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Original Article

Design, Development and Characterization of Losartan Pharmacosomes Encapsulated in Capsule Formulation

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ABSTRACT

Background: In comparison to conventional vesicular drug delivery techniques, Pharmacosomes are a potential method for vesicular drug delivery that offers a number of advantages. Pharmacosomes are phosphilipid complexes with the potential to increase the bioavailability of medicines that are poorly lipophilic and poorly water soluble. Angiotensin receptor blocker losartan is classified as a BCS class II medication with low solubility. **Materials and Methods:** Solvent evaporation method was used to prepare the Losartan Pharmacosomes. These prepared Pharmacosomes were encapsulated into capsules for easy administration. **Results:** The phospholipid complex of Pharmacosomes was made using the solvent evaporation method in 7 distinct ratios. The morphology, X-ray Diffraction, FTIR, UV and drug entrapment investigation of the synthesized losartan pharmacosomes were assessed. The synthesized compound was shown to have substantially better solubility than the pure medication Losartan. Losartan pharmacosomes were encapsulated into capsules for oral medication administration. **Conclusion:** Based on the results, we assume that the solubility as well as bioavailability problem of native losartan was reduced.

Keywords: Pharmacosomes, Losartan, Capsules, Solubility, Bioavailability.

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INTRODUCTION

Losartan is one of the anti-hypertensive medications. Angiotensin II is produced by the Angiotensin-Converting Enzyme (ACE) from angiotensin I and it stimulates the adrenal cortex to produce and release aldosterone, which causes a decrease in sodium excretion and an increase in potassium. In vascular smooth muscle, angiotension II also has vasoconstrictor properties. These medications are mostly used to treat high blood pressure. It typically travels via the first-pass metabolism pathway.[1]

Pharmacosomes are colloidal dispersion of drug, which bound to lipids, may exit ultrafine vesicular micellar are hexagonal aggregates on the chemical structure of drug lipid complex. They have amphiphilic phospholipids complexes bearing active hydrogen that binds to it, which result in enhancing the bioavailability. Pharmacosomes have been prepared for various diseases like NSAID'S, CVS drug and anticancer agents.[1] Which improve the absorption and minimize the GIT toxicity. Physicochemical stability of Pharmacosomes depends upon the drug lipid complexes, degradation velocity into active drug molecule, depends to great extent on size, functional group, chain length of lipids. They can give orally, topically, extra or intravascularly. It provides efficient method for drug delivery at site of action, which leads to reduction of drug toxicity with no adverse effect and reduces cost of therapy by improved bioavailability of medication, in case of poorly soluble drug.[1,11] It is suitable for incorporating both hydrophilic and lipophilic drug. Since the drug is covalently linked, loss due to leakage of drug does not take place, so it is good for incorporation. The entrapment efficacy is not only high but predetermined, so drug itself conjugation with lipids forms as vesicles. Drug lipid complexes are a key factor in the physicochemical stability of pharmacosomes and the size, functional group and chain length of lipids all have a significant role in how quickly they degrade into active drug molecules. The medicine is delivered at site of action in an effective manner.[2,3] Based on the above advantages we have chosen pharmacosomes to improve their bioavailability.

MATERIALS AND METHODS

A complimentary sample of losartan was obtained from Microlabs, Chennai India. A free sample of soy lecithin was obtained from HiMedia Laboratories in Nashik. Losartan pharmacosomes were created using the standard solvent evaporation method. Other compounds were all of the analytical variety.

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Preparation of Losartan Pharmacosomes

Losartan pharmacosomes was prepared by solvent evaporation technique. It was acidified with aqueous solution of losartan using 0.1N hydrochloric acid and then extracted into chloroform and subsequently recrystallized. Phosphatidycholine (PC) complex was prepared by associating losartan with PC in various molar ratios. The accurately weighed PC and losartan were placed in a 100 mL round bottom flask and dissolved in sufficient amount of dichloromethane and the mixture was refluxed for one hour after that solvent was evaporated under vacuum at 40°C in a rotary vacuum evaporator. The dried residues were collected and placed in vacuum desiccator and then subjected to characterization.[2,4]

Preformulation Studies

Compatibility Studies

The chemical interaction between API and excipients were analyzed using IR spectra. The mixtures were prepared with required quantity of KBr. Transparent pellet was prepared by using 100 mg of sample and scanned by using FTIR spectrometer.[5]

Angle of Repose

It is an angle between the surface pile of powder and the horizontal plane. It was analyzed by funnel placed vertically at a determined height. The angle of repose was performed and the funnel height was modified until the tip of the funnel touched the top of the powder stack.

