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Research Article

Preparation and evaluation of buccal patches of losartan potassium using hydrophilic polymers

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ABSTRACT

Losartan potassium is an Angiotensin II receptor antagonist with a half life of 1.5-2 hrs and an oral bioavailability of only 33% due to extensive first pass metabolism. Mucoadhesive buccal films of losartan potassium were prepared using hydroxypropyl methyl cellulose (HPMC 5cps and K100M), hydroxy propyl cellulose (HPC), Polyvinyl pyrrolidone K-30 (PVP K-30), sodium carboxy methyl cellulose (SCMC). FTIR analysis of formulations shows no interaction between drug and polymers. The films were subjected to physical investigations such as uniformity of thickness, weight, drug content, folding endurance, surface pH, percentage moisture absorption, water vapour transmission rate and mucoadhesive strength. The mucoadhesive force, swelling index, was higher for those formulations containing higher percentage of HPMC. In vitro drug release studies reveal that all films exhibited sustained release in the range of 72.09 to 97.10 % for a period of 8 hours. The data was subjected to kinetic analysis which indicated non fickian diffusion for all formulations except few. Ex vivo release studies through goat cheek mucosa indicate that films containing higher percentage of the mucoadhesive polymer SCMC showed slower permeation of the drug for 12 hours.

Keywords: Losartan potassium; HPMC; PVP K-30; SCMC

INTRODUCTION

The potential of buccal mucosal route of drug administration was first recognized by *Walton* (1935). Amongst the various routes of drug delivery, oral route is perhaps the most preferred to the patient and clinician alike. The usefulness of this route of drug administration can be easily appreciated because the oral mucosa is a highly perfuse tissue and the drug directly enters the systemic circulation, thus facilitating prompt onset of action circumventing the hepatic first pass effect. (Pandit JK et al., 1993)

1) Buccal bio-adhesive drug (BBD) devices can now be designed to remain in contact with the oral mucosa while providing controlled release characteristics over a prolonged period of time.

2) Within the oral cavity, drugs can be administered from the buccal gingiva (or) the sublingual space either for the treatment of local conditions (e.g. thrush) or for the systemic treatment of diseases (e.g. angina). The advances in bio-adhesive and controlled release technology have stimulated a renewal of interest in the delivery of drugs to or via, the buccal route.

A combination of the above two (i and ii) attributes can be achieved by the use of suitable bio-adhesive materials. Appropriate materials for the bio-adhesive drug delivery consist mainly of hydrogel forming polymers. They have been called "wet" adhesives because they require moisture to exhibit the adhesive property. This may be supplied by the saliva, which also act as the dissolution medium.

An ideal buccal film should be flexible, elastic, soft yet adequately strong to withstand breakage due to stress from mouth activities (Raghuraman S et al., 2002). Moreover, it must also possess good bio-adhesive strength; so that it can be retained in the mouth for a desired duration. The antihypertensive, Losartan potassium is an angiotensin II receptor (type AT) antagonist, orally active and undergoes substantial 1first-pass metabolism by cytochrome P450 enzymes. The terminal half-life of losartan is about 2 h. The drug is orally administered as 25 mg tablets once or twice daily with total daily doses ranging from 25 to 100 mg. Following oral administration, losartan is well absorbed (based on absorption of radiolabeled losartan) and undergoes substantial first-pass metabolism; the systemic bioavailability of losartan is approximately 33%. In view of these facts, this drug can be considered as a suitable candidate for buccal delivery. In this study, an attempt is made to investigate the feasibility of mu-

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Table 1: Composition of formulations

Formulation code	Drug reservoir in % HPMC 5cps	Rate controlling Membrane				Plasticizer (30%)	
		HPC	HPMC K100M	PVP K30	SCMC	Drug Reservoir	Rate controlling membrane
F1	4 %	5 %	0.5 %	_	_	Glycerin	Dibutyl phthalate
F2	4 %	5 %	0.75 %	_	_	Glycerin	Dibutyl phthalate
F3	4 %	5 %	1 %	_	_	Glycerin	Dibutyl phthalate
F4	4 %	5 %	_	0.5 %	_	Glycerin	Dibutyl phthalate
F5	4 %	5 %	_	0.75 %	_	Glycerin	Dibutyl phthalate
F6	4 %	5 %	_	1 %	_	Glycerin	Dibutyl phthalate
F7	4 %	5 %		_	0.5%	Glycerin	Dibutyl phthalate
F8	4 %	5 %		_	0.75%	Glycerin	Dibutyl phthalate
F9	4 %	5 %		_	1%	Glycerin	Dibutyl phthalate

