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FORMULATION AND EVALUATION OF CONTROLLED POROSITY OSMOTIC TABLET OF LOSARTAN POTASSIUM

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Abstract:

Osmotically controlled oral drug delivery systems utilize osmotic pressure as energy source for the controlled delivery of drugs. The aim of the present study is to formulate and evaluate controlled porosity osmotic tablets of Losartan Potasssium. Losartan Potassium is used in hypertension. Core tablets were prepared by direct compression technique using mannitol, fructose and NaCl as osmogens and Avicel PH101 as filler. The osmotic tablet contains pore forming water soluble additives in the coating membrane, which dissolve after coming in contact with water, resulting in formation of an in-situ micro porous structure. The core tablets were coated by dip coating using cellulose acetate as a coating agent with PEG 400 and PEG 6000 as water soluble pore former and dibutyl pthalate as plasticizer. The formulations were evaluated for precompression and postcompression parameters. The batch F8C2 containing Fructose as an osmogen and 20 % PEG 6000 as a pore forming agent showed the 91.25 % drug release for 12 hrs.

Keywords: *Antihypertensive, Losartan Potassium, Osmotic, PEG 6000, Semi Permeable Membrane.*

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INTRODUCTION: [1-7]

Osmotically controlled drug delivery systems (ODDS) are a type of NDDS which based on osmotic pressure for controlled delivery of active agent. These systems are used for both oral administration and implantation. These systems utilize osmosis as the major driving force for drug release. Adequate water solubility of the drug is essential for osmotic drug delivery system. Osmotic drug delivery devices are composed of an osmotically active drug core, which is surrounded by a rate controlling membrane. The release of drug(s) from osmotic systems is affected by various formulation factors such as osmotic pressure of the core component(s), solubility and size of the delivery orifice, and nature of semi permeable membrane. Different types of osmotic systems have been developed implantable and oral. Controlled-porosity osmotic pump (CPOP) is one type of osmotic tablets in which the delivery orifices are formed by incorporation of a leachable component into the coating solution. After coming into contact with water, this soluble additive dissolves resulting in an in situ formation of a microporous semipermeable membrane. The method to create the delivery orifice is relatively simple with the elimination of the common laser drilling technique. The mechanism of drug release from these systems was found to be primarily osmotic with simple diffusion playing a minor role. The release rate depends upon the solubility of the drug in the tablet core, the osmotic pressure gradient across the membrane, the coating thickness, and the level of leachable component in the coating. Losartan potassium, or 2-n-butyl- 4-chloro-5-hydroxymethyl-1-[(2-(1H-tetrazol-5-yl) biphenyl-4-yl) methyl] imidazole potassium is a potent, highly specific angiotensin II type 1 (AT1) receptor antagonist with anti-hypertensive activity. Losartan potassium is used in treatment of hypertension due to mainly blockade of AT1 receptors. Losartan is used to treat high blood pressure and to help protect the kidneys from damage due to diabetes.

MATERIAL AND METHODS:

Materials: Losartan Potassium was obtained as gift sample from Centurion Laboratories Ltd., Vadodara. Other chemicals were used of analytical standard.

Methods [8, 9]:

Solubility studies: Solubility of drug in three different solvents (pH 1.2 media, pH 6.8 buffer and distilled water) was carried by preparing saturated solutions of drug in respective solvents. Saturated solutions were prepared by adding excess of drug to vehicles and shaking them on shaker for 24 hrs under constant vibration. After this, the solutions were filtered and analyzed spectrophotometrically.

Formulation of Controlled Porosity Osmotic Tablet of Losartan Potassium [10-17]

The core osmotic tablets were prepared by direct compression technique using multi station rotary tablet punching machine keeping conventional punch. The tablets were coated by dip coating.