Bulk Density

Using a measuring cylinder and pre-sieved (#40 mesh) powder, the volume and weight of the mixture were measured to estimate the bulk density.

Tapped Density

The tapped density was determined by utilizing a specific amount of powder in a cylinder on the mechanical tapper apparatus, which was operated for a predetermined number of taps (about 1000) until the powder bed volume was at a minimum. The smallest volume and the sample's weight in the cylinder were used to calculate the tapped density.

Drug Content Determination

The amount of medication in the losartan pharmacosome was measured by weighing the complex equivalent to 50 mg of losartan and adding 100 mL of pH 7.4 phosphate buffers to a volumetric flask. After that, a magnetic stirrer was used to constantly swirl the volumetric flask for 24 hr. Using 205 nm UV spectrophotometry, the drug content was studied.[4,5]

Solubility Determination

By employing a phosphate buffer pH 7.4, the solubility of losartan and losartan pharmacosome was estimated. For 24 hr, the flask was shaken in a water bath at 25°C. After reaching equilibrium, the liquid was kept for 15 min at 1000 rpm, the saturated solutions were centrifuged to extract any remaining medicine. To avoid crystallization, the supernatant solution was filtered and properly diluted using the same solvent. it was then spectrophotometrically examined at 205 nm.[4,6]

X-ray Powder Diffraction (XRD) Analysis

It is determined with sample holder made of aluminum held the powder sample.[7] The radiation source for the X-ray generator was the Ka lines of cooper and it ran at 40kV tube voltages and 30 mA tube current. With a 10^{o} min^{-1} scan speed, the scanning angle ranged from 10 to 90°. X-ray diffraction was used to study the drug, phosphatidylcholine and the pharmacosome.[7]

Scanning Electron Microscopy (SEM) Analysis

To identify the surface morphology of prepared formulation SEM analysis was performed. Sample was maintained on a SEM stub for 6 min at 50 mA using double-sided adhesive tape and a sputter. To capture digital images a scanning electron microscope with a secondary electron detector was used.[8]

Formulation of Losartan pharmacosome capsules

50 mg of Losartan Pharmacosomes were encapsulated manually using a capsule filling machine in commercially available gelatin capsules (size: 5).[9,10]

Disintegration Test

The disintegration time of LPC was determined using a disintegration apparatus. The assembly should be suspended in the beaker of distilled water and maintained at constant temperature of 37.2°C. There should be 28-32 cycles per minute of raising and lowering the assembly. The time at which the capsules disintegrated completely from the tubes were noted.[5]

Dissolution study

The dissolution test apparatus Type I was used to conduct this test. Both the temperature and the stirring speed were held constant at 37°C±0.5°C. The capsule release investigation was completed by storing the capsules in 900 mL pH 7.4 phosphate buffer solutions, which served as the dissolution medium, for 10 hr. 10 mL of the sample was taken out and replaced with fresh buffer solution every predefined amount of time. At 205 nm, the sample's absorbance was determined using a double beam spectrophotometer. The standard curve was used to compute the sample's cumulative release using the appropriate equations.

Drug Release Kinetic Analysis

In vitro drug release investigations were plotted in various kinetic models to analyze the release kinetics:

Zero order as cumulative percent release vs. time.

Higuchi's model as cumulative percent drug release vs. square root of time.

A graph is drawn between time on the x-axis and the log cumulative % of the drug still to be delivered on the y-axis using a first order equation.

The Korsmeyer plot, which is a graph between log T and log percent cumulative release.[11,12]

RESULTS

Compatibility Studies

The IR spectra of the pure drug, losartan, soy lecithin and excipients were analysed using FTIR Spectroscopy. The peaks obtained at wave number 762.39 cm^{-1}, 1422.5 cm^{-1}, 2955.12 cm^{-1}, 3358.4 cm^{-1}, 1358.19 cm^{-1} and 1581.49 cm^{-1} for C-Cl stretching, C-N stretching, C-H stretching, N-H stretching, O-H stretching and C=C stretching respectively for losartan. Similarly, the combined spectra for losartan and excipients indicate the functional groups of losartan (Figures 1 and 2). This suggests that there was no incompatibility between the excipient and the drug.

Preparation of Losartan Pharmacosomes

Losartan was loaded into pharmacosomes with different concentration as mentioned in Table 1. The drug concentration was fixed and the polymer concentration was varied from 1 to 4 times with the drug concentration. The Pharmacosomes were prepared using solvent dichloromethane and dried using vacuum and stored for further analysis.

