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Research Article

FORMULATION AND EVALUATION OF FLUCONAZOLE PATCHES FOR BUCCAL DRUG DELIVERY ROUTE

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Abstract:

Fluconazole is a first-generation triazole antifungal medication that generally used to treat serious, invasive fungal infections. These are generally seen in patients who are immune compromised, and include invasive candidiasis, invasive aspergillosis, and certain emerging fungal infections. In the present study buccal drug delivery of Fluconazole was developed to overcome the first pass metabolism and to reduce the frequency of dosing compared to oral route. Matrix type of buccal patches were developed by using polymers HPMCK4M and HPMCK100M. Buccal patches were prepared by employing solvent casting method. Propylene glycol and Tween80 were selected as permeation enhancer and plasticizer. Drug excipient compatibility studies were carried out by using FTIR, and it was observed that there were no interactions. The formulations were prepared with the varying concentrations of polymers ranging from F1-F6, and all the formulations were evaluated for various parameters like Physical appearance, Flatness, Weight variation, Thickness, Folding endurance, Drug content, Moisture uptake, Moisture content and Swelling study and all the results were found to be within the pharmacopeial limits. Invitro drug release studies are done by using dialysis membrane. Among all the 6 formulations F6 formulation which contain HPMC K100M 500mg had shown 94.7% cumulative drug release within 12 hours. For F6 formulation release kinetics were plotted and the Regression coefficient value was found to be high for Korsmeyer-peppas release model i.e., 0.989.

Key words: *Fluconazole, HPMCK₄M, HPMCK100M, Buccal Patches and Buccal Drug Delivery.*

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INTRODUCTION:

There are several routes of drug administration for delivering the drug. Among them in recent years, many investigations are done in the field for delivering the drug locally to the tissues in the oral cavity, especially for treating bacterial and fungal infections, and periodontal treatments. Bioadhesive drug delivery plays an important role in delivering drug locally in the oral cavity as it retains the drug at the site of action [1]. Adhesive material may be natural or synthetic. Surface of adhesion can be either epithelial tissue or mucous coat of the tissue [2]. If adhesion is to a mucous coat, then it is referred as mucoadhesion. Over the decades mucoadhesion has become popular for its potential to optimize localized drug delivery, by retaining a dosage form at the site of action (e.g. within the gastrointestinal tract) or systemic delivery by retaining the formulation in intimate contact with the absorption site (e.g. buccal cavity) [3]. Mucoadhesive polymers have greater application in buccal drug delivery system [4]. Recently, many mucoadhesive forms have been developed like patches, films, disks, strips, ointments, tablets, gels etc. However, buccal patch offers greater flexibility and comfort than the other forms. Apart from it buccal patches can overcome problems like short residence time as that of gels which is easily washed away by saliva [5]. Buccal route of drug delivery provides high bioavailability as it has direct access to the systemic circulation through the jugular vein bypassing the first pass hepatic metabolism [6]. Apart from it, it has excellent accessibility, low enzymatic activity, suitable for drugs or excipients that mildly and reversibly damage or irritate the mucosa. Other advantages include painless drug administration, easy withdrawal. Facility to include permeation enhancer / enzyme inhibitor or pH modifier in the formulation, versatility in designing as multidirectional or unidirectional release system for local or systemic action [7]. Fluconazole is a triazole anti fungal drug which is used to treat serious fungal infections. It has very low aqueous solubility and extensively metabolized by liver [8]. Buccal route offers several advantages as it bypasses first pass metabolism, easy withdrawal, and rapid absorption [9]. Hence it leads to significant reduction of dose and related side effects. Here in the present work, an attempt was made to formulate and evaluate Fluconazole buccal patches for buccal drug delivery route.

MATERIALS AND METHODS:**Materials**

Fluconazole procured from Natco Laboratories Pvt Ltd, Hyderabad, and Telangana, India. HPMC K-4M, HPMC K-100M, PEG-400 and Tween-80 from SD fine chemical, Mumbai, India. Dichloromethane and

Methanol from Merck Specialities Pvt Ltd, India and other chemicals were consumed of laboratory grade.

Methods**Determination of UV Absorption maxima [10]**

Fluconazole solution was prepared with 6.8 pH phosphate buffer and diluted suitably. The UV spectrum of the solution was taken on Lab India 3200 UV/Vis double beam Spectrophotometer. The solution exhibited UV maxima at 274 nm. The procedure was repeated with pH 6.8 phosphate buffer.