Amount of drug loaded in each 2 cm patch = 35 mg

Table 2: Evaluation of physico chemical parameters of losartan potassium buccal patches

Formulation Code	Drug content uniformity* (mg)	Weight uniformity* (mg)	Folding endurance	Thickness* (cm)	Surface pH*	Percent moisture absorption*	Water vapour transmission rate* (rate x 10^{-3}) mg $cm^{-2}h^{-1}$
F1	35.02±0.06	195±0.79	290	0.09±0.03	6.66±1.05	5.85±0.96	$2.212x10^{-3}$ ± 5.07
F2	34.85±0.05	205±0.73	298	0.10±0.02	6.53±1.04	8.72±1.08	$2.238x10^{-3}$ ± 4.08
F3	35.08±0.06	228±0.63	301	0.13±0.05	6.71±1.06	12.29±1.17	$2.280x10^{-3}$ ± 6.09
F4	35.01±0.05	201±0.74	303	0.14±0.04	6.36±1.02	7.10±1.01	$2.228x10^{-3}$ ± 5.88
F5	34.74±0.06	194±0.69	302	0.17±0.05	6.4±1.05	11.12±1.3	$2.241x10^{-3}$ ± 5.94
F6	34.92±0.04	208±0.73	297	0.19±0.03	6.65±1.09	14.7±1.5	$2.308x10^{-3}$ ± 6.01
F7	34.85±0.05	194±0.69	305	0.08±0.02	7.10±1.03	4.35±1.1	$2.139x10^{-3}$ ± 5.86
F8	35.05±0.05	200±0.65	298	0.13±0.03	6.63±1.01	5.34±0.98	$2.154x10^{-3}$ ± 4.90
F9	34.83±0.06	230±0.55	296	0.15±0.04	6.60±1.02	8.01±1.01	$2.181x10^{-3}$ ± 5.96

*Average of three patches (Mean±S.D)

coadhesive buccal films as a medium for the sustained delivery of losartan potassium with better bioavailability.

MATERIALS AND METHODS

Losartan Potassium, HPMC and HPC, Sodium carboxy methylcellulose and polyvinyl pyrrolidone K30. Organic solvents used were of analytical grade and other chemicals of Laboratory grade.

Fabrication of Buccal Patches

Fabrication of drug reservoir film

Accurately weighed quantity of hydroxy propyl methyl cellulose – 5cps (HPMC 5 cps) was mixed with 392.7 mg of losartan potassium. Then add 8 ml of distilled water and glycerine as plasticizer. Stirring was continued until a clear solution was obtained. Then the medicated gel was left 2 hour at refrigeration temperature to ensure clear, bubble - free gels. The solution was then transferred quantitatively to glass rings (diameter 6.7 cm) kept on the surface of mercury in petriplates. The petriplates were covered with inverted funnels to allow controlled evaporation of the solvent. These were left undisturbed in room temperature for two to three days. After complete drying, the films could be retrieved intact by slowly lifting the rings from the mercury substrate. Circular patches of 2cm diameter, each containing 35 mg of drug were cut and sealed by using

