ISSN: 0976-4607
Research Article

International Journal of Innovative Pharmaceutical Research

Journal homepage: www.ijipr.com

Design and Evaluation of Losartan Potassium Fast Dissolving Films

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ABSTRACT

An attempt to design and evaluate fast dissolving film of losartan potassium for quick effect in treatment of hypertension occurring in both elder and adults has been made in the present study. Fast dissolving films allow the rapid and reproducible drug dissolution in the oral cavity and thus bypass the first pass metabolism, thereby increase the patients' compliance. The losartan potassium films were prepared by solvent casting method using different polymers HPMC, PVA, PVPK30, maltodextrin DE 18-20, and glycerol as plasticizer. Twelve formulations (F1-F12) films were prepared and evaluated for thickness, weight uniformity, folding endurance, tensile strength, % elongation, surface morphology, surface p^H, moisture uptake, moisture loss, drug content, disintegration time and *in vitro* dissolution studies. FTIR studies indicated that there is no incompatibility between drug and polymers. The formulation F6 considered as optimized containing PVA and PVPK30 at 60% (2:1) as film formers, showed the disintegration time 17.6 seconds and percent drug release 99.99% at the end of 8 minutes.

Keywords: Fast dissolving films, Hypertension, Solvent casting method.

INTRODUCTION

The fast dissolving drug delivery systems are becoming more popular dosage forms recently because of the more acceptances by the consumers due to the fast disintegration and dissolution. Oral fast dissolving films are the most advanced form of oral solid dosage forms due to its more flexibility and comfort. It improves the efficiency of active drug by dissolving within minutes in oral cavity after the contact with saliva without chewing and water for administration. The first fast dissolving oral strip was developed by major pharmaceutical company Pfizer who named it as Listerine pocket packs and were used for mouth freshening. Chloraseptic relief strips were the first therapeutic oral thin films which are used for treatment of sore throat (M.D. Nehal siddiqui *et al* 2011).

Losartan Potassium (LP) is an anti-hypertensive drug which is an angiotensin receptor II Antagonist, which inhibits the action of angiotensin II on vascular smooth muscle. One of the major problems with the drug is, it undergoes extensive first pass metabolism which results in poor bioavailability (33%) after oral administration. This further leads to delayed onset of action. So to overcome these problems, the present work aimed to formulate the drug losartan potassium in the form of fast dissolving films. The main advantage of the drug was it is freely soluble in water. This makes the drug to formulate easily into fast dissolving films.

Losartan Potassium is available as conventional tablets in market. For the treatment of hypertension where there is a requirement of fast onset of action, the conventional tablets are unsuitable. So, the drug was formulated to fast dissolving films. These fast dissolving films have many advantages like rapid disintegration and dissolution, specific onset and local action, suitable for pediatric, geriatric, bedridden patients and psychiatric patients, dose accuracy, and avoid the hepatic first pass metabolism (Rajni Bala *et al* 2013).

Initial work was focused on the development of placebo fast dissolving films with good peelability, thickness, appearance and folding endurance. After getting the films of above characteristics, the drug Losartan Potassium was loaded and formulated. Finally the Losartan Potassium fast dissolving films were formulated and evaluated with HPMC, PVA, PVPK30, maltodextrin as film formers.

MATERIALS AND METHODS

Losartan Potassium, HPMC (AtoZ Pharmaceuticals ltd, Chennai), PVA, PVPK30, Maltodextrin (Himedia Pvt. Ltd., Mumbai), Glycerol

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(Thermo fischer scientific Pvt Ltd, Mumbai). All other chemicals were used of analytical grade.

Preparation of Losartan Potassium fast dissolving films

Solvent casting method

Initially, the film forming polymer of required quantity was dissolved in sufficient distilled water, if necessary the solution was heated at 25^0c to dissolve the polymer. After complete dissolving of polymer in distilled water, the solution was kept for stirring on a magnetic stirrer for about an hour until clear solution was obtained. To the above solution the plasticizer of required quantity was added with continuous stirring. The drug of required quantity is dissolved in sufficient distilled water and added to the polymer solution with continuous stirring. The saliva stimulating agent and sweetening agent were individually dissolved in sufficient distilled water and added to the film solution with continuous stirring. Finally the flavour was added to the film solution and stirring was continued for about 2hrs or until clear solution was obtained. After formation of clear solution, the solution was kept a side for three hours to exclude the air bubbles. Then the solution was cast into the mould, which was previously lubricated with light liquid paraffin. The casted mould was kept for drying in hot air oven at 40-45^0c for about 24 hours. After complete drying of the film, the film was carefully removed from the mould and cut into 2×2 cm^2 and stored in dessicator for further evaluation of the film (Vaishali Y *et al* 2012).

Evaluation of losartan potassium fast dissolving films

Thickness of the film

The thickness of film is measured by calibrated digital vernier callipers. The thickness was evaluated at five different locations (four corners and one at centre) of the film (M.D. Nehal siddiqui *et al* 2011) and the results were tabulated in Table.2.

Weight uniformity

The film (2×2 cm) was cut at three different places. The weight of each film strip was taken and weight variation was calculated (Yallanki SK *et al* 2011) and the results were tabulated in Table.2.

Folding endurance

The folding endurance is expressed as the number of folds (number of times the film is folded at the same place) required to break the specimen or to develop visible cracks. This also gives an indication of brittleness of the film. A strip of 2×2 cm was subjected to folding endurance by folding the patch at the same place repeatedly several times until a visible crack was observed (Yallanki SK *et al* 2011), and values were in Table.2.