Preparation of Standard Calibration Curve of Fluconazole [11]

100 mg of Fluconazole was accurately weighed and dissolved in a little amount of Methanol and the final volume is made up to 100 ml with pH 6.8 phosphate buffer to prepare a stock solution. The 10 ml of stock solution was further diluted with pH 6.8 phosphate buffer in 100ml to get 100 μ g/ml (working standard). Then 0.5, 1, 1.5, 2 and 2.5 ml of working standard was taken in 10 ml standard volumetric flask and made up the volume with pH 6.8 phosphate buffer. Then the absorbance was measured in a UV spectrophotometer at 274 nm against pH 6.8 phosphate buffer as blank.

Drug excipients interaction studies ¹²

FT-IR spectrum interpretation: IR spectral analysis was carried out using FT-IR by the KBr disc method. The sample and KBr were triturated and compressed to get the discs. The samples of pure drug, dummy formulation and optimized formulation were analyzed between wave numbers 4000.0 and 400.0 cm^{-1} .

Selection of drug and other ingredients [13]

Fluconazole was selected as model drug based on its physico-chemical and biological properties and also based on its suitability for buccal drug delivery system. HPMCK4M (mg), HPMCK100M (mg) were selected as matrix forming polymers.

Propylene glycol and Tween80 were selected as permeation enhancer and plasticizer.

Formulation of Buccal patches [14]

Development of Buccal patches: Buccal drug delivery patches were prepared by solvent casting method.

Solvent casting method: Polymers HPMCK4M and HPMCK100M were weighed accurately and dissolved in dichloromethane and methanol as solvent using magnetic stirrer.

Fluconazole Propyleneglycol, Tween80 is added to the above dispersion with continuous stirring. The uniform dispersion was poured on the petri plate. The rate of evaporation of solvent was controlled by inverting cut funnel over the patches.

Table 1: Formulations of Fluconazole Buccal Patch

INGREDIENTS	F1	F2	F3	F4	F5	F6
FLUCONAZOLE	300	300	300	300	300	300
HPMCK 4M	300	400	500	-	-	-
HPMCK 100M	-	-	-	300	400	500
DICHLOROMETHANE	10ml	10ml	10ml	10ml	10ml	10ml
METHANOL	13.2ml	13.2ml	13.2ml	13.2ml	13.2ml	13.2ml
PEG 400	1ml	1ml	1ml	1ml	1ml	1ml
TWEEN 80	1ml	1ml	1ml	1ml	1ml	1ml

Evaluation of Buccal patch of physical methods [15]

Physical appearance: All the Buccal patches were visually inspected for color, clarity, flexibility and smoothness.

Thickness: This thickness of the patches was assessed at 3 different points using screw gauze. For each formulation, three randomly selected patches were used.

Weight variation: The three disks of 2x2 cm² were cut and weighed on an electronic digital balance for weight variation test. The test was done to check the uniformity of weight and thus check the batch- to-batch variation.

Flatness: Longitudinal strips were cut out from each patch, one at the center and two from either side. The length of each strip was measured and the variation in the length because of the uniformity in flatness was measured by determining present constriction, considering 0% constriction equivalent to 100% flatness.

Folding endurance: The folding endurance was measured manually for the preparation patch. A strip of the films (4x3 cm²) was cut evenly and repeatedly folded at the same place till it is broken [16].

Moisture uptake: The percent moisture absorption test was carried out to check the physical stability and integrity of the patch at high humid conditions. In the present study the moisture absorption capacities of the patch were determined in the following manner. The patches were placed in the desiccators containing 200 ml saturated solution of potassium chloride, to get the humidity inside the desiccators with 84 % RH. After 3 days the films were taken and weighed the percentage moisture absorption of the patch was found [17].

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

Moisture content: The patches were weighed individually and kept in a desiccator containing fused calcium chloride at 40 °C for 24 h. The patches were

reweighed until a constant weight was obtained. The moisture content was calculated in percentage based on the difference between the initial and the constant final weights of the patches [18].

Swelling study: Completely dried patches with a specified area (3.83 cm²) were weighed and put in desiccators for 24 h. They were removed and exposed to relative humidity conditions of 75 % (containing saturated solution of sodium chloride) in desiccators. Weight was taken on a single pan balance periodically until a constant weight was obtained. The swelling capacity of the patch (in weight %) was calculated in terms of percentage increase in weight of the patch over the initial weight of the specimen. The experiments were carried out in triplicate and the average values were used for the calculation. The percentage degree of swelling (DS) was calculated as DS (%) = $\frac{W_s - W_d}{W_d} \times 100$

Where, W_s and W_d indicate the weight of the swollen and dry patch respectively [19].