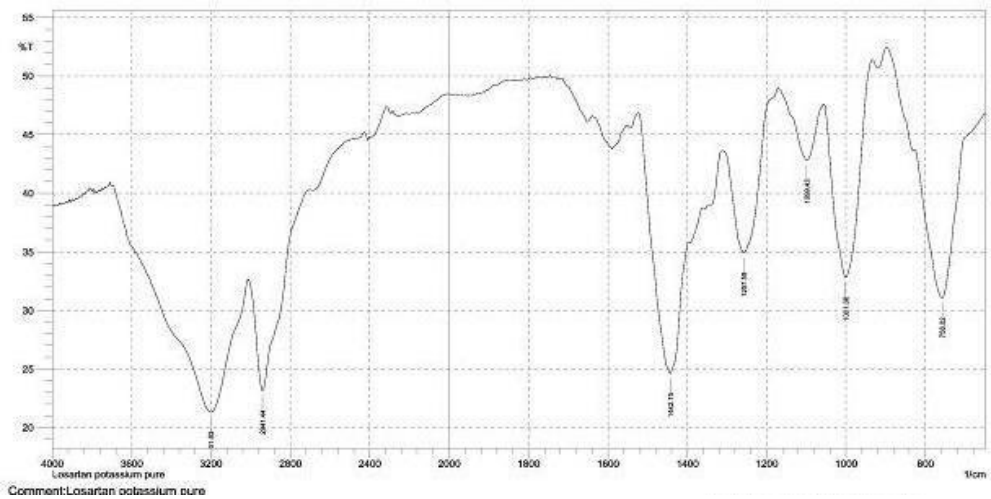


Figure 1: FTIR of Pure Losartan Potassium

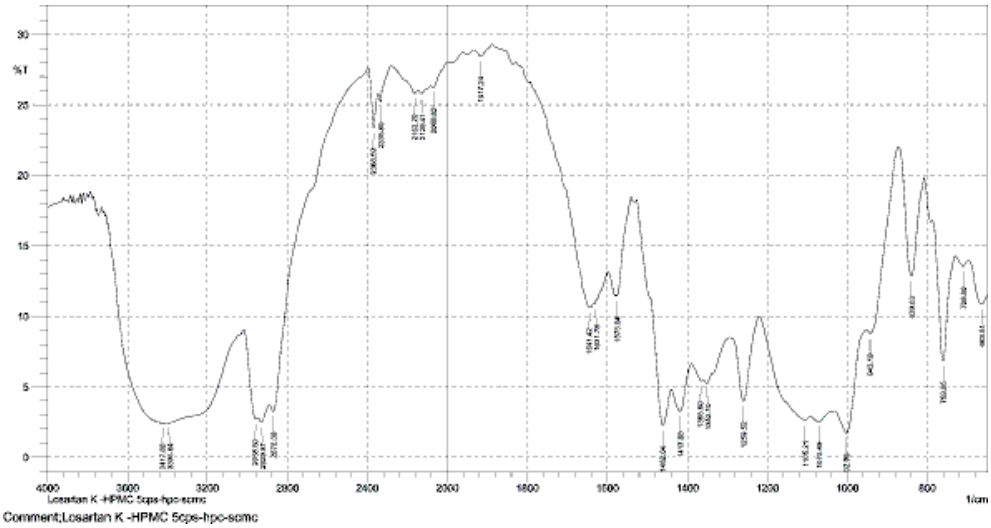


Figure 2: FTIR of Formulation containing Drug-HPMC-5cps-HPC-SCMC

rate controlling membrane on either side to control the drug release from periphery (Khanna R et al., 1997**)**.

Similarly, rate controlling membrane was prepared using polymers such as Sodium carboxy methyl cellulose, hydroxy propyl cellulose, polyvinyl pyrrolidone and hydroxy propyl methyl cellulose – K100 M. While distilled water was used as casting solvent and Dibutyl phthalate as plasticizer.

Evaluation of prepared buccal patches

Compatibility studies

About 100mg of this mixture is compressed and it is scanned from 4000 to 600 cm^{-1} in a Shimadzu FTIR spectrophotometer (Dandagi PM et al., 2005).

Drug content

The medicated patch of 2 cm diameter is allowed to dissolve in 100 ml phosphate buffer pH 7.4 analyzed for drug content spectrophotometrically at λmax of 250 nm (Noha Adel Nafee et al., 2003).

Weight uniformity

Each patch is weighed individually and average weight of three patches is found out (Semalty A et al., 2005).

Folding endurance

It is determined by repeatedly folding one patch at the same place till it broke or folded upto 300 times **(**Semalty A et al., 2005**)**.

Thickness

Thickness of the patches is measured at six different points using a vernier caliper (Noha Adel Nafee et al., 2003).

Swelling index

The sample is allowed to swell on the surface of an agar plate kept in an incubator maintained at 37^0C. Measurement of the diameter of the swollen patch is done at one hour intervals for 5 hours. Radial swelling is calculated from the following equation (Panigrahi L et al., 2005).

$$SD(\%) = \frac{D_t - D_0}{D_0} \times 100$$

Where, SD (%) is the percent swelling obtained by the diameter method, D_t is the diameter of the swollen patch after time t, D_o is the original patch diameter at time zero.

Surface pH

The patches was allowed to swell then in contact with 0.5 ml of distilled water (pH 6.5±0.5) for one hour at room temperature and pH was noted down by bringing electrode in contact to the surface, allowing it equilibrate for 1 minute.

Percent moisture absorption

Three 2 cm diameter patches are cut out and weighed accurately then the patches are placed in dessicator containing saturated solution of aluminium chloride. After 3 days the patches are removed, weighed and percentage moisture absorption is calculated. Average percentage moisture absorption of three patches are found using the formula (Shaila L et al., 2006),

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

Water vapour transmission rate

For water vapour transmission rate glass vials of equal diameter is used as transmission cells. These transmission cells are washed thoroughly and dried in an oven. About 1g of fused anhydrous calcium chloride is taken in the cells and the polymeric patches are fixed over the brim with the help of an adhesive. The cells are weighed accurately, kept in a closed dessicator containing saturated solution of potassium chloride. The humidity inside the dessicator is measured by a hygrometer. The cells are taken out and weighed after 1, 2, 3, 4, 5, 6 and 7th day of storage. From the increasing weights, the amount of water vapour transmitted is found using the formula (Kanig JL et al., 1962),

$$Water\ vapour\ transmission\ rate = \frac{Final\ weight - Initial\ weight}{Time\ x\ Area}$$