Scanning Electron Microscopy (SEM) Analysis

Scanning electron microscopy was used to examine the surface morphology of the Losartan pharmacosomes. The SEM images revealed that the needle-shaped pharmacosome particles were randomly distributed throughout the sample (Figure 3).

Solubility Determination

The Solubility of marketed losartan tablets and formulated LPC were determined and found that, the LPC showed 4-fold increased solubility in buffer than marketed tablet.

X-ray powder Diffraction (XRD) Analysis

The XRD patterns of the chosen formulation, soy lecithin and Losartan are shown in Figure (4a, 4b and 4c). For Losartan, characteristic diffraction peaks were seen. Comparatively, the diffraction peak intensity of the formulation F7 was lower than that of the pure Losartan. This indicates the decrease in crystallinity of losartan in pharmacosomes.

Drug Content Studies

It is determined by using UV spectrophotometer at 205 nm with phosphate buffer pH 7.4. The F7 formulation with high polymer ratio shows 96.83% of drug content and F6, F5, F4, F3, F2 and F1 shows 96.12, 93.38, 93.56, 90.81, 90.04 and 88.60% drug content respectively. The results (Table 2) indicates that the percentage of drug content is more in higher polymer ratio and decreases with decrease in polymer ratio.

Preformulation Studies

The flowability and compressibility of the losartan pharmacosomes were assessed using the preformulation parameters such as angle of repose, bulk density, tapped density, Hausner's ratio and Carr's index (Table 3).

The sample appears to have a decent flow character based on the parameters. The outcomes were all within the allowed ranges as per IP.

Formulation of Losartan Pharmacosome Capsule

Based on the preformulation studies, the prepared losartan pharmacosomes F1 to F7 were capsulated into hard gelatin capsules using manual capsule filling machine. 25 mg of prepared

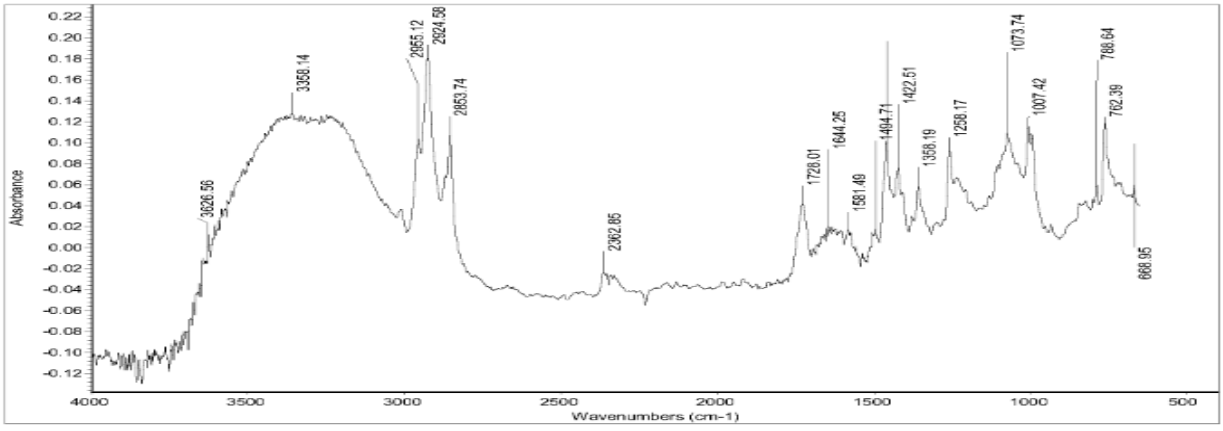

Figure 1: IR spectrum of Losartan pure drug.

Table 1: Formulations F1 to F7 with different ratios of losartan and soyalecithin.

Ingredients	F_1	F_2	F_3	F_4	F_5	F_6	F_7
Losartan: Soyalecithin	1:1	1:1.5	1:2	1:2.5	1:3	1:3.5	1:4