Drug content determination: The patch of area 3.83 cm² was cut and dissolved in phosphate buffer solution with pH 6.8. Then solvent methanol and dichloromethane, to make polymer soluble, were added to the mixture and the remaining volume was made up with buffer pH 6.8 to 100 ml in 100 ml volumetric flask. Then 1 ml was withdrawn from the solution and diluted to 10 ml. The absorbance of the solution was taken at 274 nm and concentration was calculated. By correcting dilution factor, the drug content was calculated [20].

Surface pH: For the determination of surface pH of the patch, each formulation is allowed to swell for 2 hrs in a petri dish containing 5 ml of phosphate buffer pH 6.8. The surface pH was measured by pH paper placed on the surface of patches and allowed to equilibrate for 1 min [21].

Evaluation of Buccal patch of permeation studies [22]

Diffusion cell: Permeation studies were carried out in Franz diffusion cells. The Franz diffusion cell contains two compartments, the donor and receptor

compartment. The receptor compartment is 5mm and holds a volume of 15 ml. The receptor compartment is attached to a collecting tube which allows easy collection of the sample every hour during the process of diffusion. The donor and the receptor compartment are held together with the help of a clamp and the diffusion cell was placed on the magnetic stirrer while diffusion studies carried. The total area of the receptor compartment that is exposed to the buccal patch for diffusion is 3.83 cm².

***In vitro* permeation studies using dialysis membrane[23]**

In vitro permeation of Fluconazole from Buccal patches through the dialysis membrane (Hi-Media) with molecular weight cut off of 12000 was studied. The membrane was mounted over a Franz diffusion cell along with the buccal patch. The receiver compartment of the diffusion cell was filled with 15 ml of phosphate buffer solution pH 6.8 and the setup was placed over a magnetic stirrer with temperature maintained at 37°C. Samples of 3 ml were withdrawn and replenished immediately from the receiver compartment at 1, 2, 3, 4, 6 and 12hrs. They were stored in refrigerated condition till the analysis was performed. The content of Fluconazole in the samples was analyzed by UV-Visible spectrophotometer. The concentrations of drug were determined at 274 nm.

Kinetic modeling of drug release [24]

Mechanism of drug release: Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted in zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

A.Zero order release model: To study the zero-order release kinetics the release rate data are fitted to the following equation.

$$Q = K_0 t$$

Where, Q= amount of drug released at time t, K₀=zero order release rate constant

The plot of % drug release versus time is linear.

B.First order release model: The release rate data are fitted to the following equation $\ln(100-Q) = \ln 100 - k_1 t$

Where, Q= percent drug release at time t, K₁= first order release rate constant, the plot of log % drug release versus time is linear.

C.Higuchi's Release Model: To study the Higuchi release kinetics, the release rate data were fitted to the following equation

$$Q = K_H t^{1/2}$$

Where, Q= percent drug release at time t, K_H= Higuchi's (diffusion) rate constant, In Higuchi's model, a plot of % drug release versus square root of time is linear.

D.Korsmeyer-peppas release model: The release rate data were fitted to the following equation

$$F = (M_t/M) = K_m t^n$$

Where, M_t= drug release at time t, M= total amount of drug in dosage form, F= fraction of drug release at time t, K_m=constant dependent on geometry of dosage form, n=diffusion exponent indicating the mechanism of drug release.

If n is equal to 0.89, the release is zero order. If n is equal to 0.45 the release is best explained by Fickian diffusion, and if 0.45 < n < 0.89 then the release is through anomalous diffusion or non-fickian diffusion (Swellable & Cylindrical Matrix). In this model, a plot of log (M_t/M) versus log (time) is linear.

RESULTS AND DISCUSSION:

The standard Calibration curve of Fluconazole

It was found that the estimation of Fluconazole by UV spectrophotometric method at λ_{max} 274 nm in 6.8 pH phosphate buffer had good reproducibility and this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 2-10 μg/ml.

Construction of calibration curve

The absorbance was measured in a UV spectrophotometer at 274 nm against 6.8 pH buffer. The absorbance so obtained was tabulated as in table 2. Calibration curve was plotted as shown in figure 1.

