Original Article

Preparation and Evaluation of Buccoadhesive Patches of an Antihypertensive Drug

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ABSTRACT

Buccoadhesive patches of losartan potassium were prepared by solvent casting method using mucoadhesive polymers such as PVA and chitosan in different ratios. Propylene glycol was used as a plasticizer. Backing membrane was prepared by using polymer ethyl cellulose, solvents such as isopropyl alcohol and acetone. Dibutyl phthalate was used as a plasticizer in backing membrane.

Patches were subjected to physicochemical characterization evaluation such as thickness, weight uniformity, folding endurance, drug content, swelling index, surface pH study, buccoadhesion strength, buccoadhesion time, *in vitro* drug release, *ex vivo* permeation study and stability study. The FTIR spectroscopy of polymer, physical mixture and formulation indicated the compatibility of drug with excipients. Patches were found to be satisfactory when evaluated for thickness, weight uniformity, folding endurance, drug content and swelling index. The surface pH of all the patches was found to be neutral . A combination of PVA and chitosan resulted in sustained buccal drug delivery. The *in vitro* drug release in optimized formulation F9 was found to be 94.06 % in 8 hr.

The optimized formulation F9 also showed satisfactory pH, buccoadhesion time (520 min.), swelling index (65.6%), drug content (93.42%), buccoadhesion strength (0.1695 N), *ex vivo* permeation (77.97%), effective *in vitro* drug release (94.06) and satisfactory stability study.

Keywords: Losartan potassium, PVA, Chitosan, Buccoadhesive Patches, Ethylcellulose.

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INTRODUCTION

Buccoadhesive drug delivery is an important route of drug administration and has comprehensively been investigated by many researchers. The buccal route has been preferred due to avoidance of first pass metabolism and possibility of being accessible for controlled and sustained drug release.[1] Various dosage forms for the buccal delivery of drugs can broadly be categorized as conventional matrix tablets, gels, films, patches, strips and ointment systems. The uses of various polymeric patches for buccal drug delivery are broadly investigated. Introducing various polymeric systems has been comprehensively employed in the modification of drug release.[2]

Losartan potassium is an angiotensin II receptor antagonist and is widely used in the management of hypertension to reduce cardiovascular mortality in patients with left ventricular dysfunction following myocardial infarction, and in the management of heart failure. Although it is completely absorbed from the gastrointestinal tract, the systemic availability is approximately 25–35% because of high first-pass metabolism. Higher bioavailability of losartan potassium has been observed after absorption from the buccal mucosa. This suggests that the oral availability of losartan potassium could be improved by formulating a buccoadhesive dosage form. Hence, buccoadhesive patches can be envisaged to ensure both enhanced oral availability as well as maintenance of effective plasma concentration over prolonged duration by extending the release of losartan potassium. This in turn is expected to reduce the frequency of administration by maintaining effective plasma concentration over longer duration, providing better control of hypertension and thereby, improving patient compliance. In the present study, buccal patches of losartan potassium using chitosan and polyvinyl alcohol have been developed and evaluated.[3, 4]

MATERIALS

Losartan potassium was obtained from Lark Laboratories, Biwari as gift sample. Polyvinyl alcohol and chitosan were obtained from S.D. Fine chemical ltd. Ethyl cellulose, isopropyl alcohol, acetone, dibutyl phthalate, glycerin, acetic acid of laboratory grade were used.

Preparation of Buccoadhesive Patches [5, 6, 7]

Buccal patches of losartan potassium were prepared by solvent casting technique, using combination of two polymers chitosan and polyvinyl alcohol (PVA). PVA was dissolved in hot water and chitosan was dissolved in 1 % acetic acid solution. Then both solutions were mixed together with slow stirring to get a clear viscous solution. Propylene glycol was used as plasticizer. The solution was poured in a petridish and allowed to dry over night at room temperature to remove the bubbles. Then solution was dried in an oven maintained at 40ºC till a flexible patch was formed. The dried patch was carefully removed from the petridish and cut into squares of 2 cm^2.

Preparation of Backing Membrane [5, 6, 7]

The ethyl cellulose backing membrane was prepared by solvent casting technique. Ethyl cellulose was dissolved in 30 ml mixture of acetone and isopropyl alcohol and kept for 1 hour in magnetic stirrer for continuous stirring. Dibutyl phthalate was added in above solution as plasticizer. This solution was poured in a petridish and kept overnight for drying at the room temperature to obtain the backing membrane.

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EVALUATION OF BUCCAL PATCHES

1. Thickness

The thickness of each patch was measured using brainier caliper. The mean ± SD value were calculated of all formulation.

2. Weight uniformity

Patches of size 2 × 2 cm^2 were cut. The weights of five patches were taken using Shimadzu balance of (Shimadzu, Tokyo, Japan) and the weight variation was calculated.