***In vitro* drug release studies**

Commercial semi permeable membrane is employed in this study. The membranes were transparent, regenerated cellulose membranes, which are permeable to low molecular weight substances. The semi permeable membrane is tied to one end of the two sided open ended cylinder, which acted as donor compartment. The buccal patch having the diameter of 2 cm containing 35 mg of Losartan potassium is kept on the semi permeable membrane, in such a way that the entire surface of the patch is in contact with the semi permeable membrane. Then the donor compartment is fixed, so that the semi permeable membrane is in contact with the receptor medium, 100 ml of phosphate buffer, (pH 7.4) in the receptor compartment. The contents of the receptor compartment are agitated by a magnetic stirrer. Samples of 1ml are withdrawn at periodic intervals from the receptor compartment and replaced with the fresh phosphate buffer immediately and after suitable dilution the drug content is analyzed spectrophotometrically at 250 nm against a blank (Kumar GVP et al., 2005).

***Ex Vivo* Drug permeation studies**

An e*x vivo* diffusion study of losartan potassium is carried out. Fresh goat cheek pouch membrane procured from local slaughter house, is tied to one end of an open-ended cylinder, which acts as a donor compartment. The patch should be placed in such a way that it should be stuck on the mucous membrane. The receptor compartment was filled with isotonic phosphate buffer pH 7.4. The assembly is maintained at 37°C and stirred magnetically. Samples are withdrawn at one hour intervals for 12 hours and analyzed using UV spectrophotometer at 250 nm (Harris Shoaib M et al., 2006).

***In vivo* drug release studies**

Selection of Animals

Rabbits 10-12 weeks old, weighing 2.5 to 3 kg were selected.

Method

Among the twelve formulations prepared and tested, the best formulation is chosen for animal studies. Male healthy rabbits weighing 1.5 to 2 kg were chosen for this study. Rabbits are fasted over night and are divided into 3 groups of 4 rabbits each. The rabbits are kept in cages with husk bedding. The fore limbs and hind limbs are tied into the iron rod of the mini operation table, so that the rabbit is in dorsal position (Subash Pillai et al., 2010).

To the group I, 17.5 mg of losartan potassium is given orally with the help of plastic tube. To the group II, buccal patches having the size of 1 cm containing 17.5 mg of losartan potassium is placed in the cheek pouch of the rabbit with the help of a clip. To the group III, buccal film without drug (placebo) is placed in the cheek pouch, which acted as control. Dextrose solution is transfused continuously throughout the period of studies. Periodically 1 ml blood samples are withdrawn from the marginal ear vein of the rabbit at hourly intervals using a syringe containing 3.8% of sodium citrate to prevent blood clotting.

To the above sample 0.5 ml of 0.5 N sodium hydroxide and 0.5 ml of 10% zinc sulphate was added to precipitate blood protein. Then it was filtered through Whatmann filter paper and after suitable dilution, these samples were analyzed at 250 nm using spectrophotometer against a blank. This process was continued upto 8 hours.

Accelerated Stability Studies

Among the twelve formulations prepared F7, F8 and F9 (which showed the best release from *In vitro* dissolution data) were selected for stability studies. The losartan potassium buccal patches is packed in aluminium

Table 3: Study of percentage radial swelling index

Formulation Code	Percentage Swelling index* (Mean ± S.D) Time in hours				
	1 hr	2 hr	3 hr	4hr	5hr
F1	4.5±0.86	12.09±1.3	20.18±1.5	27.27±1.8	27.27±2.1
F2	9.13±1.2	20.18±1.7	31.82±2.6	36.36±2.6	36.36±2.5
F3	13.55±1.5	22.72±3.3	33.27±2.1	40.08±2.8	40.90±2.6
F4	4.9±0.81	11.09±1.5	19.18±2.3	22.72±2.3	22.72±1.9
F5	9.09±1.4	12.63±1.6	22.72±3.6	29.27±1.9	29.27±2.1
F6	13.63±1.9	21.18±1.7	27.27±2.7	36.31±2.44	36.31±2.46
F7	4.5±0.81	9.13±1.4	18.28±1.8	20.72±2.1	20.72±1.8
F8	7.07±1.5	18.18±1.7	22.72±1.7	24.52±1.6	24.52±2.3
F9	9.09±1.7	15.63±1.4	27.27±2.3	30.81±2.6	30.81±1.9