Table 2: Standard calibration curve values of Fluconazole in 6.8 pH

S. No	Concentration (μg/ml)	Absorbance (at 274 nm)
1	0	0
2	0.5	0.126
3	1	0.248
4	1.5	0.362
5	2	0.487
6	2.5	0.599

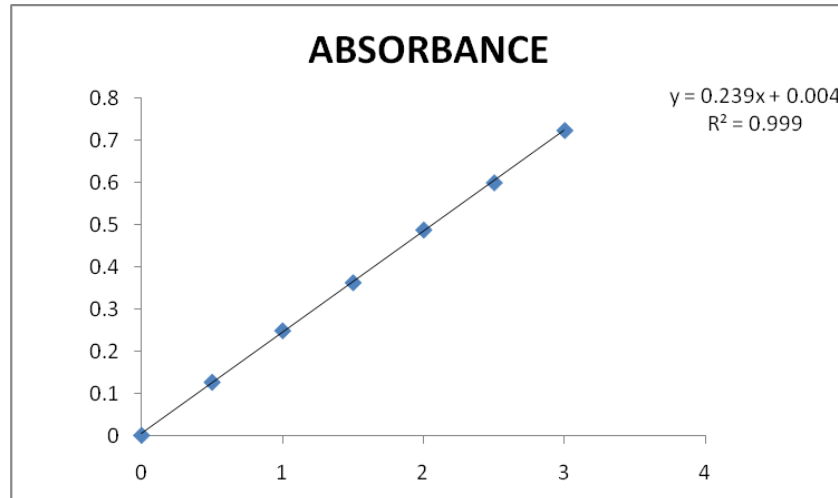


Fig. 1: Calibration curve of Fluconazole in pH 6.8 Phosphate buffer

FT-IR Spectrum study

The FT-IR spectrum did not show the presence of any additional peaks for new functional groups, indicating no chemical interaction between drug and polymers. The FT-IR results were shown in the figure number 2 –3.



Fig. 2: FT-IR of Pure Drug

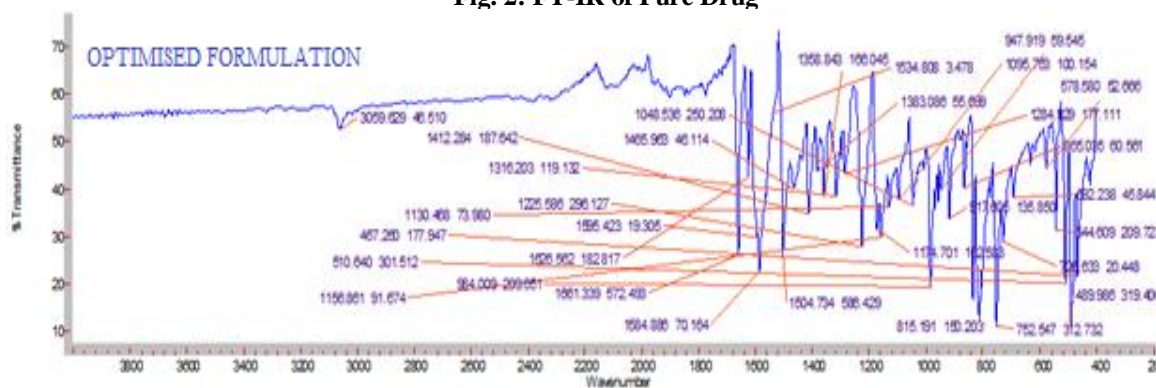


Fig. 3: FT-IR of Optimized Drug

Selection of Drug and other ingredients

Fluconazole is selected based on suitability for buccal drug delivery system, biological and physico-chemical properties. Polymers HPMC K4M, HPMC K100M were selected. FT-IR studies showed there were no interactions between drug and polymers. Propylene glycol, Tween 80 was selected as permeation enhancer

and plasticizer as given good results in studies observations.

Formulation of Fluconazole buccal patches

Buccal patches were prepared by solvent casting method. The prepared patches were as shown in the figure 4.