3. Folding endurance[8]

Folding endurance of the patches was determined by repeatedly folding one patch at the same place till it broke or folded upto 300 times manually, which is considered satisfactory to reveal good patch properties. The number of times a patch could be folded at the same place without breaking gave the value of the folding endurance. This test was done on all the patches three times.

4. Drug content [9]

Drug content uniformity was determined by dissolving the patch by homogenization in 50 ml of an isotonic phosphate buffer pH 6.8 for 2 hr with occasional shaking. Aliquot 1 ml was withdrawn and diluted with isotonic phosphate buffer pH 6.8 up to 10 ml and the resulting solution was filtered through a 0.45 mm Whatman filter paper. The drug content was then determined after appropriate dilution by using spectrophotometer at 206 nm.

5. Surface pH [10]

The surface pH of the patch was determined by the method similar to that used by Bottenberg et al. (1991). The patches were allowed to swell by keeping them in contact with 1drop of distilled water for 2 h at room temperature and pH was noted down by bringing the electrode in contact with the surface of the patch, allowing it to equilibrate for 1 min.

6. Swelling studies [11]

The degree of swelling of bioadhesive polymer is an important factor affecting adhesion. The swelling rate of buccoadhesive patch was evaluated by placing the patch in phosphate buffer solution pH 6.8 at 37 ± 1ºC. The patches of each batch were cut and weighed (W_1). The patches were placed in phosphate buffer and were removed at time intervals of 0.5, 1, 2, 3, 4, 5, 6, 7 and 8 hr. Excess water on the surface was carefully absorbed using filter paper and swollen patches were reweighed. The average weight W_2 was calculated and the swelling index was calculated by the formula:

$$\text{Swelling index} = [(W_2 - W_1) \div W_1] \times 100$$

Where, W_1 = Initial weight of the patch

W_2 =Final weight of the patch

7. *In vitro* drug release [12]

In vitro drug release studies were carried out in 100 ml of beaker using 50 ml of phosphate buffer pH 6.8 as the dissolution medium at 50 rpm at 37 ±0.5ºC for 8 hr. To provide unidirectional release, one side of each patch was attached to a glass disk with the help of cyanoacrylate instant adhesive. The beaker was kept in magnetic stirrer in which the temperature and rpm were maintained. An aliquot of 0.1 ml of sample was withdrawn with the help of micropipette at suitable time intervals and replaced with fresh phosphate buffer pH 6.8 maintained at the same temperature. The samples were filtered through Whatman filter paper and analyzed after appropriate dilution by uv spectrophotometer at 206 nm.

8. *Ex-vivo* buccoadhesion time [13]

The *ex- vivo* buccoadhesion time was examined after application of the buccal patch on a freshly cut porcine buccal mucosa. The

fresh porcine buccal mucosa was adhered with the help of cyanocrylate on the glass slide and the buccoadhesive side of each patch was wetted with 1 ml of phosphate buffer pH 6.8 and pasted to the porcine buccal mucosa by applying a light force with a fingertip for 30 seconds. The glass slide was then put in the beaker, which was filled with 50 ml of phosphate buffer pH 6.8 and kept at 37 ± 1ºC. After 2 minutes, stirring was applied slowly to simulate the buccal cavity environment and patch was monitored. The time for the patch to detach from the porcine buccal mucosa was recorded as the buccoadhesion time.

9. Measurement of buccoadhesive strength[14]

Buccoadhesive strength of the buccal patches was measured on the "Modified Physical Balance method". The method used porcine buccal membrane as the model mucosal membrane. The fresh porcine buccal mucosa was cut into pieces and washed with phosphate buffer pH 6.8. A piece of mucosa was stuck on a metal slide which was moistened with phosphate buffer pH 6.8. The patch was stuck to the lower side of another metal slide with glue. Then both pans of the balance were balanced by adding an appropriate weight on the left hand pan. The metal plate with mucosa was placed with appropriate support, so that the patch touches the mucosa. Previously weighed beaker with water was placed on the right hand pan and water (equivalent to weight) was added slowly to it until the patch detached from the mucosa surface. The weight required to detach the patch from the mucosal surface gave the buccoadhesive strength.