Table 1: Formulation Composition of Core Tablets

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Losartan Potassium	100	100	100	100	100	100	100	100	100
Sodium Chloride	50	100	150	-	-	-	-	-	-
Mannitol	-	-	-	50	100	150	-	-	-
Fructose	-	-	-	-	-	-	50	100	150
Avicel PH 101	176	126	76	176	126	76	176	126	76
PVP K30	17	17	17	17	17	17	17	17	17
Magnesium stearate	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Talc	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Total weight (mg)	350	350	350	350	350	350	350	350	350

Table 2: Composition of Coating Solution

Ingredients	C1	C2
Cellulose acetate	3 g	3 g
PEG 400	20% w/w	-
PEG 6000	-	20% w/w
Dibutyl pthalate	10% w/w	10% w/w
Weight gain	4%	4%
Coating Solvent: (Acetone: Isopropyl alcohol) in ratio of 4:1		

Evaluation of Tablets [18-20]

Hardness: The tablet hardness is defined as the force required break a tablet in a diametric compression test. To perform this test, a tablet was placed between two anvils, force is applied to the anvils & the crushing strength that just caused the tablet to break was recorded. The hardness was measured using Monsanto hardness tester. It is expressed in kg/cm^2.

Friability Test: The friability of the tablets was determined using Roche friabilator. It is expressed in percentage (%). Approximately 4 g (W_o) of dedusted tablets were subjected to 100 free falls of 6 inches in a rotating drum and were then reweighed (W). The friability is given by

$$F = 100 \times (1 - W_o/W)$$

Weight Variation Test: Twenty tablets were weighed individually, average weight was calculated & individual tablet weights were compared to the average weight. The tablets met the USP test if no more than 2 tablets are outside the percentage limit & if no tablet differs by more than two times the percentage limit.

Drug Content: 10 tablets were randomly selected and average weight was calculated and powdered in a glass mortar. Powder equivalent to 100 mg of drug was weighed and dissolved in 100 ml of distilled water, filtered and drug content analyzed spectrophotometrically at 250 nm wavelength.

Thickness: The thicknesses of ten tablets were measured using vernier calipers.

In Vitro Dissolution Studies: Dissolution test was performed using a USP type-2 paddle apparatus at 37 ± 0.5° C in 900 ml of 1.2 pH buffer with a speed of 50 rpm. After 2 hrs of release, pH 1.2 buffer medium changed to pH 6.8 phosphate buffer for next 10 hrs. Samples were withdrawn at predetermined time intervals and drug release was measured using a UV spectrophotometer at a 250 nm wavelength.

RESULTS & DISCUSSION:

Solubility Studies

Table 3: Solubility Studies of Losartan Potasssium

Solubility	Results
In Distilled water	96.89 mg/ml
In 0.1 N HCl	4.60 mg/ml
In 6.8 pH Buffer	94.44 mg/ml

Evaluation of Controlled Porosity Osmotic Tablets of Losartan Potassium:

Table 4: Pre Compression parameters of Losartan Potassium mixture

Formulation Code	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Carr Index %	Hausner's Ratio	Angle of Repose (θ)
F1	0.50±0.04	0.66±0.03	24.24±0.13	1.32±0.02	32.21±1.13
F2	0.49±0.09	0.64±0.04	23.43±0.02	1.30±0.01	32.15±1.23
F3	0.45±0.03	0.60±0.06	25.11±0.11	1.33±0.04	33.27±1.09
F4	0.54±0.01	0.70±0.05	22.85±0.04	1.29±0.01	34.45±1.04
F5	0.42±0.08	0.58±0.03	27.58±0.15	1.38±0.04	31.22±1.30
F6	0.46±0.06	0.62±0.04	25.80±0.07	1.34±0.03	32.67±1.19
F7	0.47±0.04	0.61±0.02	22.95±0.12	1.29±0.02	33.80±1.05
F8	0.48±0.02	0.65±0.03	26.15±0.09	1.35±0.02	30.10±1.35
F9	0.46±0.03	0.59±0.03	22.03±0.03	1.28±0.01	31.89±1.14

