vitro/in-vivo* performance and effect of ageing International Journal of Pharmaceutics, 264;1-14.
12. Kapil, K.P., Manoj, K.J., Asha, S.J., Shivanand, K. (2010). Formulation and evaluation of Timolol maleate buccal mucoadhesive patches Journal of Pharmacy Research, Vol (3) Issue (8), 2031-1035.
13. Doijad, R.C., Manvi, F.V., Malleswara, R., and Patel, P.S.(2006). Buccoadhesive drug delivery system of isosorbide dinitrate: Formulation and evaluation. Indian Journal of Pharmaceutical Sciences; 68(6):744-748.
14. Perioli, L., Ambrogi, V., Angelici, F., Ricci, M., Giovagnoli, S., Capuccella, M., Rossi, C. (2004). Development of mucoadhesive patches for buccal administration of ibuprofen. Journal of Control Release. (99)73- 82.
15. Patel, V.M., Prajapati, B.G., Patel, M.M. (2007). Design and characterization of chitosan-containing mucoadhesive buccal patches of Propranolol hydrochloride Acta Pharma. (57) 61-72.
16. Deshmane, S.V., Channawar, M.A., Chandewar, A.V., Joshi, U.M., Biyanikar. (2009). Chitosan based sustained released mucoadhesive buccal patches containing Verapamil HCL. International Journal of Pharmacy and Pharmaceutical Sciences Vol;1;Nov-Dec.

17. Giradkar, K.P., Channawar, M.A., Kajale, A.D., Sridhar, E., Kamble, RS., Bakde, B.V., Chandewar, A.V.(2010) Design development and *in-vitro* evaluation of bioadhesive dosage form for buccal route. International Journal of Pharma. Research and Develop; Vol-2/Issue-6.

18. Alagusundaram, M., Chengaiah, B., Ramkanth, S., Parameswari, SA., Chetty, C.M., Dhachinamoorthi, D.(2009). Formulation and evaluation of mucoadhesive buccal films of ranitidine International Journal of Pharma Tech Research; Vol 1. No.3. P557-563.

19. Raghavendra Rao, N.G., Suryakar, V.B., Thube, K., (2010). Development of mucoadhesive films for buccal administration of montelukast International Journal of Pharmacy and Technology; Vol (2); issue (1) 1-15.

Corresponding Author:

Dr.N.G Raghavendra Rao*,

Professor and HOD, PG Dept of Pharmaceutics,

Luqman College of Pharmacy, Old Jewargri Road,

Gulbarga-585102, Karnataka.

Email: *ngraghu@rediffmail.com*