Table 4: T_{80} values for the buccal patches of in vitro diffusion studies through artificial membrane

Formulation Code	T_{80} Values (In minutes)
F1	384
F2	404
F3	424
F4	420
F5	424
F6	464

foil and stored at a temperature of 25ºC ± 1 at 60 % relative humidity and 40 ± 1ºC at 75 % relative humidity, and physico chemical parameters like drug content, folding endurance and surface pH and *In vitro* drug release study is determined spectrophotometrically at 250 nm. The selected film (F8) was packed in glass petri dish lined with aluminium foil and plastic packets and maintained temperature at 40°C/75 % relative humidity for 45 days. The change in appearance was investigated using Scanning Electron Microscopy (Banker G.S et al., 1991).

RESULTS AND DISCUSSION

Evaluation of Prepared Films

The FTIR indicates that there was no chemical interaction or bonding decomposition of losartan potassium employed in the formulation with various polymers, results are given in figure 1-2. From the results of the tests for physical characterization conducted, it is observed that the weight and thickness of all film samples was uniform within each formulation. Films formulated from EC were smooth whereas those prepared from Eudragit were slightly rough in texture. All films were translucent and flexible. All film formulations exhibited good folding endurance exceeding 290, indicating that they are tough and flexible. The results were given in the table 2.

Percent Moisture Absorption and Water Vapour Transmission

Percentage Moisture absorption studies revealed that buccal patches containing Polyvinyl pyrrolidone showed maximum percent moisture absorption while the buccal patches containing Sodium carboxy methyl cellulose showed minimum percentage of moisture absorption.

The water vapour transmission studies were also conducted to find out the order of hydrophilicity of the polymers and the buccal patches containing polyvinyl pyrrolidone exhibited maximum water vapour transmission. The descending order of hydrophilicity of the polymers used in study is as follows Polyvinyl pyrrolidone> Hydroxy propyl methyl cellulose> Sodium carboxy methyl cellulose. This can be attributed to the higher affinity, solubility and low viscosity of polyvinyl pyrrolidone, which altogether contributed to maximum water absorption and transfer characteristics. The results were given in the table 2.

Surface pH

All the formulations had near to neutral pH and hence will not create any difficulty or irritation while placing in the buccal membrane. The results of them are shown in the table 2.

Swelling Index

The descending order of swelling for the formulations according to the swelling index was, Hydroxy propyl methyl cellulose> Polyvinyl pyrrolidone> Sodium carboxy methyl cellulose. The differences in the radial swelling might be contributed to the water solubility of the polymers. Hydroxy propyl methyl cellulose being highly water soluble and having the maximum tendency to absorb water has swelled a lot. While Sodium carboxy methyl cellulose being the least water soluble polymers has swell only to a limited extent that was evident from the reports obtained for the formulations. The results are shown in table 3.

Table 5: *In vitro* diffusion kinetic profiles of the buccal patches through artificial membrane

Formulation Code	Zero order Equation (r^2)	Higuchi's Models (r^2)	Korsmeyer-Peppa's Models (r^2)	Diffusion Exponent (n)
F1	0.9979	0.9851	0.9928	0.818
F2	0.9933	0.9737	0.9922	0.958
F3	0.9934	0.9698	0.9944	1.117
F4	0.9857	0.9561	0.9641	0.614
F5	0.9858	0.9575	0.9616	0.676
F6	0.9918	0.9678	0.9742	0.799
F7	0.9972	0.9896	0.9967	0.749
F8	0.9980	0.9897	0.9979	0.814
F9	0.9942	0.9764	0.9916	0.901

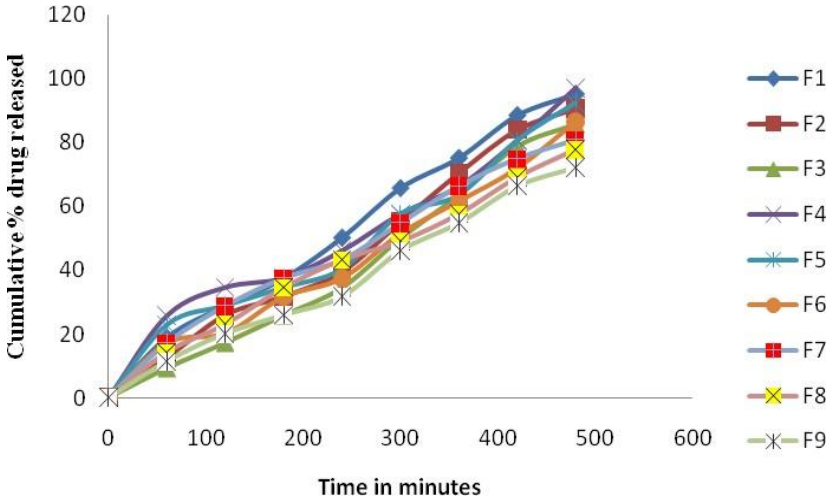


Figure 3: Graph for *In vitro* release profile of formulations in pH 7.4 buffer solution