Surface p^H

The surface p^H of the films was determined in order to investigate the possible side effects due to change in p^H *in vivo*, since an acidic or alkaline p^H may cause irritation to the buccal mucosa. Surface p^H was calculated by using p^H meter. The film was allowed to swell by keeping them in contact with 1ml of distilled water for 2 hours at room temperature. The p^H was noated down by bringing the electrode in contact to the surface of the film, allowing it to equilibrate for one minute (Yallanki SK *et al* 2011) and p^H was tabulated in Table.2.

Disintegration

The disintegration time is the time when a film starts to break or disintegrate. The *in vitro* disintegration time was determined visually by placing the film in glass beaker containing 25ml of simulated salivary fluid with swirling for every 10 seconds. Average disintegration time was noated (Rajni Bala *et al* 2013) and the results were tabulated in Table.2.

Tensile strength

The tensile strength was conducted using texture analyzer (Acquati, I), equipped with 5N load cell. The film was cut into 6×2 cm strips. The strips were held between two clamps positioned at a distance of 3cm. During measurement, the strips were pulled at a specified speed, the force and elongation were measured when the film broke.

Two mechanical properties namely, tensile strength and percentage elongation were calculated for the evaluation of film. Tensie strength is the maximum stress applied at a point at which breaks (Vaishali Y *et al* 2012).

$$\text{Tensile strength} = \frac{\text{Force at break}}{\text{Intial cross sectional area of sample (mm2)}}$$

Percentage Elongation can be calculated from the formula:

$$\%\ \text{Elongation at break} = \frac{\text{Increase in length}}{\text{Orginal length}} \times 100$$

The obtained tensile strength and % Elongation values are tabulate in Table.3.

Drug content

The drug content test was performed to ensure uniform and distribution of drug. 2×2 cm^2 film was cut, weighed and dissolved in 25ml simulated salivary fluid. The solution was filtered. From the filtered solution 1ml was withdrawn and transferred to 10ml volumetric flask and mark up the solution with simulated salivary fluid. Secondary dilution was done such that the final concentration of the solution is 8µg/ml. The final diluted solution was analyzed spectrophotometrically at 205nm wavelength. The content of the losartan potassium in 2×2 cm^2 film was calculated by using standard calibration curve of losartan potassium and results were tabulated in table No. 3

$$\%\ \text{Drug content} = \frac{\text{Observed value}}{\text{Actual value}} \times 100$$

Dissolution

Dissolution studies of fast dissolving films of losartan potassium was carried out using USP type II (paddle apparatus) with 300ml of simulated salivary fluid

(p^H 6.8) as a dissolution medium maintained at 37 ± 0.5^0c. The losartan potassium film of 2×2 cm^2 was stick to the side of the dissolution beaker. The medium was stirred at a speed of 50 rpm. The specified amount of sample was withdrawn for every two minutes interval. The sample withdrawn was replaced with the same amount of simulated salivary fluid p^H 6.8 to maintain the sink conditions. After final appropriate dilution of the samples, the final concentration of the samples was assayed spectrophotometrically at a wave length of 205nm. Percentage of drug dissolved at various time intervals was calculated by plotting time on X-axis against percent cumulative drug release on Y-axis (Francesco Cilurzo *et al* 2010).The results were shown in Table.3 and Figure.1.

Moisture uptake study

The film sample was weighed and placed on a pre-weighed stainless steel wire mesh. The wire mesh was then submerged in a petridish containing 20 ml of distilled water. Increase in weight of the film was determined at regular intervals until a constant weight was obtained. The hydration ratio of the film was calculated using following formula:

$$\% \text{ Hydration ratio} = \frac{Wt - W0}{W0} \times 100$$

Where,
Wt = weight of film at time t
W0 = weight of at zero time
The results were tabulated in table No. 3

Moisture loss study

The percent moisture loss was determined by placing film in dessicators containing anhydrous calcium chloride. After three days the film was taken and reweighed (Yallanki SK *et al* 2011). The percent moisture loss was calculated using following formula:

$$\% \text{ Moisture loss} = \frac{W0 - Wt}{W0} \times 100$$

W0, Wt are initial weight and final weight of films respectively.
The results were tabulated in Table.3.

Characterization of films

FT- IR Spectroscopy

Fourier transform infrared (FT-IR) spectral measurements were performed using Thermo-IR 200 FT-IR spectrophotometer. Potassium bromide palette method was employed. The pure drug and pure drug along with polymer mixture used for preparation of films was finely grounded with KBr to prepare pellets under a hydrollic pressure of 600 psi and background spectrum was collected under identical conditions. Each spectrum was derived from 16 single average scans collected in the range of 4000-400 cm^{-1} at the spectral resolution of 2cm^{-1}.

Differential scanning calorimetry (DSC)

Thermal analysis of Losartan Potassium and physical mixture of the formulations was recorded with Netzsch STA449F3 with a range of 29/20.0 (k/min)/500. The temperature axis and cell constant of DSC were previously calibrated with indium. A heating rate of 5^0c/min was employed over a temperature range of 0-350^0c with pure nitrogen (Dr Anna Balaji *et al* 2014).

Scanning electron microscopy (SEM)

The surface morphology of pure drug and formulated films was assessed using a scanning electron microsope JSM-6610. Samples were mounted on round brass stubs (12mm diameter) using double – backed adhesive tape and then sputter coated for 8 minutes under argon atmosphere with gold before examination under the scanning electron microscope. Pictures were then taken at an excitation voltage of 15 kV.