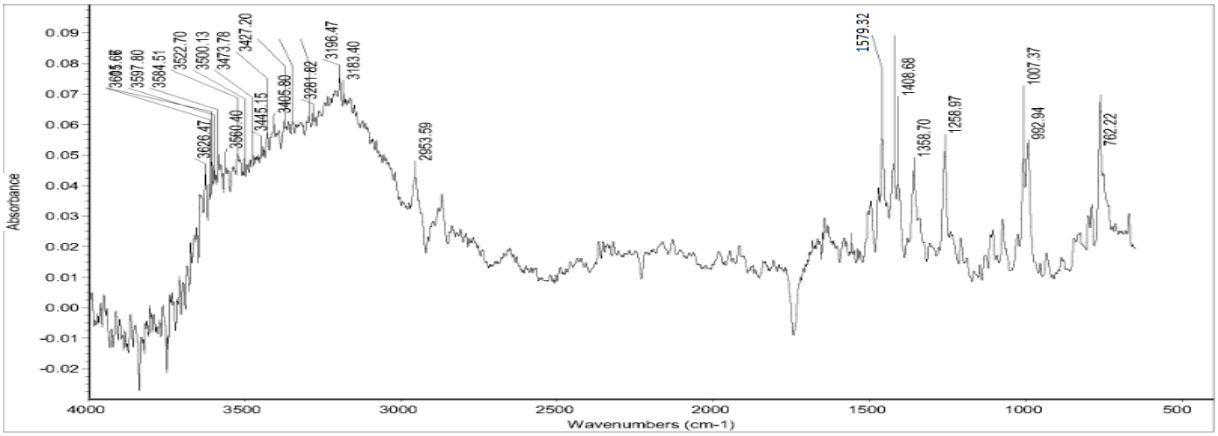

Figure 2: IRSpectrum of Losartan+Soya lecithin.

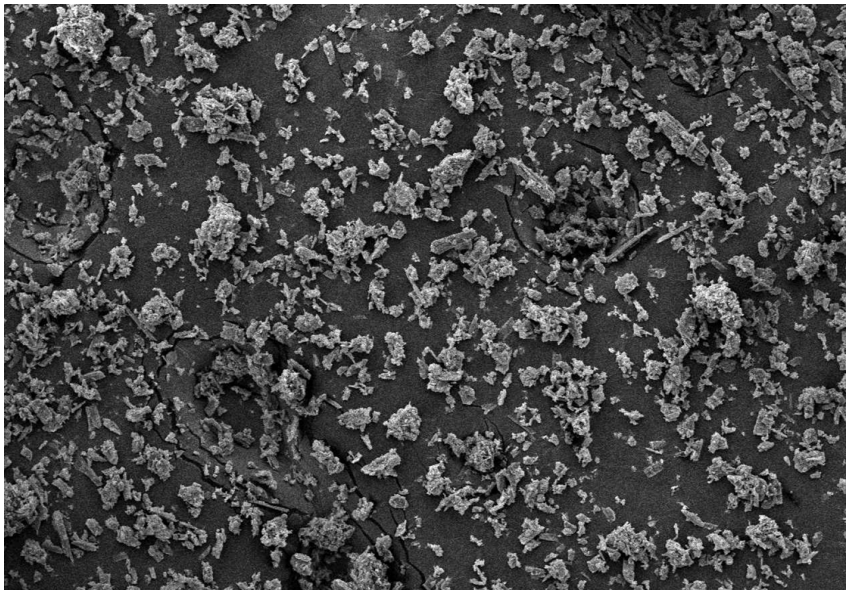

Figure 3: SEM image of Losartan pharmacosomes.

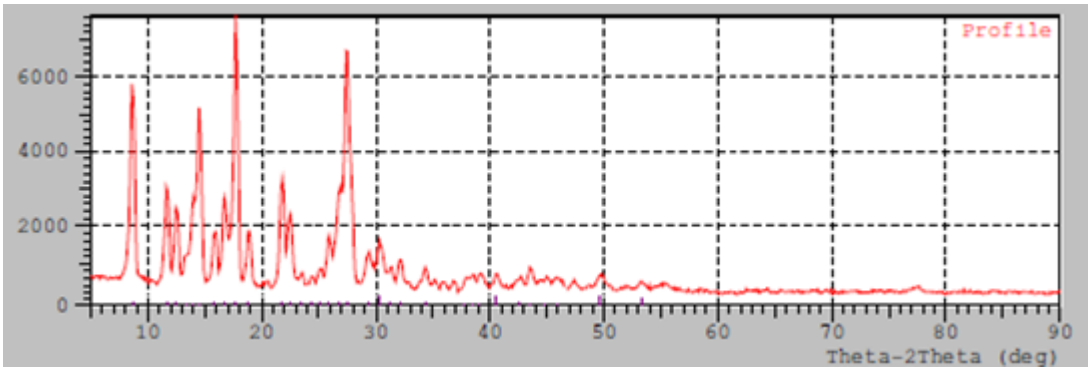

Figure 4a: XRD pattern of pure drug (Losartan).