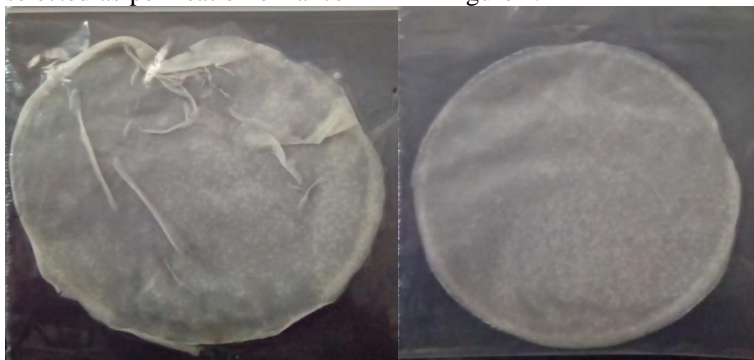


Fig.4: Fluconazole buccal patches

Evaluation of Fluconazole Buccal patches

The prepared Fluconazole Buccal patches were evaluated for Physical appearance, Flatness, Weight variation, Thickness, Folding endurance, Drug content, Moisture uptake and Moisture content and all the results were found to be within the pharmacopeia limits as shown in the table 3.

Physical appearance: All the Buccal patches were visually inspected for colour, clarity, flexibility.

Flatness: All the Buccal patches were found to be flat without any foam.

Evaluation of buccal patches by *In-vitro* permeation studies using a dialysis membrane

The prepared Fluconazole Buccal patches were evaluated for *In-vitro* permeation studies using dialysis membrane, Among all the 6 formulations F6 formulation which contain HPMC K 100M had shown a 94% cumulative drug release within 12 hours, HPMC K 100M showed a better drug release profile and the results are as shown in the table 4.

Table 3: Evaluation of Buccal patch by physical methods

Formulation Code	Thickness (mm)	Folding endurance	Drug content (%)	Moisture uptake (%)	Moisture content (%)	Surface pH	Weight variation
F1	0.3569	20	45	7.98	3.77	6.59	2.09
F2	0.3520	25	65	25.05	9.2	6.34	1.97
F3	0.3470	27	57.5	13.09	5.16	5.89	2.13
F4	0.3496	24	60	15.63	5.66	6.34	2.11
F5	0.3460	30	67.5	11.73	4.87	6.18	1.97
F6	0.3517	32	92.5	19.65	12.67	5.98	2.18

Table 4: Evaluation of Buccal patch by *In-vitro* permeation studies using dialysis membrane

Time (hrs)	F1	F2	F3	F4	F5	F6
1	9.05	15.1	10.1	9.49	10.9	20.2
2	13.3	19.8	12.8	11.3	19.6	27.8
4	14.6	28.3	21.5	22.6	24.9	42.8
6	21.9	34.1	25.9	32.3	31.2	53.5
8	32.7	41.1	33.4	43.9	38.0	66.3
10	40.4	50.1	44.5	56.3	50.3	82.0
12	54.2	65.8	56.7	69.4	65.9	94.7

***In vitro* permeation studies using a dialysis membrane**

The results were plotted to assess the permeation pattern as given in Figure 5 and table 5. All results suggest that the permeation was similar to the *in vitro* dissolution studies in most cases and the amount permeated is slightly less than the actual amount of drug dissolved under similar conditions.

Table 5 represents the kinetic parameters of *in vitro* dissolution studies. The zero order, first order, Higuchi diffusion and Korsmeyer – Peppas drawn as represented in Figures 6 –9. Results suggest that the Fluconazole buccal patches could release the drug following first order.

Table 5: kinetics of *In-vitro* permeation studies using dialysis membrane

CUMULATIVE RELEASE Q (%)	TIME (T)	ROOT (T)	LOG(RELEASE (%)	LOG (T)	LOG (%) REMAIN
0	0	0			2.000
20.2	1	1.000	1.305	0.000	1.902
27.8	2	1.414	1.444	0.301	1.859
42.8	4	2.000	1.631	0.602	1.757
53.5	6	2.449	1.728	0.778	1.667
66.3	8	2.828	1.822	0.903	1.528
82	10	3.162	1.914	1.000	1.255
94.7	12	3.464	1.976	1.079	0.724