Table.1 Composition of Losartan potassium fast dissolving films (2×2 cm)

S.No.	Ingredients	Formulation code											
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	Drug	25	25	25	25	25	25	25	25	25	25	25	25
2	HPMC	25	40	60	-	-	-	8.4	16.6	-	-	20	30
3	PVA	-	-	-	16.6	26.6	40	16.6	8.4	20	30	-	-
4	PVPK30		-	-	8.4	13.4	20	-	-	-	-	-	-
5	Maltodextrin DE 18 to 20	-	-	-	-	-	-	-	-	20	30	20	30
6	Glycerol	20	15	10	20	15	10	20	20	15	10	15	10
7	Citric acid	6	5	2	6	5	2	6	6	5	2	5	2
8	Aspartame	6	5	2	6	5	2	6	6	5	2	5	2
9	Flavouring agent	18	10	1	18	10	1	18	18	10	1	10	1

All the weights are taken in mg

Table.2 Thickness, weight uniformity, Folding endurance, Surface p^H, Disintegration time if films

S.No.	Formulation	Thickness (mm)	Weight uniformity (mg)	Folding endurance	Surface p^H	Disintegration time (seconds)
1	F1	0.116±0.014	98.66±0.577	480.33±0.709	6.76±0.061	83±1
2	F2	0.213±0.0057	98.66±1.15	561.33±1.15	6.93±0.057	67.33±0.67

3	F3	0.243±0.0057	99.33±1.154	591.66±1.527	6.76±0.057	41.33±0.67
4	F4	0.166±0.115	103.33±0.96	411.33±0.67	6.66±0.057	28±1
5	F5	0.256±0.0058	101±2	656.66±0.577	6.76±0.061	23.3±0.577
6	F6	0.283±0.009	101±1	772.33±1.527	6.66±0.15	17.6±0.577
7	F7	0.136±0.023	98.33±0.0027	426.66±0.577	6.66±0.115	12.6±0.577
8	F8	0.32±0.02	104.33±0.004	713.33±1.54	6.76±0.058	5.3±0.577
9	F9	0.116±0.018	97.19±0.87	485.33±4.5	6.84±0.201	9.66±0.577
10	F10	0.146±0.058	97.84±0.689	537.33±19.55	6.78±0.126	21±1
11	F11	0.086±0.018	94.77±0.540	412.33±4.16	6.84±0.033	28±1
12	F12	0.163±0.151	97.22±0.678	611.66±12.58	6.82±0.021	32.66±3.055

Mean±SD, n=3

RESULTS AND DISCUSSION

Thickness

The thickness of the films was found to be in the range of 0.086 to 0.320 mm as shown in table N0.2. The thickness is low for formulation F11 which contains 40% carrier concentration Matodextrin:HPMC (1:1) and high for the formulation F8 which contains 25% of carrier concentration HPMC:PVA(2:1). Obtained results shown that, as the concentration of polymer increases the thickness of film also increases. It was observed that the films containing maltodextrin as film forming polymer, has the low thickness because of the less viscous nature of the maltodextrin.

Folding endurance

The folding endurance of the films was found to be in the range of 411 to 772 seconds as shown in table No.2. The folding endurance was low for the formulation F4 containing 25% of polymer concentration PVA: PVPK30 (2:1) and high for formulation F6 containing 60% of polymer concentration PVA:PVPK30 (2:1). From the obtained results it was observed that the folding endurance of the film increases with the thickness of the film. As the concentration of polymer increases, the folding endurance also increases. The folding endurance for all the films was found to be greater than 400, therefore the fast dissolving films exhibit the good physical and mechanical properties.

Weight uniformity

The weight of film strip units varies from 94.77 to 103.33 mg and results were shown in table No.2. This weight uniformity test was performed to ensure uniform distribution of drug in casted films. The results obtained indicate that, the selection and proportion of carriers used for the preparation of films have reduced the weight variation and improves the uniformity of drug distribution in casted films.

Surface p^H

The surface p^H was found to be in the range of 6.66 to 6.93 as shown in the table No.2. The surface p^H of the films was determined in order to investigate the possible side effects due to change in p^H *in vivo*, since an acidic or alkaline p^H may cause irritation to the buccal mucosa. From the results it is clear that all films have p^H value closer to the neutral P^H, which indicates films doesn't cause any irritation to the buccal mucosa.

Moisture uptake study

The moisture uptake study defines the ability of films to absorb water from environment or from dissolution media. The percent moisture uptake for the films ranges from 3.58 to 35.71%. Moisture uptake values of all formulations are shown in table No. 3. A moisture uptake value gives an idea of films dissolution time and disintegration time. Higher values of moisture uptake indicate the films dissolve faster and easily. The percent moisture uptake was highest for the formulation F7 containing film former concentration of 25% PVA:HPMC (2:1), which has the less disintegration time.

Moisture loss study

This moisture loss study is also termed as moisture vapour transmission (MVT). MVT is defined as the quantity of moisture transferred through the unit area of film in unit time. The percent moisture loss for the films ranges from 0 to 22.22% and results were tabulated in table No.3. The moisture loss study gives an idea about films stability nature ability of films to withstand its physicochemical properties under normal conditions. It also gives an idea about hydrophilicity of film formulations. Formulation F9 containing 40% of Maltodextrin:PVA (1:1) has the grater moisture loss and formulation F1 containing 25% of HPMC has the nill moisture loss.

Disintegration

The disintegration time is the time when a film starts to break or disintegrate. Disintegration time for all formulated films is tabulated in Table.2. Disintegration time for all the formulations were in a range of 5 to 83 seconds. The disintegration time was lowest for the formulations F7 and F9 containing 25% of HPMC: PVA (1:2) and 40% of Maltodextrin:PVA (1:1) respectively. The disintegration time is highest for the formulation F2 containing 40% of HPMC in the total film concentration. The disintegration time of the fast dissolving films depends upon the type and percentage of film forming polymers used in the film formulations.

Tensile strength

The tensile testing of a film gives an indication of its strength and elasticity. It is reflected by the parameters tensile strength, elastic modulus and elongation at break. A soft and weak polymer is characterized by a low tensile strength, elastic modulus

and elongation at break. A hard and brittle polymer is characterized by a moderate tensile strength, high elastic modulus and low elongation at break; a soft and tough carrier is characterized by a moderate tensile strength and high elongation at break. The tensile strength and % elongation values are given in table No.3. The tensile strength values ranges from 0.641 to 0.704 MPa and % elongation ranges from 12.25 to 24.56. As the concentration of carrier increases the tensile strength of the films also increases and it was highest for the films made up of PVA and PVPK30 in 2:1 ratio. The %elongation was found to be more for the films made up of HPMC as a carrier.