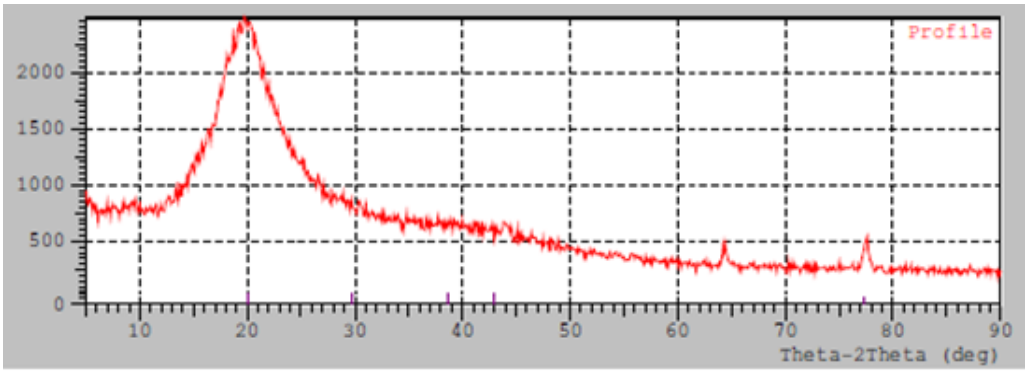

Figure 4b: XRD pattern of soya lecithin.

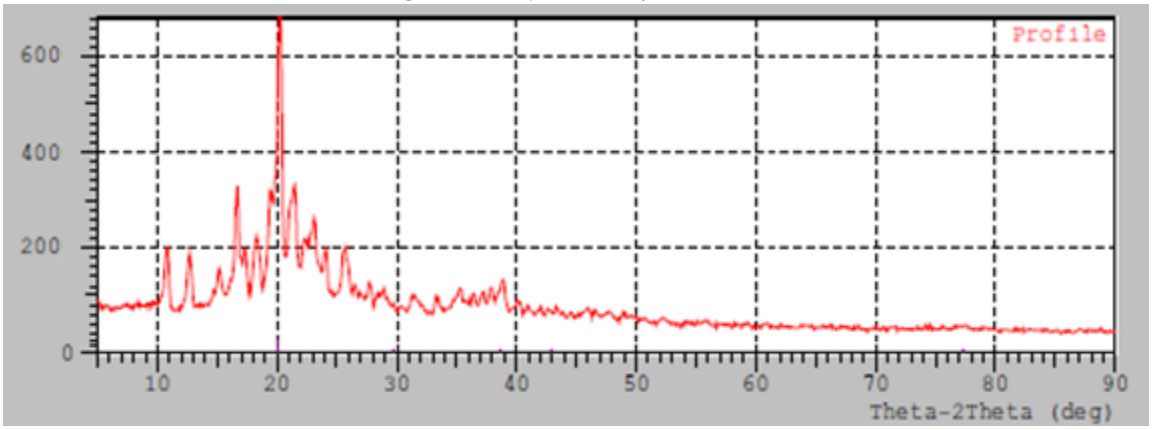

Figure 4c: XRD pattern of Losartan pharmacosomes (F_1).

Table 2: Percentage drug content of F1 to F7 formulations.

Formulation	F1	F2	F3	F4	F5	F6	F7
Percentage of drug loaded (%w/w)	88.60	90.04	90.81	93.56	93.38	96.12	96.83

losartan pharmacosomes were loaded into hard gelatin capsules and evaluated.

Evaluation of Losartan Pharmacosome Capsules

The prepared capsules were evaluated for disintegration test and the time taken for disintegration was tabulated in Table 4.

In vitro Dissolution Studies

In vitro release study was carried out for 0 to 10 hr for all formulations. Plots were created based on the drug release using the data collected (Table 5 and Figure 5) and the percentage cumulative release was calculated using the data.

For all 7 formulations, the capsules containing Losartan pharmacosomes displayed a better dissolving profile, with a percentage cumulative drug release that ranged from 79.49 to 94.69%. At the tenth hour, the formulation F1 with a drug: soya lecithin in the ratio of 1:1 shown the greatest release of 94.69%; similarly, the formulation F7 demonstrated a release of 79.49% due to an increased soya lecithin ratio. The release of the losartan from pharmacosomes due to the phospholipids present in the formulation. This indicates the enhanced bioavailability of losartan when compared to marketed tablets. The complex process of solid dispersion is influenced by a number of variables, including particle size, crystal habit, surface area, surface energy and wettability. Phospholipids, an amphiphilic surfactant, have wetting and dispersion qualities that improve the complex's dissolution profile by making the medication more soluble.