Table 5: Post-Compression Parameters of Core Tablets

Formulation Code	Wt. Variation n=20(±SD) (mg)	% Friability n=6	Hardness n=3(±SD) (kg/cm^2)	Drug Content n=10(±SD) (%)	Thickness n=3(±SD) (mm)
F1	349.1±2.33	0.59	5.1±0.065	99.59±0.23	3.91±0.024
F2	350.2±1.10	0.62	5.4±0.067	100.45±0.62	3.99±0.023
F3	349.8±2.22	0.51	5.2±0.070	98.54±0.79	3.93±0.035
F4	350.4±1.43	0.40	5.1±0.069	97.69±0.14	4.09±0.045
F5	349.5±1.31	0.48	5.2±0.070	98.37±0.97	3.94±0.065
F6	347.6±3.32	0.55	5.5±0.065	97.54±0.34	3.97±0.052
F7	351.8±2.05	0.37	5.4±0.071	101.45±0.67	3.95±0.054
F8	350.5±0.45	0.31	5.3±0.069	99.56±0.56	4.11±0.019
F9	348.9±2.12	0.44	5.2±0.068	100.43±0.29	4.19±0.025

Table 6: Physicochemical Parameters of Coated Tablets

Formulation Code	Thickness n=10(±SD) (mm)	Wt. Variation n=20(±SD) (mg)	% Weight Gain n=10(±SD)
F1C1	4.01±0.073	363.7±0.33	4.17±0.010
F1C2	4.03±0.065	363.2±0.23	4.02±0.014
F2C1	4.07±0.085	365.3±0.17	4.31±0.021
F2C2	4.09±0.099	365.3±0.10	4.31±0.032
F3C1	4.04±0.029	364.7±0.22	4.25±0.012
F3C2	4.02±0.035	365.2±0.25	4.40±0.017
F4C1	4.16±0.047	364.6±0.43	4.05±0.026
F4C2	4.17±0.050	365.5±0.46	4.03±0.035
F5C1	4.05±0.066	364.7±0.31	4.34±0.011
F5C2	4.06±0.070	364.1±0.33	4.17±0.025
F6C1	4.06±0.041	362.3±0.32	4.20±0.013
F6C2	4.05±0.046	361.8±0.35	4.05±0.032
F7C1	4.03±0.055	365.8±0.05	4.01±0.029
F7C2	4.02±0.057	366.5±0.09	4.20±0.018
F8C1	4.22±0.053	365.3±0.45	4.37±0.022
F8C2	4.25±0.048	365.3±0.47	4.36±0.031
F9C1	4.29±0.021	364.1±0.12	4.34±0.009
F9C2	4.31±0.029	363.3±0.16	4.11±0.013