Drug content

The drug content for the formulations was performed to ensure the uniform and accurate distribution of drug in the prepared formulations. The drug content was performed for all the twelve formulations and results were tabulated in table No.3. The drug content was found to be in the range of 92.31 to 99.87% The results obtained assured that the drug loss in all the formulations was as possible as less and drug uniformity is also more.

***In vitro* dissolution studies**

Among the films F1 to F3, the formulation F3 showed the highest drug release 98.75% at the end of 16 minutes. This is due to the increased wettability of the HPMC in the dissolution medium. The drug release was highest for formulation F6 almost 100% for drug was released at the end of 8^{th} minute. On comparison of drug release profiles for the films made up of PVA: PVPK30=2:1 and the films made up of HPMC, it is clear that the drug release was more for the films PVA: PVPK30=2:1. This is due to the HPMC has poor water solubility and more viscous compared to the PVA and PVPK30. The viscous nature of the HPMC, results in the formation of thick matrix gel upon contact with the dissolution fluid. This matrix gel hinders the drug release from the films. Both PVA and PVPK30 are less viscous in nature and PVA has a nature of fully degradable and dissolves quickly, PVPK30 is readily soluble in water and readily absorbs up to 40% of its weight in atmospheric water and has excellent wetting property. So the combination of both these carriers releases the drug quickly and instantly. But when F7 was compared to that of F6 formulation, the F7 released the slowly and constantly due to the presence of HPMC, which releases the drug from its thick matrix gel. Among the formulation F9 and F10, made up of 40 and 60% w/w of maltodextrin and PVA in 1:1 respectively, the drug release was more for the F9 i.e; 98.14% drug was released at the end of 12 minutes. But still upon increasing the concentration of carrier the drug release was decreased may be due to the saturation of carrier in the dissolution medium.

The films F11 and F12 containing 40 and 60% w/w of maltodextrins and HPMC in 1:1 respectively release the slowly and constantly due to the hindering of drug release from the films by the HPMC. The formulation F6 containing 60%w/w of PVA: PVPK30=1:1 showed the highest drug release almost 100% at the end of 8^{th} minute and on the basis of drug release the formulation F6 was concluded as optimized formula.

Characterization

The FTIR studies was carried out for the pure drug – Losartan potassium, formulations F3, F6, F7, F9, F11 containing of different excipients mixture and their spectra are shown in figure 2,3,4,5,6 and 7 respectively. The pure drug losartan potassium showed the principal absorption peaks at 1261.51 cm^{-1} (C-N aryl stretching), 763.85 cm^{-1} (C-Cl stretching), 1111.06 cm^{-1} (C-O stretching) and 1377.25 cm^{-1} (C-H bending). Same peaks of functional groups C-CN, C-Cl, C-O, C-H bonds were present as that of pure drug without any shifting in the spectra of formulations F3, F6, F7, F9, F11 formulations containing of drug and different excipients mixture. This suggests that there is no chemical interaction between drug and excipients or drug is compatible with the excipients used in the formulations.

Differential scanning calorimetry (DSC)

The DSC graphs of Losartan Potassium and its films made up of different carriers like HPMC, PVA: PVPK30=2:1, HPMC : PVA=2:1 and 1:2, maltodextrin : PVA=1:1 and maltodextrin :HPMC=1:1 were shown in figure No 8,9,10,11,12,13 respectively. From the DSC Thermograms, the melting point of pure Losartan Potassium was found to at 275^0c. The formulations F3, F6, and F7 containing HPMC, PVA:PVPK30(2:1), HPMC:PVA(1:2) along with drug respectively showed the thermogram peak at the temperature 275^0c as that of pure drug Losartan Potassium. Though the thermogram show the exothermic peak for the formulations F9 and F11 containing maltodextrin:PVA(1:1), maltodextrin:HPMC (1:1) along with drug respectively but they are in the same range i.e; 275^0c for F9 formulation and 260^0c with slight decrease for F11 formulation. So, from the obtained DSC thermograms, it is clearly indicated that all the polymers used in alone or in combination in different concentrations for the film formulation are compatible with drug Losartan Potassium.

Scanning electron microscopy (SEM)

The SEM pictures of pure drug and its films made up of different carriers like HPMC, PVA:PVPK30=2:1, HPMC:PVA=2:1&1:2, Maltodextrin: PVA=1:1and Maltodextrin:HPMC=1:1 were shown in figure No. 14,15,16,17,18,19 respectively. From the above SEM pictures it is clearly evident that the films made up of PVA and PVPK30 combination has uniform distribution of drug and film appears to be clear when compared to the films made up of other polymers. This is due to the less viscous nature of PVPK30 and PVA and its freely soluble nature made the uniform distribution of drug.