Release Kinetic Analysis

The formulation F1 was examined for the release kinetic studies based on the information gained from the *in vitro* drug release investigations. To determine the pattern of release and to determine the mechanism of release from the formulated pharmacosomes, the cumulative release of the drug was fitted into a variety of plots, including the Zero order, First order and Higuchi models (Figure 6). Based on the value of the regression coefficient for each model, the model that best matches the release data is chosen. For the zero order, higuchi, first order and korsmeyer-peppas models, F1 displays r^2 values of 0.9662, 0.9822, 0.9871 and 0.8539, respectively.

Table 3: Preformulation Studies of prepared losartan pharmacosomes.

Formulation	Angle of Repose	Bulk Density (g/cm³)	Tapped Density (g/cm³)
F_1	24°15'	0.554	0.624
F_2	26°53'	0.401	0.453
F_3	24°82'	0.500	0.570
F_4	27°08'	0.433	0.500
F_5	28°30'	0.454	0.525
F_6	27°56'	0.415	0.500
F_7	27°63'	0.500	0.624

Table 4: Disintegration test for F1 to F7 formulation.

Formulation	F_1	F_2	F_3	F_4	F_5	F_6	F_7
Disintegration time (min)	3.7	4.1	3.9	4.1	4.0	3.9	4.3

From the values obtained it was observed that the disintegration time were within the range.

Table 5: Percentage cumulative release of F1 to F7 formulations.

Time (hr)	Percentage Cumulative Release						
	F_1	F_2	F_3	F_4	F_5	F_6	F_7
0.25	4.60	3.29	2.83	2.85	3.07	3.95	3.07
0.5	11.58	10.37	9.88	8.64	9.54	7.85	6.19
1	21.29	18.07	16.94	14.21	15.73	14.26	13.42
2	33.16	27.68	25.65	20.14	23.46	23.02	18.85
3	40.64	38.42	34.49	33.24	41.51	29.51	21.52
4	53.21	46.63	42.92	40.23	47.43	41.46	32.94
5	58.55	53.17	48.19	45.75	50.85	49.00	45.18
6	65.77	59.40	52.08	46.98	52.30	50.76	53.62
7	73.50	64.81	57.30	51.27	56.74	53.95	54.05
8	84.16	71.54	62.69	60.20	62.25	63.16	59.54
9	90.19	82.79	71.20	74.48	74.25	72.60	73.60
10	94.69	90.05	85.07	83.05	84.44	83.34	79.49

It was found that the formulation f1 follows zero order kinetics based on the values of the regression coefficients. Since the formulation used a non-Fickian diffusion mechanism for drug release, the slope value (n) from the peppas plot was 0.8539.

DISCUSSION

High blood pressure is an arterial disease that affects 1.3 billion people and also it kills 10 million people worldwide every year. Peripherally-acting antihypertensive drug by depleting or inhibiting the release of catecholamine from the peripheral nerve ending or altering the response at alpha 1- and alpha 2-receptor sites. In this research we have chosen Losartan a class of angiotensin II blocker and it also stimulates the adrenal cortex to produce and release aldosterone, which causes a decrease in sodium excretion and an increase in potassium. In vascular smooth muscle, angiotension II also has vasoconstrictor properties. It typically travels via the first-pass metabolism pathway.[1] Administration of Losartan via oral route has low bioavailability profile. To increase the bioavailability, formulating losartan pharmacosomes using phopsphatidylcholine as a carrier.

Totally 7 formulations from F1 to F7 were prepared using different concentration of polymer. The prepared pharmacosomes were dried using vacuum and the compatibility studies were carried out by FTIR spectroscopy. The results revealed that functional groups of Losartan and excipients in formulation were disintictive, which indicates that there were no incompatibility issues between the excipient and the Losartan. The surface morphology study by SEM analysis reveals needle shaped pharmacosomes and it was randomly distributed.

The XRD determination for soy lecithin and the pure Losartan shown diffraction peaks in the spectra and the intensity of peak for the formulation F1 was lower than that of the pure Losartan.