***In vitro* Drug Release Study:**

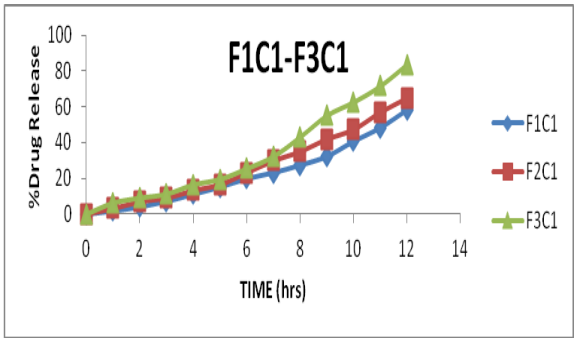

Fig 1: *In vitro* Drug Release of F1C1-F3C1

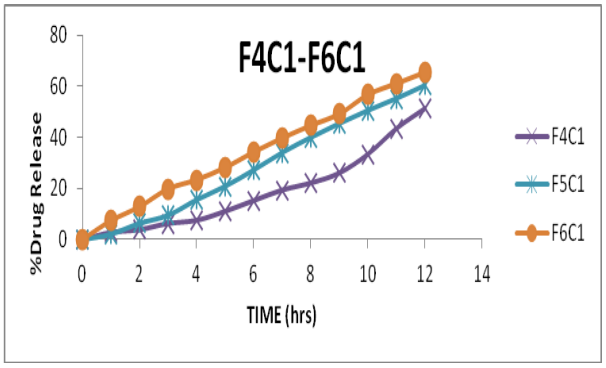

Fig 2: *In vitro* Drug Release of F4C1-F6C1

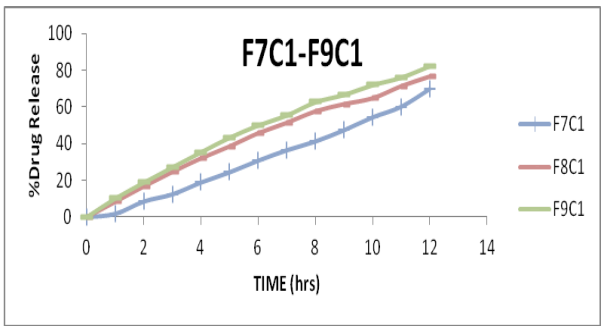

Fig 3: *In vitro* Drug Release of F7C1-F9C1

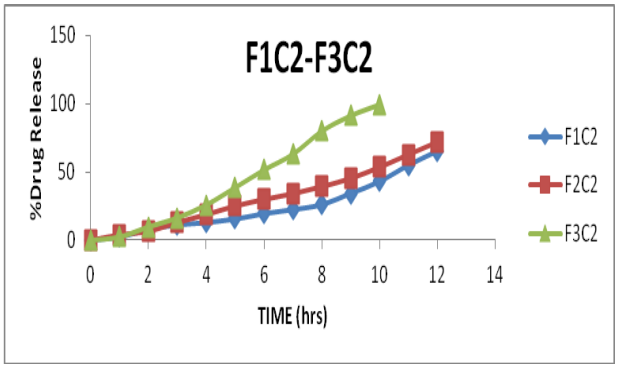

Fig 4: *In vitro* Drug Release of F1C2-F3C2

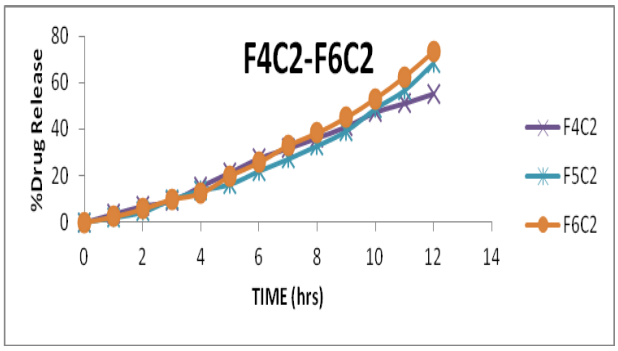

Fig 5: *In vitro* Drug Release of F4C2-F6C2

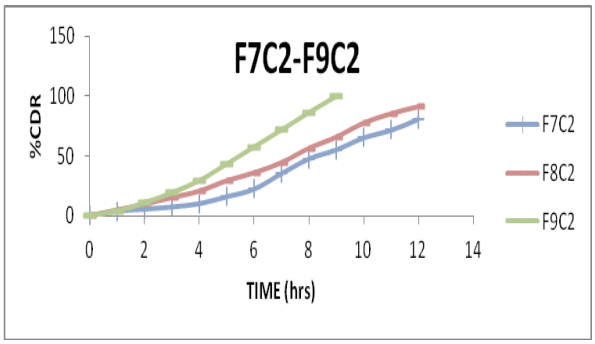

Fig 6: *In vitro* Drug Release of F7C2-F9C2

SUMMARY & CONCLUSION:

The solubility of Losartan Potassium was found to be maximum in distilled water an pH 6.8 buffer. Directly compressible core tablets showed acceptable physical properties like hardness, friability, weight variation test. The core tablets were coated by coating agent cellulose acetate with PEG400 and PEG6000 as water soluble pore former and dibutyl pthalate as plasticizer. The drug release of formulations coated with coating solution 1 were found to be between 51.12 % to 83.81 % and formulations coated with coating solution 2 were found to be between 55.41 % to 99.45 % . The batch F8C2 containing Fructose as an osmogen and 20 % PEG 6000 as a pore forming agent showed the 91.25 % drug release for 12 hrs.

REFERENCES:

1.Leon L., Herbert LA., Joseph KL: The theory and practice of industrial pharmacy. Varghese publishing house, Second edition.
2.John C., Morten C: The Science of Dosage Form Design Aulton: Modified release peroral dosage forms. Churchill Livingstone.