Table.3 Tensile strength, % Elongation, Moisture uptake, Moisture loss, Drug content of Films

S.No.	Formulation	Tensile strength (MPa)	% Elongation	Moisture uptake (%)	Moisture loss (%)	Drug content (%)
1	F1	0.506	24.56	3.58	0	94.87
2	F2	0.594	21.21	9.37	4.76	95.13
3	F3	0.678	18.54	10.0	4.56	98.59
4	F4	0.619	15.32	9.47	5.0	99.74
5	F5	0.671	13.17	17.3	4.16	99.6
6	F6	0.704	12.25	22.2	3.57	99.74
7	F7	0.499	15.51	35.71	15.38	98.9
8	F8	0.455	16.14	17.80	6.25	99.87
9	F9	0.641	14.73	33.33	2.22	97.82
10	F10	0.687	13.16	22.83	7.5	97.18
11	F11	0.636	20.04	12.92	12.0	92.31
12	F12	0.691	18.51	10.52	10.0	95.51

Fig.1 %Drug release of formulations F1 to F12

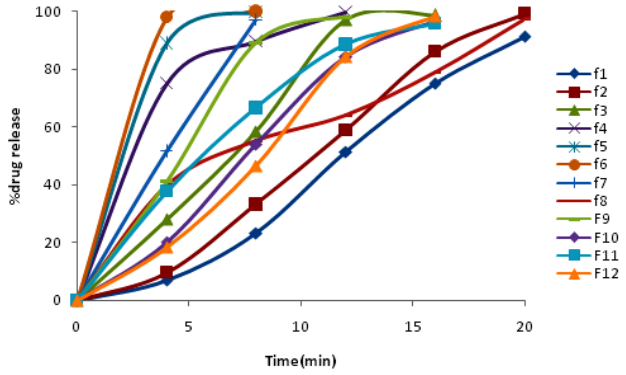


Fig.2 FT-IR Spectra of Losaratn potassium

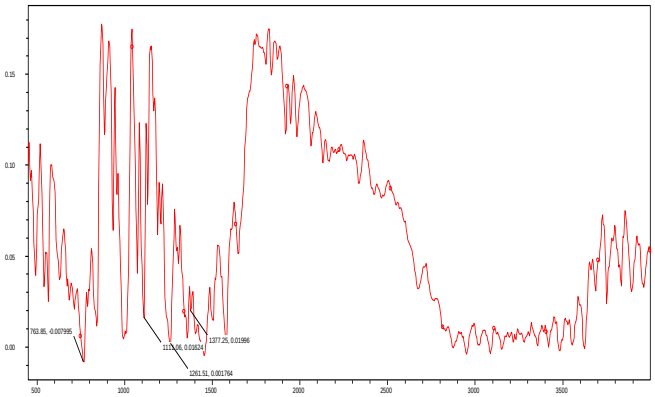


Fig.3 FT-IR Spectra of Formulation F3

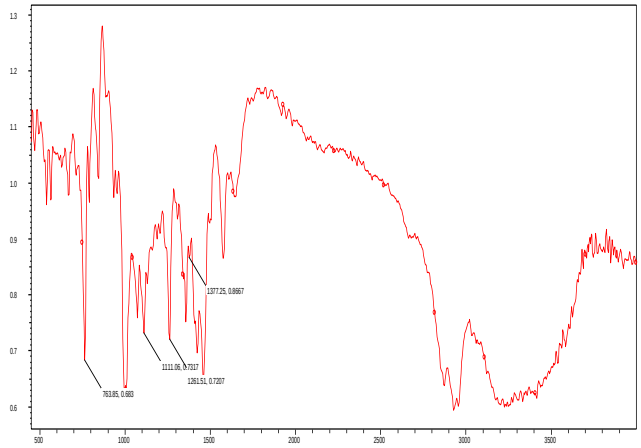


Fig.4 FT-IR Spectra of Formulation F6

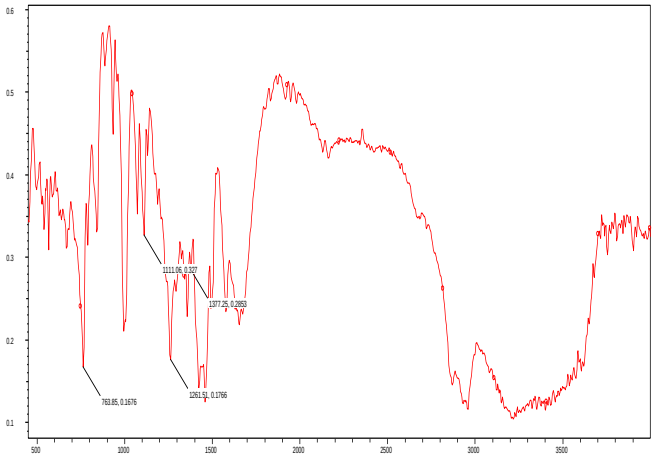


Fig.5 FT-IR Spectra of Formulation F7

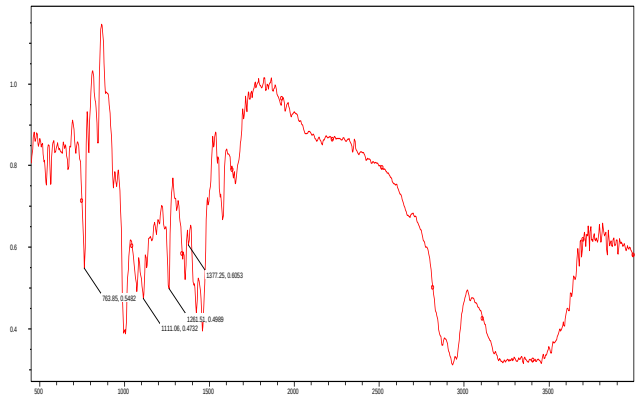


Fig.6 FT-IR Spectra of Formulation F9

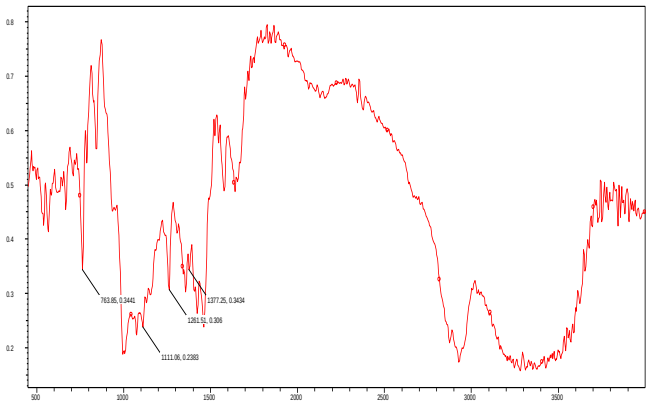


Table.4 % Drug release of Films (Mean±SD, N=3)