10. *Ex-vivo* permeation study

In this study, porcine buccal mucosa was used as a barrier membrane. Diffusion studies were carried out, to evaluate the permeability of drug across the porcine buccal mucosal membrane, by using glass surface Franz diffusion cell. Porcine buccal mucosa was obtained from local slaughter house and used within 2 hrs of slaughter. The tissue was stored in phosphate buffer pH 6.8 solution upon collection. The epithelium was separated from underlying connective tissues with surgical scissors clamped between donor and receiver chamber of diffusion cells for permeation studies. The smooth surface of the mucosal membrane faced the donor chamber and receiver chamber was filled with phosphate buffer of pH6.8. Whole assembly was placed on a magnetic stirrer maintained at 37±1^{0}C. Buccal epithelium was allowed to stabilize for 1hr and receiver chamber was maintained by stirring with magnetic bead at 50 rpm. After the stabilization of buccal epithelium, the patch was kept on buccal epithelium and 3ml of phosphate buffer pH 6.8 was added in donor chamber. Then samples of 0.1 ml were withdrawn at time intervals of 1 hour up to 8 hrs and replaced with equal volume of fresh dissolution medium. Sink condition was maintained throughout the study. The withdrawn samples were diluted to 10 ml. The amount of losartan potassium was determined by UV-VIS Spectrophotometer at 206 nm.

11. Stability study

Stability of the product may be defined as the capability of a particular formulation to remain with the physical, chemical, therapeutic and toxicological specification. Study of storage stability is an important concern in the development of pharmaceutically acceptable product. In present work stability studies of prepared formulation (losartan potassium patch) were carried out at 40ºC±2ºC and 75±5% for 1 month. The formulations were evaluated for drug content, buccoadhesive strength and % drug remaining. The initial drug content was considered as 100%.

12. Release kinetics [15]

In order to investigate the mode of drug release from losartan potassium patch, the release data were analyzed with the following mathematical models: zero-order kinetic ($Q = k_0 t$); first order kinetic ($\ln (100-Q) = \ln Q_0 - k_1 t$); higuchi equation ($Q = kH t^{1/2}$); peppas exponential model $Mt/M_\infty = Kt^n$, where Mt/M_∞ is fraction of drug released after time 't' and 'K' is kinetic constant and 'n' is release exponent which characterizes the drug transport mechanism; Hixon crowell erosion equation $Q_0^{1/3} - Q_t^{1/3} = K_{HC} t$ where Q_t is the amount of drug released in time t, Q_0 is the initial amount of the drug in patch and K_{HC} is the rate constant for Hixson-Crowell rate equation.

RESULT AND DISCUSSION

1. Thickness

Thickness of the formulated patches was measured on three different places to ensure the uniformity of patches. Average and standard deviation of all three readings were calculated and recorded in table 4. Thickness was found to be in the range of 0.66 ± 1.54 mm to 0.82 ± 0.57 mm. From the results obtained it was confirmed that all the patches were uniform and did not have any significant differences in the thickness at different points. F1 batch showed the minimum thickness while F9 batch showed the maximum. Thickness of the patch was increasing with increase in concentration of polymers.

2. Weight Uniformity

Weight uniformity of all the batches were determined by weighing three 2 x 2 cm^2 sections of each patch and then average weight was calculated. From the results shown in table 4, it was observed that all the batches were uniform in weight and there was no significant difference in the weight of the individual formulations from the average value and the variations were all within normal limits. Weight uniformity was found to be in range of 273.33 ± 0.77 mg to 329.33 ± 0.04 m.

3. Folding Endurance

The recorded folding endurance of all the formulations was above the 300, which indicates good flexibility. Table 4 shows the folding endurance value of all the formulations.

4. Drug Content

Drug content of all the formulations was determined using UV-Visible spectrophotometer and result showed that the drug was uniformly distributed throughout the patches and standard deviation of all the batches is very less and within the limits as recorded in table 4. Drug content was found to be in range of 89.16 ± 0.54 % to 93.42 ± 0.68 %.

5. Surface pH

Surface pH of patches of all the batches was determined by using pH meter and recorded in table 4. Surface pH ranged from 6.41 ± 0.3 to 6.76 ± 0.21. Surface pH of all formulations was near to neutral pH hence, should not cause any irritation in the buccal cavity.

6. Swelling study

Swelling studies of prepared patches were performed using 6.8 pH phosphate buffer for 8 hr and the results are shown in table 5. Swelling behavior of a buccal drug delivery system is an important property for uniform and prolonged release of the drug and effective mucoadhesion. The effect of various compositions of patches on the swelling index of the patches was studied by plotting the graph between percent swelling and time as shown in fig.1. Maximum swelling was observed in batch F9 (65.6 %) while batch F4 showed minimum swelling (43.37 %). Maximum swelling percentage was observed for F9 batch because of more

concentration of hydrophilic polymers. Weak aqueous solubility of chitosan, which is a cationic polymer, limited the swelling of the patches.