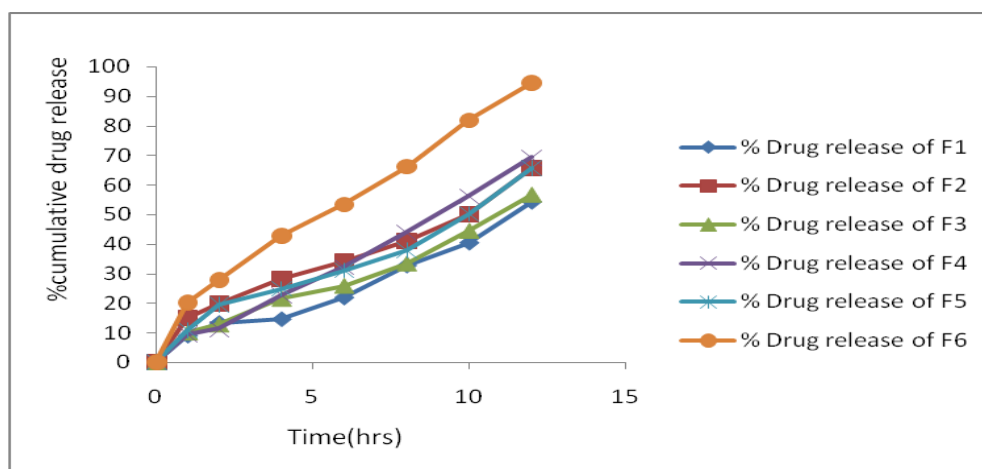


Fig. 5: Release profile of *In-vitro* permeation studies using dialysis membrane Drug release kinetics studies