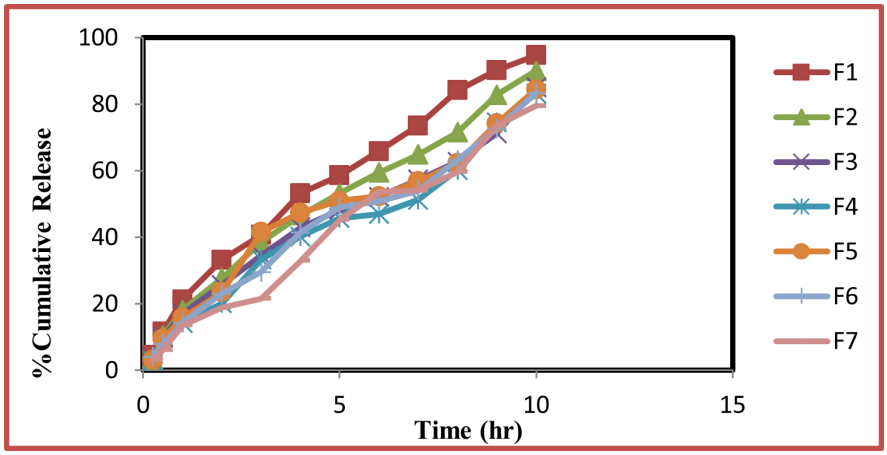

Figure 5: *In vitro* comparative dissolution Profile of pharmacosomes containing Losartan.

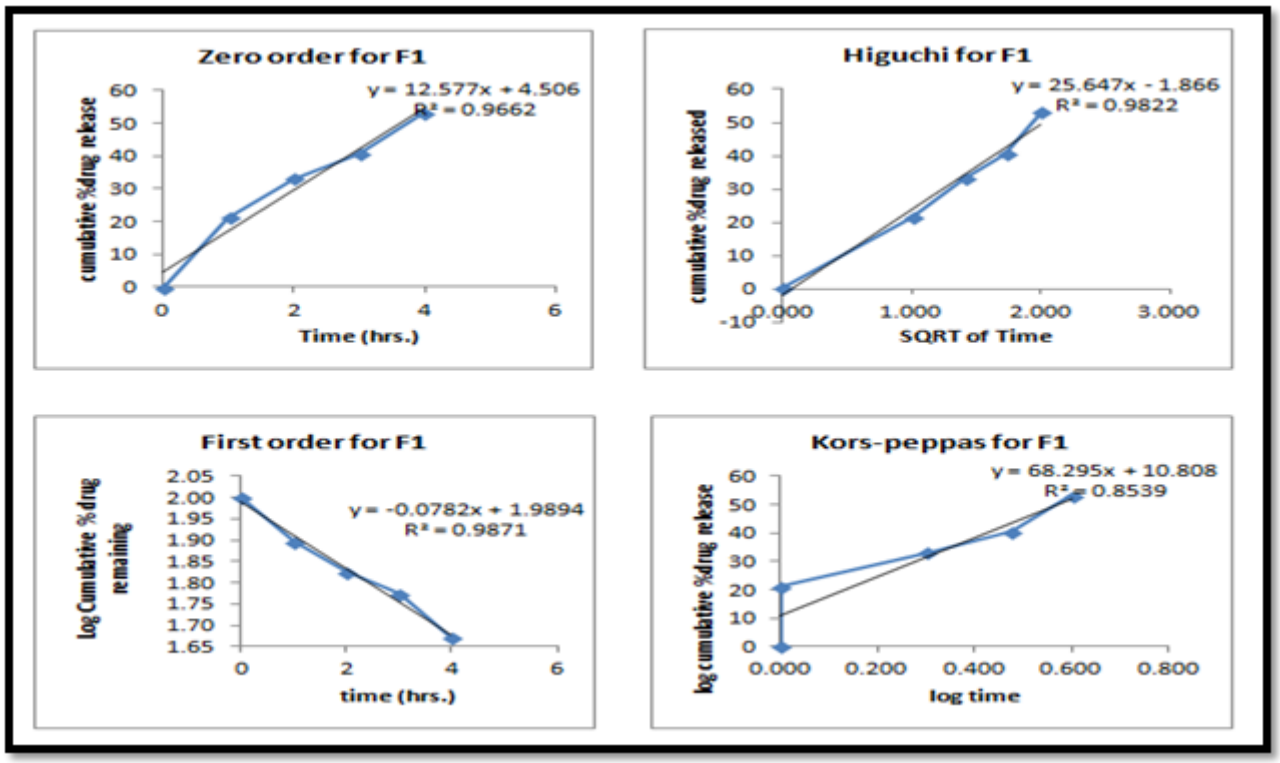

Figure 6: Different release kinetics of F1 formulation.

This demonstrated the decrease in crystallinity of losartan in pharmacosomes. Drug content of Losartan in the complex, as determined by UV Spectrophotometry and it was found to be 96.8% (w/w). The assessment of the preformulation parameters such as angle of repose, bulk density, tapped density, Hausner's ratio and Carr's index, shown the outcomes were all within the normal ranges.