7. *In-vitro* Drug Release

In-vitro release studies of buccoadhesive patches were carried out in 6.8 pH phosphate buffer at 37±2 °C. Dissolution medium was continuously stirred at a speed of 50 rpm. The data obtained from *in-vitro* drug release study performed up to 8 hr gives a clear indication that prepared patches showed necessary controlled release profile. The results for release studies are shown in table 6. The graph was plotted between cumulative percentage drug release and time as shown in fig. 2. *In-vitro* drug release studies showed that release rate of drug increased with increasing concentration of hydrophilic polymer. Thus, diffusion of drug through patches can be controlled by the concentration of hydrophobic polymer. Release of losartan potassium from patches was also increased with increased swelling index of patches. Chitosan patches produced sustained release in all formulations due to water insolubility of chitosan. Maximum *in-vitro* release was found to be 94.06 % over a period of 8 hr in batch F9 while minimum *in-vitro* release was found to be 82.47 % in batch F3. These results were further supported by swelling studies results, where highest swelling was shown by batch F9and hence resulting in faster drug release.

8. *Ex-vivo* buccoadhesion time

The buccoadhesion time was evaluated and reported in table 7. Maximum buccoadhesion time was shown by formulation F9 which was 520 min. and minimum bioadhesion time was 380 min. in formulation F1. Formulation F1 has minimum amount of PVA and chitosan and formulation F9 has maximum amount of PVA and chitosan. The decrease in the polymer concentration resulted in a decrease in buccoadhesion time.

9. Measurement of buccoadhesive strength

All the batches showed good mucoadhesive strength. Results were expressed as detachment stress (N) and are shown in table 6. Mucoadhesive strength of patches was found to be maximum in case of F9 batch (0.1695 N) while minimum in case of F1 batch (0.0391 N). Mucoadhesive strength of the formulations was found to be dependent on the concentration of the chitosan. Mucoadhesive strength of the formulations increased with increase in concentration of the mucoadhesive polymer chitosan while there was slight change in mucoadhesive strength with change in concentration of the hydrophilic polymer. It showed that hydrophilic polymer has less mucoadhesive property. Mucoadhesive strength of chitosan can be explained by the presence of chitosan in the cationic (protonated) form which led to electrostatic interactions between chitosan and negatively charged mucus membrane. Time required for complete detachment of patches from the mucosa was found satisfactory and is recorded in table 7.

10. *Ex-vivo* permeation study

The *ex-vivo* drug permeation studies were performed using porcine buccal mucosa as a model membrane using franz diffusion cell. The study was conducted at 37 ± 2 °C for 8 hr. The result of *ex-vivo* drug permeation study is shown in table 8. From the results, it was observed that after 8 hr the drug permeation from buccal mucosa was found in F9 formulation (77.97 %).

11. Stability study

Stability studies of the formulation F9 of losartan potassium buccoadhesive patches were conducted to determine the effect of formulation additives on the stability of the

drug and also to determine the physical stability of the formulation. The stability studies of the best formulation were conducted for one month at 40±2ºC and 75±5% RH. Formulation F9 was observed for thickness, weight uniformity, drug content, folding endurance, buccoadhesion time and drug release. There was no significant change in the preparation of formulation F9.

12. Release kinetics

For all the formulations, various kinetic models were applied and results were interpreted. On the basis of kinetic assessment, the values were obtained and the best fitted model was decided. Zero order kinetics is followed where drug release rate is independent of its concentration and sink condition is maintained. Kinetics for zero order is represented by graph of cumulative percentage drug release versus time. The pharmaceutical dosage forms following this profile release the same amount of drug by unit of time and are the ideal characteristics to achieve sustained or controlled drug delivery. The equations based on first order kinetics follow Noyes-whitney equation, explaining the mechanism that drug release rate from the systems is dependent on concentration. Higuchi kinetics describes that fraction of drug release from a matrix is proportional to square root of time and drug releases from the formulations through the process of diffusion. According to Korsmeyer-Peppas kinetics, drug from the formulations diffuses through the time dependent release mechanism. Values of various constants and regression coefficient for each model are shown in table 10.

As discussed before, regression coefficient plays an important role in deciding best fitted kinetic model for each formulation. From the result of kinetic modeling and the comparison of the regression coefficients values of all models, it was observed that drug release from batch F1, F2, F6 and F9 follow higuchi kinetics and show a favorable response as desired. Higuchi kinetics is based where concentration profile exists after the administration of dosage form and the drug diffusion is through the matrix slowly depending upon the concentration of drug in blood plasma maintaining the sink condition.

The ‘n’ values can be used to characterize diffusion release mechanism. The ‘n’ value for the F1, F2, F3, and F8 formulations were between 0.45 to 0.89, which indicate both drug diffusion in the hydrated matrix and the polymer relaxation called anomalous (non-fickian) diffusion. From the ‘n’ value, it can be concluded that drug release mechanism from film is diffusion with swelling of polymer.

CONCLUSION

Buccoadhesive patches for oral cavity are a promising drug delivery system for losartan potassium. The combination of polymers, PVA and chitosan showed good mucoadhesion time, mucoadhesive strength, swelling properties, *in vitro* drug release and *ex vivo* permeation study characteristics. An increase in chitosan concentration brought about an increase in mucoadhesion time, mucoadhesive strength and swelling properties. The drug release rate increase on inclusion of PVA into the chitosan base matrix system. We conclude that, chitosan with PVA can meet the ideal requirement for buccal drug delivery and which can be a good way to bypass the hepatic first pass metabolism and increase bioavailability.