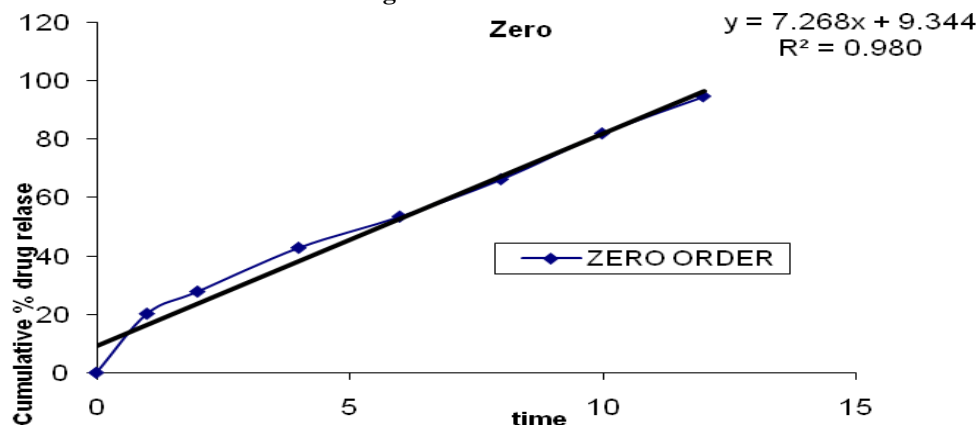


Fig. 6: Zero order kinetics

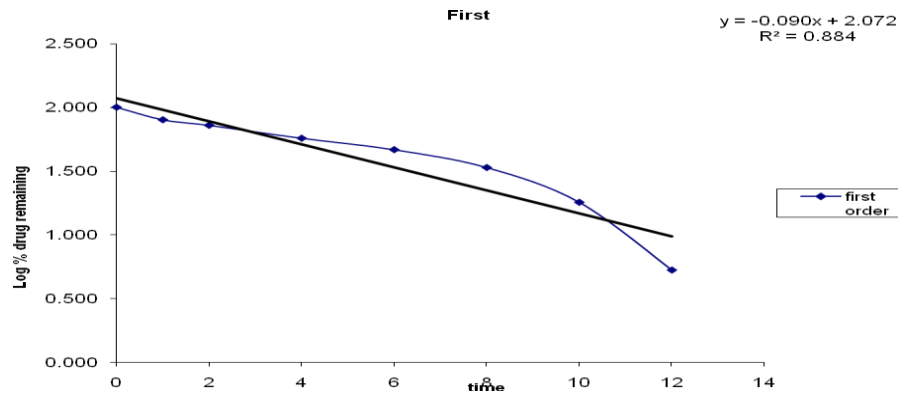


Fig. 7: first order kinetics

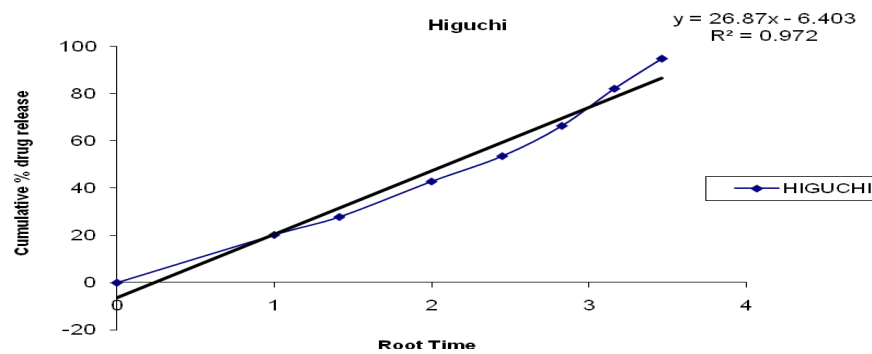


Fig. 8: Higuchi plot

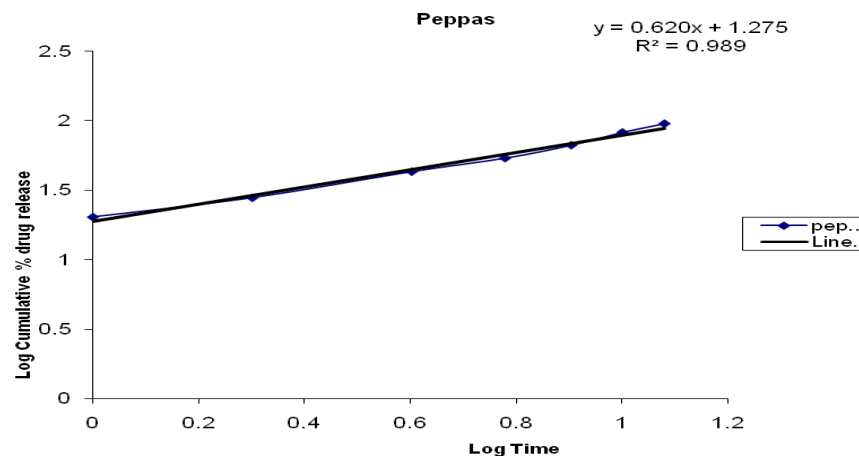


Fig. 9: Korsmeyer – Peppas plot

CONCLUSION:

In the present study buccal drug delivery of Fluconazole patches was developed to overcome the first pass metabolism and to reduce the frequency of dosing compared to oral route. Matrix type of buccal patches was developed by using polymers HPMCK4M and HPMCK100M. Buccal patches were prepared by employing solvent casting method. Propylene glycol and Tween80 were selected as permeation enhancer and plasticizer. Drug excipient compatibility studies were carried out by using FTIR, and it was observed that there were no interactions. The formulations were

prepared with the varying concentrations of polymers ranging from F1-F6, and all the formulations were evaluated for parameters like Physical appearance, Flatness, Weight variation, Thickness, Folding endurance, Surface pH, Drug content, Moisture uptake, Moisture content and Swelling study and all the results were found to be within the pharmacopeial limits. *In vitro* drug release studies are carried out by using a dialysis membrane. Among all the 6 formulations F6 formulation which contain HPMC K100M 500mg had shown 94% cumulative drug release within 12 hours. For F6 formulation

release kinetics were plotted and the Regression coefficient value was found to be high for Korsmeyer-peppas release model i.e., 0.989.

REFERENCES:

1. P. Sandhya, NazeraTazyeen , M. Sunitha , M. Sirisha , R. Sunil Formulation And Evaluation Of Buccal Films Of Ketorolac Tromethamine Journal of Global Trends in Pharmaceutical Sciences,2013;4(3):1184-1192.
- 2.NagaveniSomepalli , Chandra SekharMoru , Dinesh BabuGottipati , Vamshi Krishna Voruganti Formulation And Evaluation of Buccal Films of Salbutamol Sulphate Mintage journal of Pharmaceutical & Medical Sciences;37-40.
- 3.N. G. RaghavendraRao, Sunil Firangi, Keyur Patel Formulation and in-vitro evaluation of mucoadhesivebuccal patches containing zolmitriptan using gel forming polymers Pelagia Research Library Der Pharmacia Sinica, 2012; 3 (1):47-57.
- 4.Shalini Mishra, G. Kumar , P. Kothiyal Formulation and Evaluation of Buccal Patches of Simvastatin by Using Different Polymers The Pharma Innovation,2012;1(7):60-67.
- 5.S.Himabindu, D. Sathish and Shayeda Formulation and *In-vitro* Evaluation of MucoadhesiveBuccal Patches of Cyproheptadine Hydrochloride Journal of Applied Pharmaceutical Science,2012;2 (7):196-201.
- 6.NavneetVerma and PronobeshChattopadhyay Preparation of Mucoadhesive Patches for Buccal Administration of Metoprolol Succinate: *In Vitro* and *InVivo* Drug Release and BioadhesionTropical Journal of Pharmaceutical Research,2012;11(1):9-17.
- 7.Kashappa Goud H. Desai and T.M. Pramod Kumar. P reparation and Evaluation of a Novel Buccal Adhesive System, AAPS PharmSci Tech, 2004;5(3): 35:1-9.
8. Prasanth V.V, Mamatha. Y, SelviArunkumar , Sam T Mathew , Abin Abraham Formulation and Evaluation of MucoadhesiveBuccal Patches of Aceclofenac Scholars Research Library Der Pharmacia Lettre, 2012; 4 (1):297-306.
- 9.M.Jyostna, Bhaskar Reddy , E.Mohanambal , S.Narendiran , M.Murugan , M.Nishanthi Formulation and in vitro evaluation of buccal patches of Desloratidine, ijntps.org,2012;2(4):2277 – 2782.
- 10.RohitChaudhary, Md. ShamimQureshi , Jitendra Patel , Uttam Prasad Panigrahi , I.C.Giri Formulation, Development and In-Vitro Evaluation of MucoadhesiveBuccal Patches of Methotrexate,International Journal of Pharma Sciences and Research,2010;1(9): 357-365.
- 11.Amit Khairnar, Parridhi Jain , DheerajBaviskar and Dinesh Jain Developmement of MucoadhesiveBuccal Patch Containing Aceclofenac: *In Vitro* Evaluations International Journal of PharmTech Research,2009;1(4): 978-981.
12. Panigrahi L, Pattnaik S and Ghosal SK. Ind J Pharm Sci, 2005;67 (3):319-326.
13. Pintu K De1, Jibitesh Paul, Sanjoy K Dey, Subas C Dinda, SoumenRakshit. Der Pharmacia Sinica, 2011; 2 (5):98-109.
14. Kapil KP, Manoj KJ, Asha SJ, Shivanand K. J Pharm Res, 2010,3 (8),2031-2035.
15. Shalu Rani, Kamal Saroha, NavneetSyam, PoojaMathur. Der Pharmacia Sinica, 2011,2 (5),17-29.
16. SatishBabu BK, Srinivasan BP. Ind J Pharm Sci, 2008;175-179.
17. Koland M, Sandeep VP, Charyulu NR. J Young Pharm, 2010;2 (3):216-222.
18. Yehia SA, Gazayerly ON, Basalious EB. Current Drug Delivery, 2009;(6):17-27.
- 19.Pokhariyal Tarun, Singh Vikas Kumar, Tiwari Ajay Kumar. Formulation and evaluation of buccal patch of selective receptor blocker prazosin Hcl,Indo American Journal of Pharmaceutical Research, 2015; 4293-4303.
20. Ajitha K Cherian, SR Daisy PA, Noby Thomas, Praveen Raj, Liji Jacob, Boby Johns George, and SR Betty Carla, Formulation and Evaluation of Cefpodoxime Proxetil Buccal Film, Indo American Journal of Pharmaceutical Research, 2015; 6(1):1256-1273.
21. C.Sarath chandran,Shijith, K.V,Vipin, K. V, Augusthy, Ann Rose, Formulation and Evaluation of Bisoprolol Fumarate Buccal Patches By Using Selected Polymers, International Journal of Pharmaceutical, Chemical and Biological Sciences,2013; 3(3):854-860.
- 22.Debarshi Datta, S.Jigisha, Reshma.S, V.Lavakumar,M.Niranjan Babu, Formulation and Evaluation of Mucoadhesive Buccal Patches Containing Nifedipine, Indo American Journal of Pharm Research,2013;3(9):7603- 7608.
- 23.Mohasin Lodhi, Akhilesh Dubey, Reema Narayan, Prabhakara Prabhu, Sneha Priya, Formulation and evaluation of buccal film of Ivabradine hydrochloride for the treatment of stable angina pectoris,International Journal of Pharmaceutical Investigation,2013; 3(1):47-53.
24. Prasanth V.V, Mamatha. Y, Selvi Arunkumar , Sam T Mathew , Abin Abraham, Formulation and Evaluation of Mucoadhesive Buccal Patches of Aceclofenac, Scholars Research Library, Der Pharmacia Lettre, 2012; 4 (1):297-306.