Time (min)	% Drug release											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
2	0	6.74±0.026	15.04±0.04	64.39±0.107	75.08±0.015	88.33±0.01	41.53±0.01	39.64±0.02	0	0	0	0
4	7.06±0.015	9.56±0.005	28.05±0.035	75.17±0.07	88.96±0.02	97.95±0.01	51.54±0.04	39.87±0.02	41.24±0.02	20.10±0.00	37.7±0.095	18.36±0.33
6	12.59±3.195	19.64±0.095	41.56±0.316	77.67±0.026	98.97±0.02	99.88±0.03	85.36±0.02	46.43±0.03	70.06±0.01	36.11±0.03	50.89±0.07	30.29±0.23
8	23.39±6.218	33.09±0.051	58.34±0.015	89.65±0.047	99.87±0.015	99.99±0.00	97.15±0.03	55.14±0.03	89.15±0.01	53.89±0.01	66.59±0.06	46.46±0.34
10	37.75±8.322	45.63±0.211	80.96±0.025	99.36±0.02	99.99±0.005		98.55±0.02	61.92±0.02	97.34±0.01	69.16±0.02	78.19±0.14	81.88±0.45
12	51.36±0.02	58.93±0.026	97.35±0.485	99.65±0.032				64.24±0.02	98.14±0.01	84.30±0.07	88.58±0.41	84.32±0.25
14	63.90±0.488	71.67±0.098	98.55±0.092	99.89±0.01				65.43±0.04		90.64±0.55	95.55±0.42	98.05±0.04
16	75.09±0.03	86.19±0.02	98.73±0.03					79.13±0.02		96.50±0.41	95.76±0.13	98.35±0.04
18	84.34±0.036	98.04±0.03						88.36±0.02		97.75±0.21	96.50±0.45	98.64±0.03
20	91.32±0.032	99.35±0.015						97.57±0.02				