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Table 1. Formulation of buccoadhesive patches

S. No.	Formulation Code	Drug (mg)	PVA (mg)	Chitosan (mg)	Propylene Glycol (ml)	Solvent (water:1% acetic acid) (ml)
1	F1	50	150	350	2	25
2	F2	50	150	400	2	25
3	F3	50	150	450	2	25
4	F4	50	200	350	2	25
5	F5	50	200	400	2	25
6	F6	50	200	450	2	25
7	F7	50	250	350	2	25
8	F8	50	250	400	2	25
9	F9	50	250	450	2	25

Table 2. Composition of backing membrane

Ingredient	Quantity
Ethyl cellulose	1.5 gm
Acetone	19 ml
Isopropyl alcohol	11 ml
Dibutyl phthalate	2 ml

Table 3. Kinetic order and their parameter

S. No.	Kinetic order	Parameter
1.	Zero- order	Cumulative percent drug release Vs Time
2.	First- order	Log cumulative percent drug release Vs Time
3.	Higuchi model	Cumulative percent release Vs Root time
4.	Peppas model	Log cumulative percent drug release Vs Time
5.	Hixson crowell's erosion equation	(% Retained) $^{1/3}$ Vs Time

Table 4. Physical Characterization of the Prepared Losartan potassium Buccoadhesive Patches

Formulation	Thickness (mm)	Weight (mg)	Surface pH study	Folding endurance	Drug contents (%)
F1	0.66±1.54	273.33±0.77	6.75±0.12	>300	90.82±0.56
F2	0.68±1.52	288.33±2.88	6.68±0.25	>300	89.16±0.54
F3	0.74±2.51	303.33±1.52	6.76±0.21	>300	91.22±0.42
F4	0.70±1.15	287.33±0.42	6.74±0.18	>300	90.43±0.53
F5	0.75±2.3	307.33±0.49	6.41±0.3	>300	90.44±0.66
F6	0.77±1.52	323.66±0.57	6.59±0.16	>300	93.27±0.62
F7	0.76±3.75	304.66±1.03	6.53±0.25	>300	92.48±0.6
F8	0.78±2.08	322.66±2.51	6.73±0.14	>300	91.78±0.51
F9	0.82±0.57	329.33±0.04	6.72±0.18	>300	93.42±0.68

Table 5. Percent Swelling Index of Losartan Potassium Buccoadhesive Patches from F1 to F9 Formulations

Formulation code	Swelling index (%)
F1	51.90±0.80
F2	53.35±0.58
F3	58.32±0.82
F4	43.37±0.65
F5	51.47±0.67
F6	62.52±0.59
F7	48.37±0.57
F8	58.97±0.88
F9	65.60±0.68

Table 6. *In-vitro* Release Data of All Formulations of Losartan potassium buccoadhesive patches

Time (min.)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
60	29.83	32.03	32.46	36.33	36.81	37.80	37.12	35.45	43.90
120	37.69	40.09	38.39	39.14	40.72	44.66	42.52	43.76	49.83
180	46.56	44.52	43.82	44.47	45.27	52.14	47.36	46.22	58.28
240	51.74	51.58	50.93	49.55	50.76	58.90	53.19	54.18	67.19
300	58.67	61.67	57.98	57.57	56.82	64.22	61.22	63.55	74.86
360	65.27	68.91	64.74	72.34	74.81	72.75	70.39	78.64	85.37
420	72.75	76.46	75.27	87.33	89.09	80.14	75.29	84.15	93.05
480	84.09	87.10	82.47	89.82	92.06	88.28	83.44	89.41	94.06

Table 7. Measurement of buccoadhesive strength and buccoadhesion Time of F1 to F9 Formulations

Formulations code	Buccoadhesion strength (N)	Buccoadhesion time (min.)
F 1	0.0391	380
F 2	0.0894	400
F 3	0.0816	425
F 4	0.0620	435
F 5	0.1154	450
F 6	0.1368	485
F 7	0.0691	470
F 8	0.1011	505
F 9	0.1695	520

Table 8. *Ex-vivo* permeation study of F9 Formulations

Time (min)	cum % drug permeated
0	0
60	20.96
120	32.09
180	42.51
240	50.77
300	58.10
360	63.90
420	75.14
480	77.97

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Table 9. Stability Data of Formulation F9

Formulation	Thickness (mm)	Folding Endurance	Drug Content (%)	% CDR	Buccoadhesion Time (min.)
F 9	0.81±0.17	**>** 300	92.82±0.08	93.58	505