3.Shah N., Patel N., Patel KR., Patel D., A review on osmotically controlled oral drug delivery systems, J. Pharm. Sci. Bio. Res. 2012; 2:5:230-237.
4.Thummar A., Kalyanwat R., Tiwari A., Shrivastav B., Kyada C., An overview on osmotic controlled drug delivery system, Int. J. Pharm. Res. Sch. 2013; 2:2: 209-225.
5.Babu A., Rao MP., Ratna VJ., Controlled-porosity osmotic pump tablets-an overview, J. Pharm. Res. Health Care 2010; 2:1:114-126.
6.Keraliya RA., Patel C., Patel P., Keraliya V., Soni TG., Patel RC., Patel MM., Osmotic drug delivery system as a part of modified release dosage form, Int. Sch. Res. Net. 2012; 2012.
7.Singh K., Walia MK., Agarwal G., Harikumar SL., Osmotic pump drug delivery system: a noval approach, J. Drug. Del. Thera. 2013; 3:5:156-162.
8.Reddy KR., Srinivas M., Srinivas R., Once-daily sustained-release matrix tablets of nicorandil: formulation and in vitro evaluation, AAPS Pharm. Sci. Tech. 2003; 4:4:1-9.
9.Khan ZA., Tripathi R., Mishra B., Floating elementary osmotic pump tablet (FEOPT) for controlled delivery of diethylcarbamazine citrate: a water-soluble drug, AAPS Pharm. Sci. Tech. 2011; 12:4:1312-1323.
10.Sharma F., Jain H., Kanzariya V., Upadhyay U., Formulation and evaluation of controlled release osmotic tablet of metoprolol succinate, Asian. J. Pharm. Clin. Res. 2014: 7:3:38-43.
11.Kapoor D., Chauhan CS., Gupta AK., Formulation and evaluation of controlled porosity osmotic pump of valsartan, Int. J. Pharm. Bio. Arc. 2011; 2:3:967-972.
12.Shah N., Patel KR., Design and development of osmotic drug delivery system for anti-hypertensive agent, Int. J. Pharm. Res. Sch. 2013; 2:2:40-46.
13.Ning M., Zhou Y., Chen G., Mei X., Preparation and in vitro /in vivo evaluation of vinpocetine elementary osmotic pump system, Adv. Pharmacol. Sci. 2011; 2011.
14.Khan ZA., Tripathi R., Mishra B., Design and evaluation of enteric coated microporous osmotic pump tablet (ECMOPT) of quetiapine fumarate for the treatment of psychosis, Acta. Poloniae. Pharm. Drug. Res. 2012; 69:6:1125-1136.
15.Verma S., Saini S., Rawat A., Kaul M., Formulation, evaluation and optimization of osmotically controlled colon targeted drug delivery system, J. Pharm. Sci. Res. 2011; 3:9:1472-1485.
16.Emara HL., Taha FN., Badr MR., Mursi MN., Development of an osmotic pump system for controlled delivery of Diclofenac Sodium. Drug Disc. Thera. 2012; 6:5:269-277.
17.Elbary A., Tadros M., Alaa-Eldin A., Development and in vitro/in vivo evaluation of etodolac controlled porosity osmotic pump tablets, AAPS Pharm. Sci. Tech. 2011; 12:2: 485-494.
18.Poptani SD., Gohel MC., Parikh RK., Patel VP., Preparation and evaluation of osmotic controlled drug delivery system of metoprolol tartarate, Int. Bulletin Drug Res.; 1:1:84-93.
19.Samal HB., Sreenivas SA., Dey S., Sharma H., Formulation and evalution of sustained release zidovudine matrix tablets, Int. J. Pharm. Pharm. Sci. 2011; 3:2:32-41.
20.Patel H., Patel U., Kadikar H., Bhimani B., Daslaniya D., Patel G., Formulation and evaluation of controlled porosity osmotic pump tablets of glimepiride, Int. J. Drug. Del. 2012; 4:1:113-124.