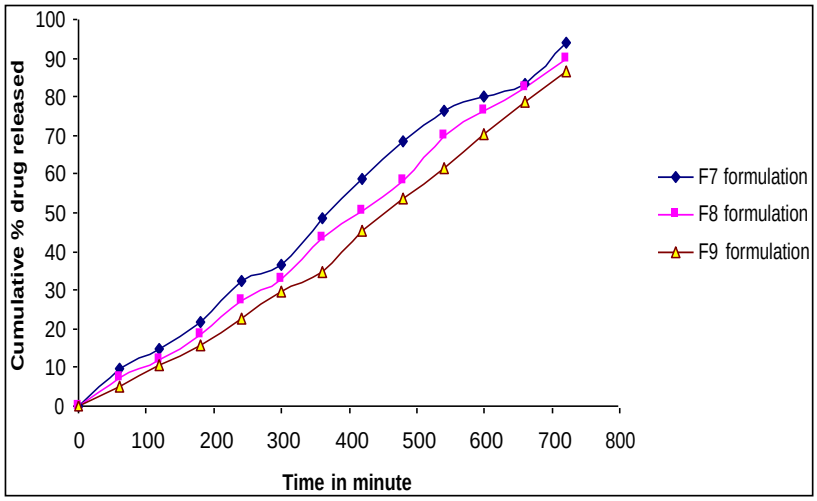


Figure 4: Graph for *Ex vivo* diffusion studies of F7, F8 and F9 formulation through fresh goat cheek membrane

***In vitro* drug release studies**

From the results, hydroxy propyl methyl cellulose K100M (F1, F2 and F3) gave 95.32, 90.55 and 85.93 percentage drug release respectively. Polyvinyl pyrrolidone K30 (F4, F5 and F6) gave percentage drug release of 97.10, 92.38 and 86.85 respectively. Sodium carboxy methyl cellulose (F7, F8 and F9) gave 80.75, 77.83 and 72.09 percentage drug release respectively. The results were given in the table 4.

Polyvinyl pyrrolidone exhibited higher drug release within 8 hours and will be devoid of the drug molecule within 8 hours. This was evident from the t_{80}% values given in the table 5.

Polyvinyl pyrrolidone, having more hydrophilicity than other polymers, enhanced possibility of hydrogen bond formation and easy penetration of dissolution might have lead to the fast depletion of the drug molecule from the matrix. So it has made a negative impact on

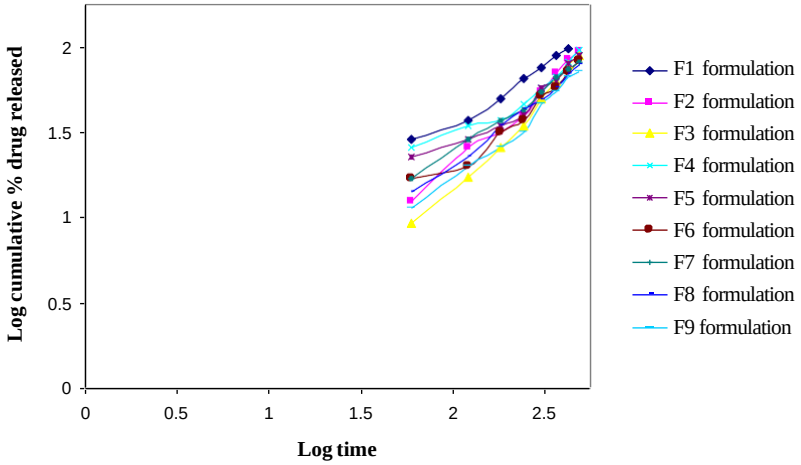


Figure 5: Graph for korsmeyer-peppa's plot of *In vitro* diffusion studies through artificial membrane