Table 10. Release kinetics of Losartan potassium buccoadhesive patches

Form.	Higuchi		Hixon		Koresmayer			Zero order		First order	
	R^2	K	R^2	K	R^2	K	n	R^2	K	R^2	K
F1	0.970	3.659	0.956	-0.003	0.955	1.058	0.827	0.933	0.147	0.944	-0.001
F2	0.956	3.826	0.950	-0.003	0.933	1.016	0.875	0.937	0.154	0.935	-0.001
F3	0.952	3.547	0.959	-0.003	0.913	0.982	0.893	0.927	0.145	0.952	-0.001
F4	0.882	4.086	0.894	-0.004	0.810	0.997	0.905	0.927	0.164	0.887	-0.001
F5	0.873	4.176	0.883	-0.005	0.816	0.968	0.934	0.924	0.168	0.872	-0.002
F6	0.972	3.536	0.964	-0.003	0.938	0.888	1.026	0.896	0.152	0.949	-0.001
F7	0.954	3.320	0.966	-0.004	0.859	0.943	0.964	0.895	0.143	0.957	-0.001
F8	0.940	3.886	0.951	-0.005	0.851	0.934	0.882	0.926	0.164	0.945	-0.001
F9	0.975	3.907	0.968	-0.005	0.943	0.825	1.128	0.882	0.169	0.953	-0.002

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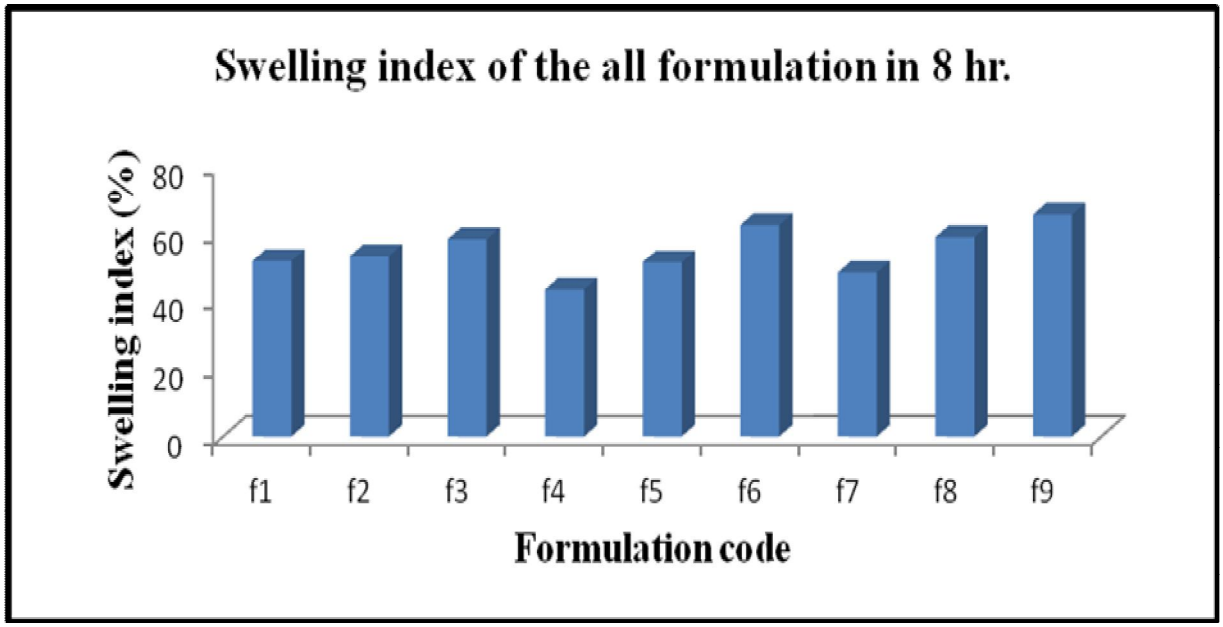

Figure.1. Comparative Swelling index of All Formulations.