Disintegration test on different ratios of losartan pharmacosomes shown that the disintegration time was in the range of 3.5 to 4 min, which passed the test for disintegration. *In vitro* dissolution study were carried out for a total of 10 hr for all formulations and it was found that the percentage cumulative release of losartan pharmacosomes was ranged from 79.49 to 94.69%. At the 10th hr, the formulation F1 with a Losartan: soya lecithin in the ratio of 1:1 shown the greatest release of 94.69%. In this all investigation, we have concluded that phopsphatidylcholine which is incorporated with Losartan can increase the bioavailability of losartan.

CONCLUSION

Losartan, an antihypertensive drug with low solubility and bioavailability was chosen to overcome its drawback through formulation approach. Pharmacosomes using phospholipids were formulated by solvent evaporation method. Losartan pharmacosomes shows 4 fold increased solubility when compared to marketed tablet. Hence this losartan pharmacosomes were capsulated into hard gelatin capsules and evaluated for drug

release studies. Based on the release pattern, we assume that the solubility as well as bioavailability problem of native losartan was reduced. In future, *in vivo* studies will add more reliable data for further use of losartan pharmacosomes orally.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

w/w: Weight by weight; **i.e:** That is; **e.g.**: Example; **PC:** Phosphatidylcholine; **HDL:** High density lipoprotein; **FT-IR:** Fourier transform infrared spectroscopy; **SEM:** Scanning electron microscopy; **XRD:** X-ray powder diffraction; **mg:** Milligram; **µg:** Microgram; **°C:** Degree centigrade; **hr:** Hour; **mL:** Mililiters; **rpm:** Rotation per minute; **min:** Minute; **nm:** Nanometer; **rpm:** Rotation per minute; **min:** Minute; **vs:** Versus; **RH:** Relative humidity; **ICH:** International Council for Harmonisation.

SUMMARY

In the present study Losartan-phospholipid complex (pharmacosomes) were prepared by a simple and reproducible method and evaluated for various physicochemical parameters. The physicochemical investigations showed that Losartan formed a complex with phospholipids with better solubility and dissolution profile. Thus, it can be concluded that the pharmacosomes of Losartan is effective in improving bioavailability and gastrointestinal safety of the drug.

REFERENCES

1. Hussain MD, Mirza S, Miroshnyk I, Habib MJ BJ. Enhanced dissolution and oral bioavailability of losartan formulation: Modulting effect of phospholipids. Pharmaceutics. 2010;2:339-350.
2. Semalty A, Semalty M, Rawat BS, Singh D RM. Pharmacosomes: the lipid-based new drug delivery system. Expert Opin Drug Deliv. 2009;6(6):599-612. doi:10.1517/17425240902967607
3. Sangiovanni E, Angarano M. Phytosomes as Innovative Delivery Systems for Phytochemicals : A Comprehensive Review of Literature.; 2021.
4. Semalty A, Semalty M, Rawat BS, Singh D RM. Development and evaluation of pharmacosomes of aceclofenac. Indian J Pharm Sci. 2010;72(5):576-81.
5. Lachman L, Lieberman HA KJ. The Theory and Practice of Industrial Pharmacy. Varghese Publishing House; 1991.
6. Semalty A, Semalty M, Singh D RM. Development and Physico-chemical evaluation of pharmacosomes of diclofenac. Acta Pharm. 2009;59(3):335-44. doi:10.2478/v10007-009-0023-x
7. Patil SD, Chatap VK PP. *In vitro*, *ex vivo* characterization of Furosemide bounded pharmacosomes for improvement of solubility and permeability. Adv Pharmacol Pharm. 2014;2(5):67-76.
8. Kamalesh M, Baviskar D, Wagh K BK. Formulation and evaluation of pharmacosomes of ketoprofen. Indo J Pharm Res. 2014;2(3):1363-8.
9. Singh D. Niosomal Encapsulation of Curcumin : Formulation and Characterization Niosomal Encapsulation of Curcumin : Formulation and Characterization. 2023;(2021). doi:10.9734/jpri/2021/v33i43B32556
10. Raikhman LM, Ivanov VE MY. Development of ibuprofen pharmacosomes for enhancing the bioavailability. Drug Dev Indian Pharm. 2002;28(5):473-82.
11. Costa P SLJ. Modeling and comparison of dissolution profiles. Eur J Pharm Sci. 2001;13(2):123-33.
12. Sica DA, Gehr TW GS. Clinical pharmacokinetics of losartan. Clin Pharmacokinet. 2005;44(8):797-814.

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