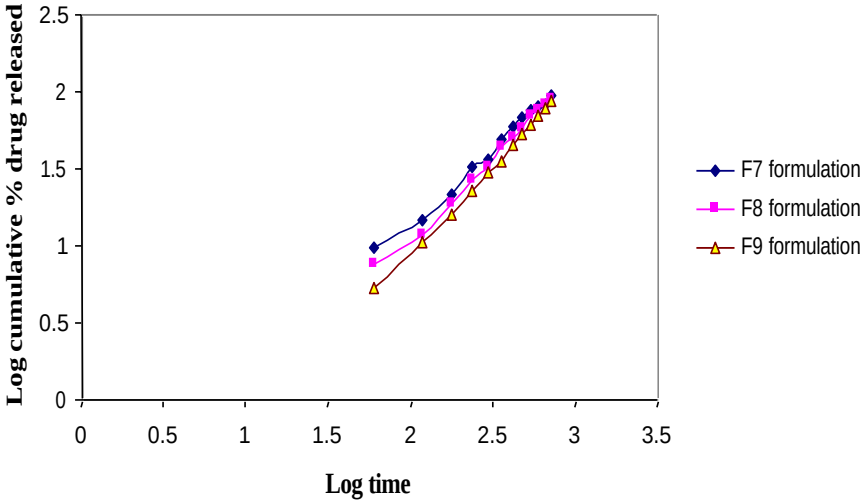


Figure 6: Graph for korsmeyer-peppa's plot of Exvivo diffusion studies of F7, F8 and F9 formulation through fresh goat cheek pouch membrane

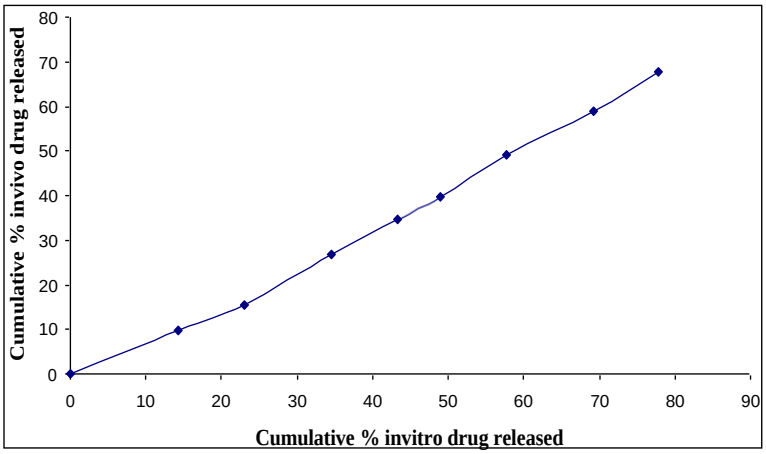
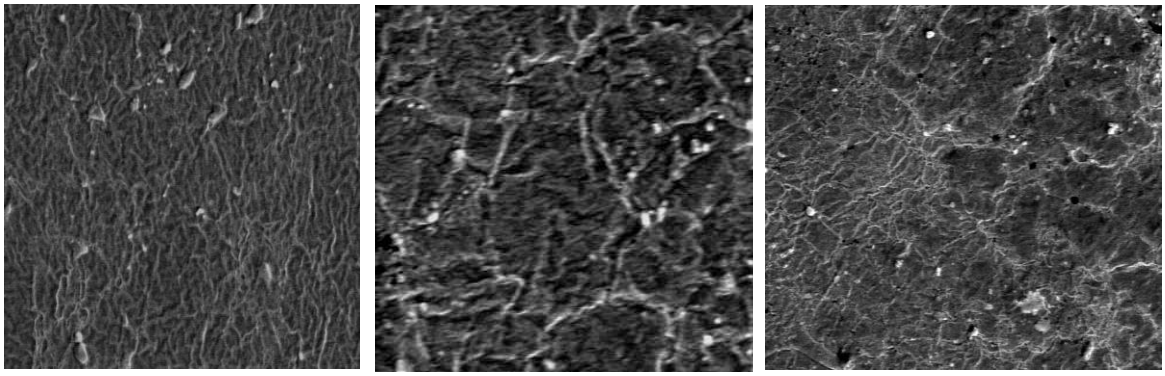


Figure 7: *In vitro- In vivo* correlation graph for Formulation F11

the release retardant ability of the buccal patch. During dissolution studies the buccal patches formulated using polyvinyl pyrrolidone swelled extensively forming a gel layer on the exposed film surfaces. The loosely bound polymer molecules were easily eroded allowing the faster release of losartan potassium from the buccal patch. This was also evident from the t_{80}% values which revealed the increasing concentration of polyvinyl pyrrolidone produced disproportionately less retardant ability. Sodium carboxy methyl cellulose, being a high molecular weight polymer has extensive release retardant ability when compared with the other three polymers, since it has increased the t_{80} values more than 8 hours. Sodium carboxy methyl cellulose at pH 7.4 tends to form a good rate controlling membrane which has hindered the drug release for a time interval of more than 8 hours. Since sodium carboxy methyl cellulose (F7, F8 and F9) had good mucoadhesiveness, good



(a) (b) (c)

Figure 8: Scanning electron micrographs of losartan potassium hpmc, hpc, scmc films (a) fresh, (b) stored 45days in petri dish and (c) stored 45 days in plastic packets

release retardant ability for losartan potassium, it was taken for further studies. The further studies like the *ex vivo* studies and in vivo studies were carried out for the formulations F7, F8 and F9.