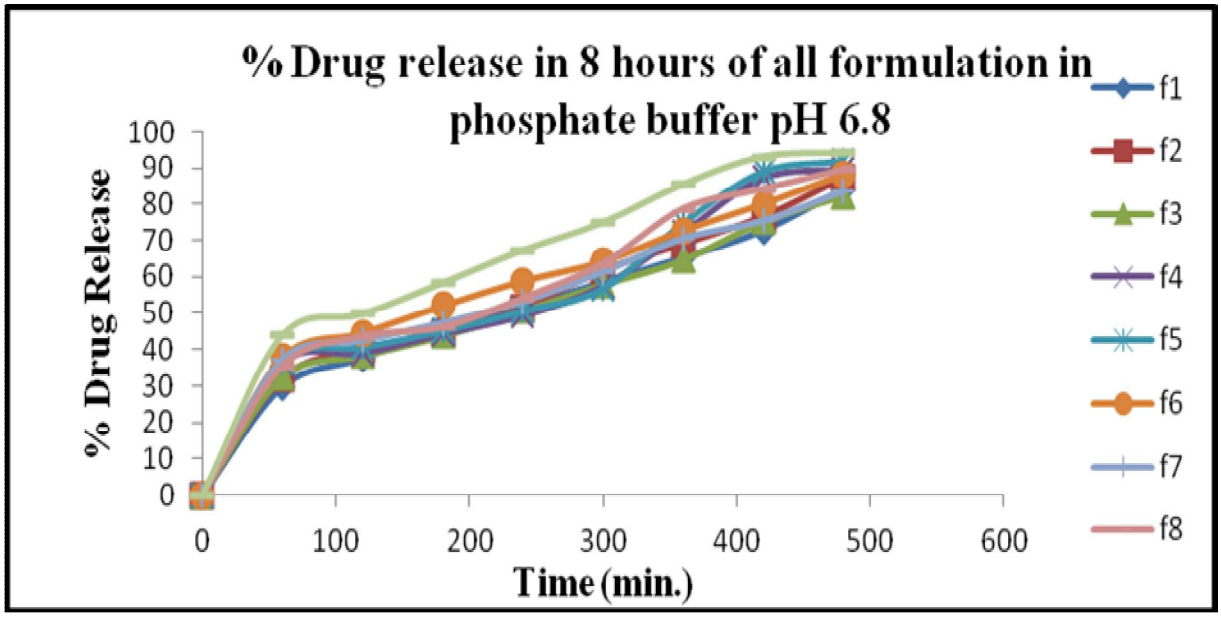

Figure.2. Comparative *In-vitro* Release Profile of F1 to F9 Formulations.

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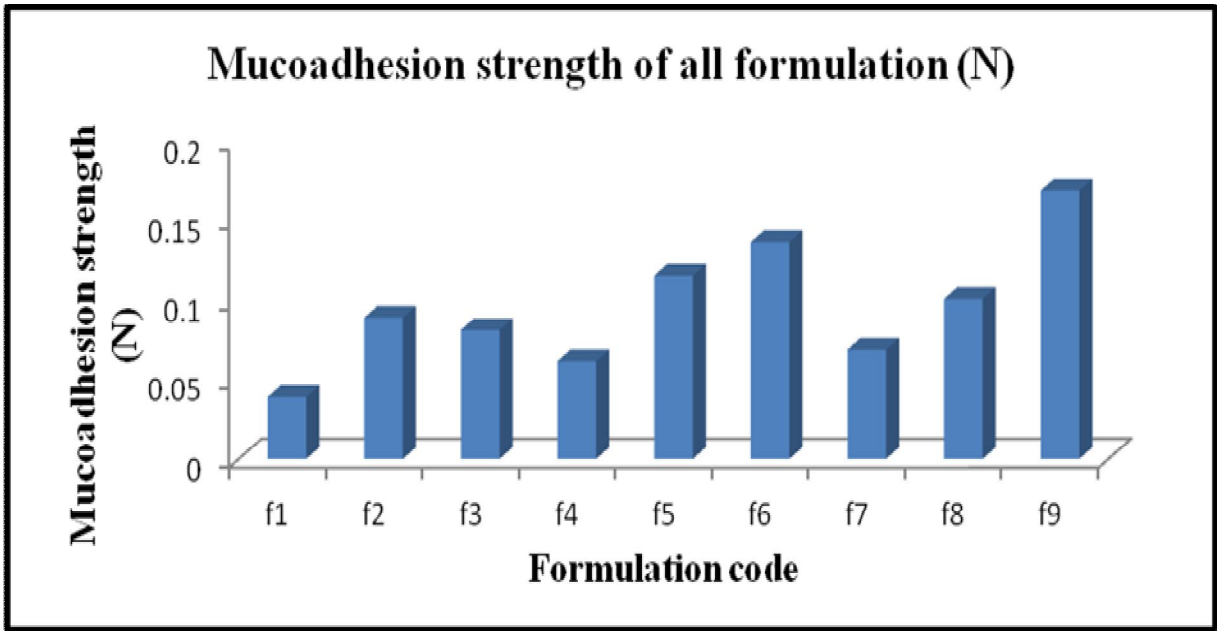