Fig.7 FT-IR Spectra of Formulation F11

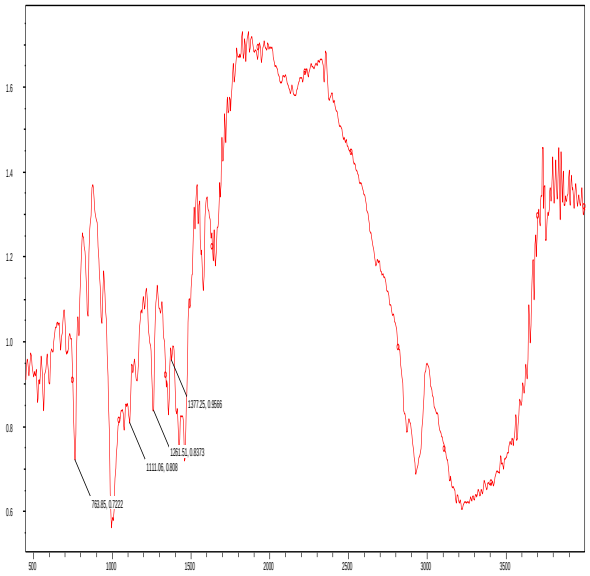


Fig.8 DSC of Losaratn potassium

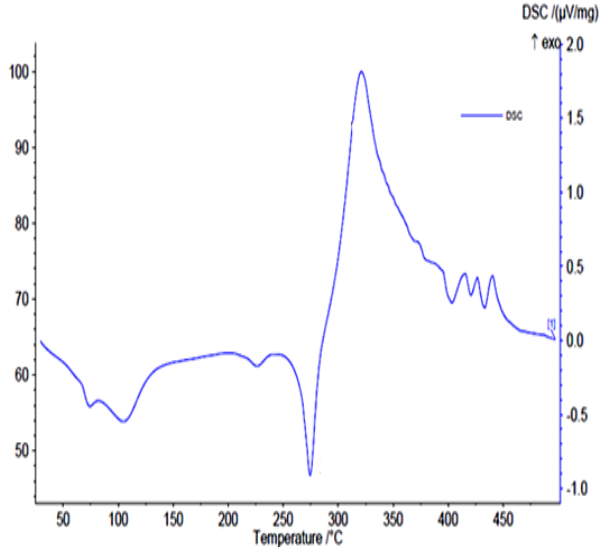


Fig.9 DSC of Formulation F3

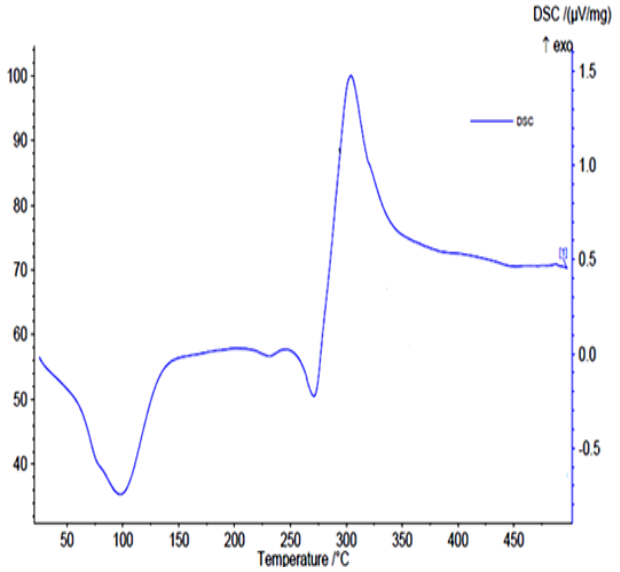


Fig.10 DSC of Formulation F6

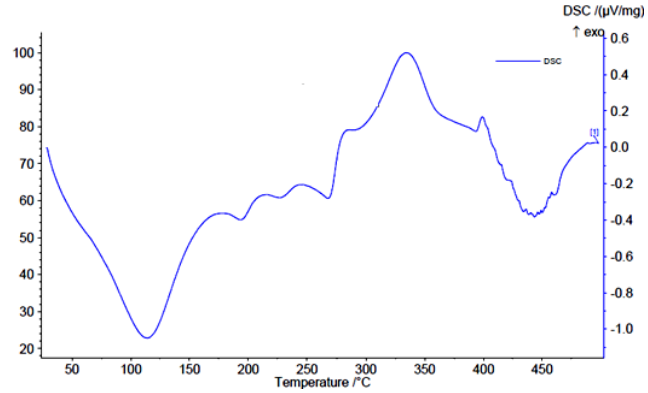


Fig.11 DSC of Formulation F7

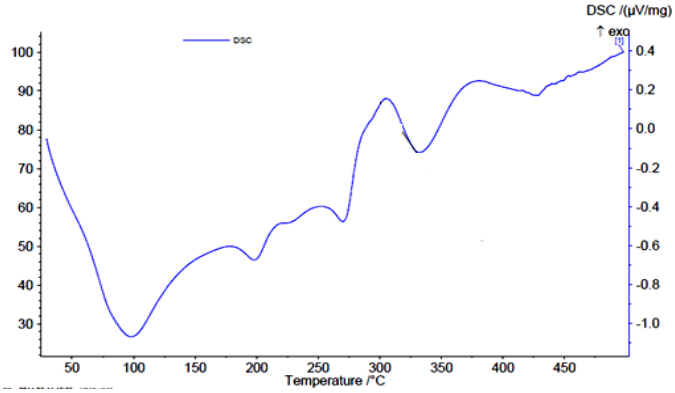


Fig.12 DSC of Formulation F9

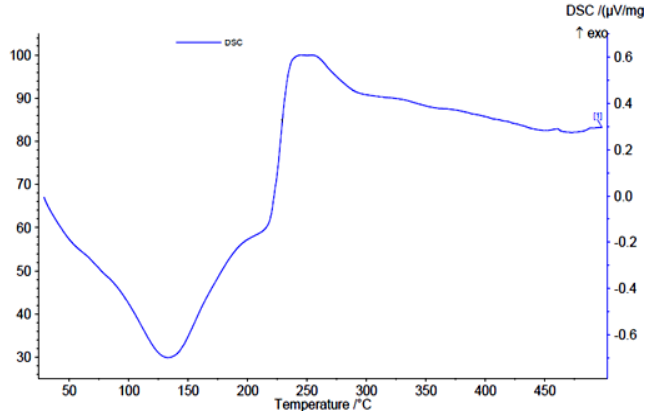


Fig.13 DSC of Formulation F9

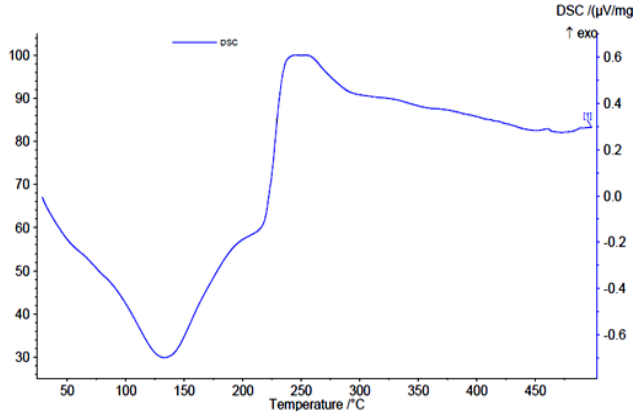


Fig.14 SEM of Losaratn potassium

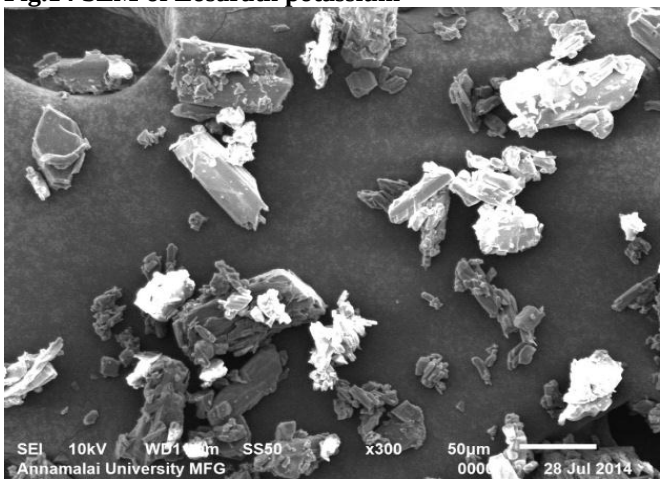


Fig.15 SEM of Formulation F3

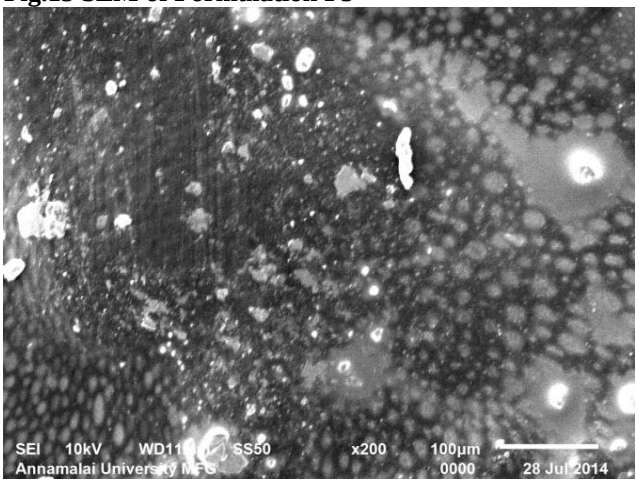
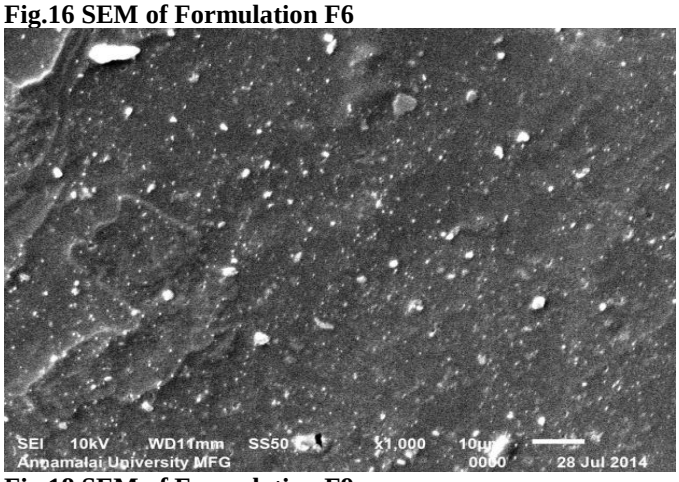


Fig.16 SEM of Formulation F6

Fig.17 SEM of Formulation F7



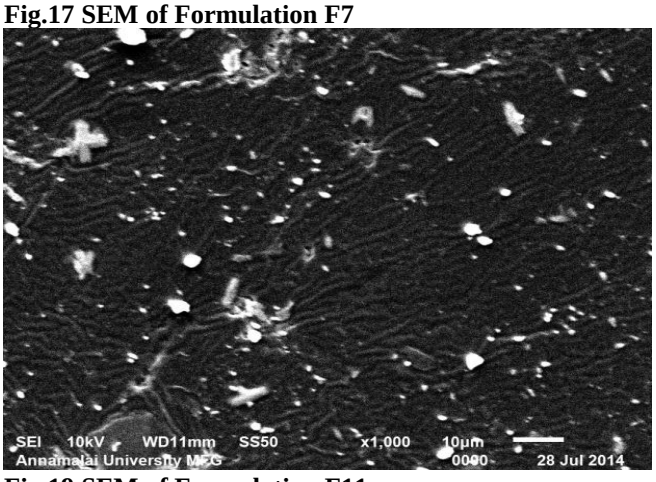
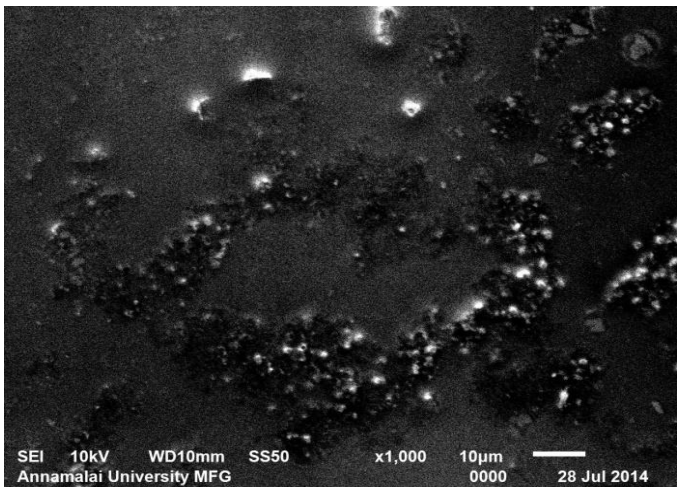
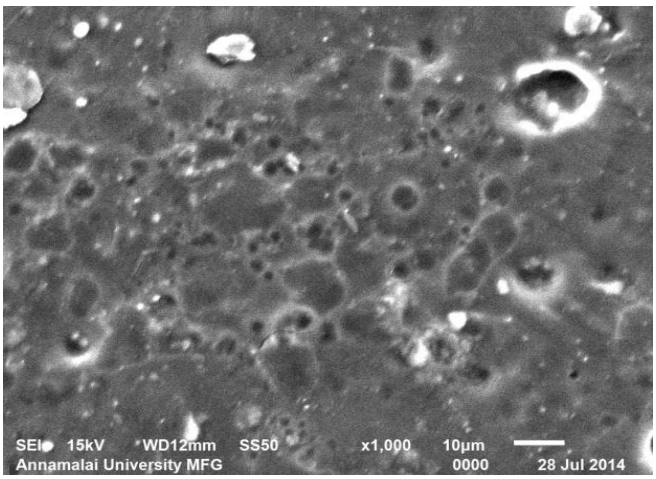


Fig.18 SEM of Formulation F9

Fig.19 SEM of Formulation F11





CONCLUSION

Losartan Potassium was successfully formulated as fast dissolving films by using various film formers alone or in combination such as HPMC, PVA, PVPK30, Maltodextrin (DE 18-20) at different concentrations and glycerol as plasticizer by solvent casting method. All the films have the smooth textured and possess the adequate mechanical strength. Amongst all the prepared formulations from F1 to F12, the formulation F6 possessing PVA and PVPK30 as a film former at a concentration of 60% in 2:1 ratio and glycerol as plasticizer at 10% concentration considered as optimized formulation on the basis of % drug release, mechanical strength and surface morphology. The optimized formulation F6 releases almost 100% of drug at the end of 8^{th} minute. The mechanical strength is also high for the optimized formulation F6 and has the clear surface morphology compared to other formulations. The study clearly evident that the Losartan potassium fast dissolving films provide the fast onset of action by bypassing the first pass metabolism, which is essential requirement for the hypertension patients.

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