***Ex vivo* drug permeation studies**

The further studies for the formulations F7, F8 and F9 were carried out for 12 hours using fresh goat cheek membrane because these three formulations gave an extended release pattern in *in vitro* release study and the results are tabulated in the table 6. From the results it was revealed that patches had good permeability for the *ex vivo* studies also.

The *ex vivo* studies conducted using goat cheek membrane not only affirmed the ability of formulation F8 to release the drug in a concentration independent manner but also the adaptability of the system to release the drug in an expected pattern through the biological membrane. The t_{80}%values revealed that increase in polymer concentration produced retardant ability. The results are given in table 7.

Kinetic analysis of release data

Then the *In vitro* kinetic data was graphically treated according to zero order, first order equation and Higuchi to elucidate the mode of release and treated according to Korsmeyer-Peppas models to confirm the mechanism of release. The results for Korsmeyer-Peppas are given in table 8-9. Test for zero correlation was done for all graphical fits and the correlation coefficients were found to be significant. Graphical best fit for the aforementioned models were drawn and the regression analysis was carried out to ensure the authenticity of best fit and the regression values for the graphical fit are shown in the table 10. From the results it was revealed that the drug release took place totally by zero order kinetics.

Mechanism of drug release

When n = 0.45 fickian diffusion is observed and the release rate in dependent on t, and if the values found $0.45 < n < 0.89$ indicate anomalous (non-fickian) transport and when n = 1, the release is zero order. All the formulations showed good linearity (r^2 = 0.97 to 0.99) with slope (n) between 0.614 - 0.849 except few (which showed zero order release), which appears to indicate a coupling of diffusion and erosion mechanisms so called anomalous diffusion. Therefore the release of drug from the prepared patches was controlled by the swelling of the polymer followed by drug diffusion through the swelled polymer and slow erosion of the patch. From the release exponent in the Korsmeyer-Peppa's model, it can be suggested that the mechanism that led to the release of losartan potassium was an anomalous transport with constant release rate adequate for a controlled release dosage form. The diffusion exponent value of formulation F8 with SCMC is 0.814 indicating that it followed non-fickian transport mechanism. The correlation (r^2) was used as an indicator of the best fitting for each of the models considered. Diffusion coupled with erosion might be the mechanism for the drug release. The results are given in table 10.

***In vivo* diffusion study**

In vivo studies inspite of substantial reduction in total amount of drug release from the formulation F8, fair correlation (r^2 = 0.9905) was observed between *In vitro* and *In vivo* profiles. Changes observed in total amount of drug release can be attributed to reduction in volume of blood supplied due to reduction in cardiac activity of anaesthetized rabbit. The formulation F8 (4% HPMC 5cps as drug reservoir and 0.75% SCMC, 5%HPC as rate controlling membrane) possessing good mucoadhesiveness and good release retardant ability has fulfilled the objectives of the present study. The result is shown in table 12.

Stability studies

The losartan potassium buccal patches is packed in aluminium foil and stored at a temperature of 25 ± 1°C at 60% relative humidity and 40 ± 1°C at 75% relative humidity, physico chemical parameters like drug content, folding endurance, surface pH and *In vitro* drug release study is determined spectrophotometrically at 250 nm.

There is no significant change in release characteristics and physicochemical properties of the buccal patch used in the release study. Based on result it is found that formulated patch were stable at different temperature and different relative humidity over a period 45 days. The results are given in table 13 and 14.

During the storage in different conditions like petridish and plastic packets, the physical appearance of the patch changed a bit when examined with scanning electron microscopy, and it was found that the patch stored in plastic packet was in better condition than that stored in petridish.

Even though its stability is assured for 45 days, further study at different temperature and humidity condition for longer period of time are needed to establish its shelf life.

CONCLUSION

The result and discussion of the study indicates that formulation F8 was found to be best among all other formulations, because of its consistent release, bioadhesive strength, swelling index was better and gave satisfactory results compared to others. The good correlation observed between the *in vitro* and *in vivo* profile revealed the ability of the formulation F8 to reproduce the *in vitro* release pattern through the biological membranes. Hence the polymers HPMC, HPC and SCMC in combination fulfills the objectives of the present study, improves the bioavailability by avoiding the first pass metabolism, reduced side effect and improved patient compliance by reducing the number of doses and effective management of hypertension.

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