Figure.3. Comparative Mucoadhesion Strength of All Formulation

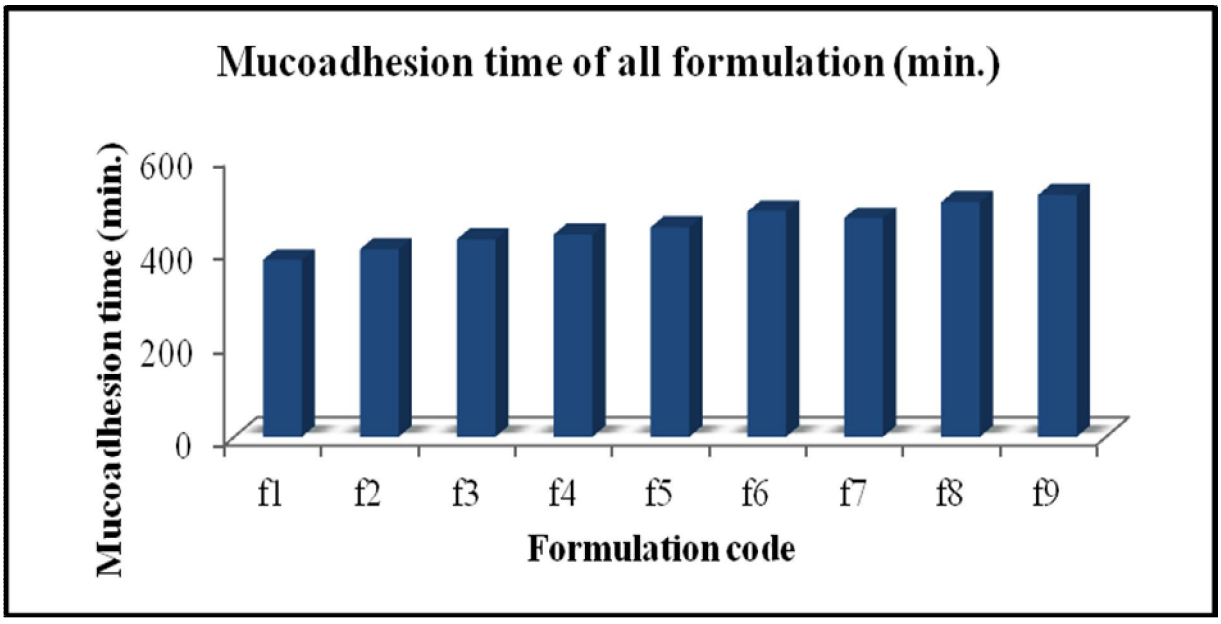

Figure.4. Comparative Mucoadhesion time of All Formulations.

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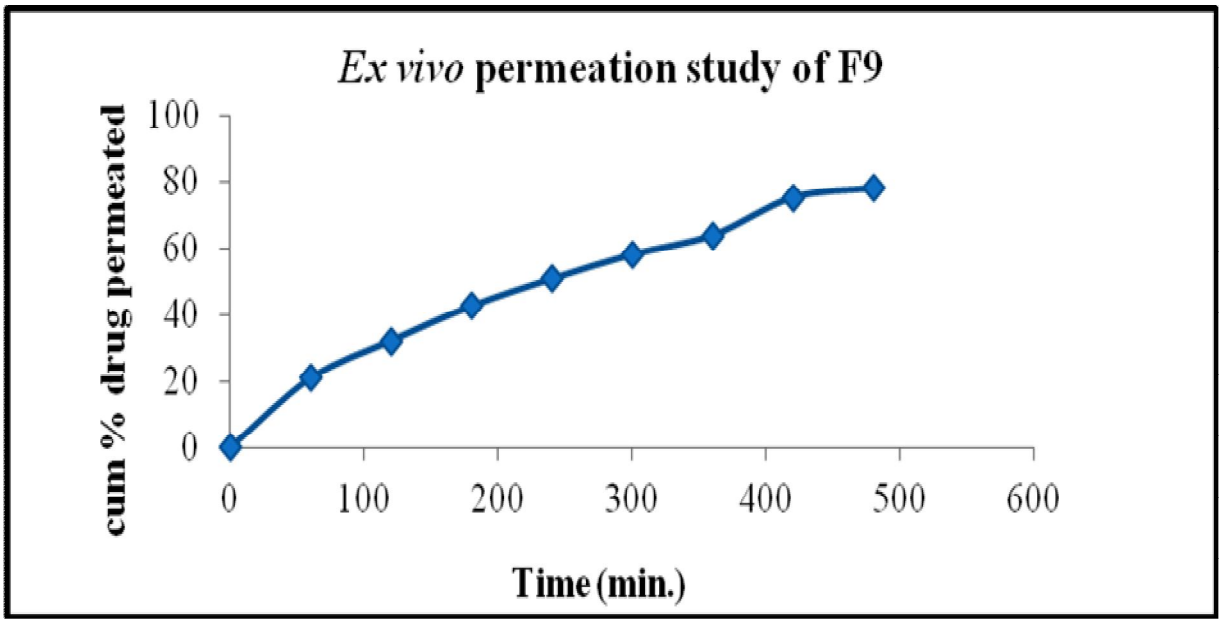

Figure.5. Study of *Ex-vivo* Drug Permeation of F9 Formulations