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FORMULATION AND EVALUTION OF CONTROLLED POROSITY OSMOTIC DRUG DELIVERY SYSTEM OF METOPROLOL SUCCINATE

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ABSTRACT

The aim of the current study was to develop a controlled porous osmotic pump (CPOP) drug delivery system of metoprolol succinate. The osmotic system utilizes the principle of osmotic pressure, as an energy source for the delivery of drugs. Metoprolol succinate was chosen as a model drug to develop this delivery system because, its plasma half life ranges from 3-4 hrs, its dose is 47.5 mg (equivalent to 50 mg of metoprolol tartrate) and it is required to administer 2-3 times per day. First, an elementary osmotic pump with delivery orifice (0.4 mm) containing drug and osmogens (lactose and fructose) was developed to select suitable osmogen for the development of CPOP drug delivery system. Core tablets containing drug with different osmogens of different ratios were prepared and coated with cellulose acetate (4% w/w) containing diethtylphthalate used as plasticizer. Further, 0.4 mm delivery orifice was drilled on one side of the tablet. From *in vitro* release studies of this elementary osmotic pump, the formulation containing suitable osmogen was selected for further characterization. The selected formulation was then coated with cellulose acetate containing different concentrations of pore-forming polymers (10% w/w and 20% w/w) (PEG 400 and dibutylphthalate DBP) in the coating membrane. Release studies of the CPOP showed that the coating containing hydrophilic pore forming agents controlled the drug release in a better manner than the hydrophobic pore forming agents. All the formulation follows zero order kinetics and Higuchi equation ensures the drug release follows diffusion mechanism. The IR spectral studies showed no interaction between drug and osmogens. The short term stability studies showed no appreciable changes in drug content.

Key words: Osmotic drug delivery system, Metoprolol succinate, Osmogen, Semi-permeable membrane, Pores forming agent.

INTRODUCTION

In the recent years, pharmaceutical research has led to the development of several novel drug delivery systems and the main reason for this paradigm shift is relatively low

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development cost and time required for introducing a novel drug delivery systems as compared to a new chemical entity[1]. Among the various novel drug delivery system available in the market, per oral controlled release system hold the major market share because of their obvious advantages of ease in administration and better patient compliance[2].

Conventional drug delivery systems have little control over their drug release and almost no control over the effective concentration at the target site[3]. This kind of dosing pattern may result in constantly changing, unpredictable plasma concentration[4.] Controlled drug delivery system should be primarily deemed to achieve more predictable and increased bioavailability[5]. Drug can be delivered in a controlled pattern over a long period of time by the process of osmosis. Drug delivered from this system is not influenced by the different physiological factors within the gut lumen and the release characteristics can be predicted easily from the known properties of the drug and the dosage form. Osmotic devices are the most promising strategy for controlled drug delivery. They are the most reliable controlled drug delivery systems and could be employed as the oral drug delivery has been popular as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs[6].

The Elementary osmotic Pump (EOP) consists of drug core, containing osmogen, surrounded by a semi-permeable membrane with a delivery orifice on one side. In operation, the drug osmotic core acts by imbibing water from the surrounding medium via the semi-permeable membrane, dissolving the drug and the osmogen and delivering the drug with constant rate under the effect of constant osmotic pressure generated inside the core[7].

Recently, osmotic tablets have been developed in which the delivery orifice is formed by the incorporation of a leachable component in the contact with the aqueous environment, water diffuses into the core through the micro porous membrane leaving behind the pores through which the drug solution is pumped out. The drug release rate from these types of system is dependent on the coating thickness, level of leachable components in the coating, solubility of the drug in the tablet core, and osmotic pressure difference across the membrane. Metoprolol succinate is a β_1–selective adrenergic blocking agent and widely used for the treatment for hypertension, angina pectoris and arrhythmias. When administered orally, frequent dosing is needed due to short plasma half life of 3-4 hrs. When metoprolol succinate conventional tablets are administered with food rather than an empty stomach, peak plasma concentration is higher and the extent of absorption of the drug is increased. The maintenance of a constant plasma level of cardiovascular drug is important in ensuring the desired therapeutic responses. Multiple doses are needed to maintain a constant plasma concentration for a good therapeutic response, improved patient compliance and reduced to minimum side effects.

Hence, the present work was aimed to design, develop and evaluate the controlled porous osmotic drug delivery system of metoprolol succinate. The tablets were coated with cellulose acetate as the semi-permeable membrane containing different channeling agents viz PEG400, DBP.

EXPERIMENTAL

Materials and methods

Metoprolol succinate was obtained as a gift sample from Madras Pharmaceuticals Chennai, India. Dicalcium phosphate (SD Fine chemicals, Mumbai) and polyvinyl pyrrolidone (PVP K30) (SD Fine chemicals Mumbai), fructose (CDH, Mumbai), lactose (CDH, Mumbai) and poly ethylene glycol 400 (PEG400) (CDH, Mumbai), dibutylpthalate (DBP) (Loba chemicals), purified talc (Loba chemicals) and magnesium stearate (Loba chemicals) were purchased locally. All the chemicals used were of analytical grade.

Preparation of core tablets[8]

The core tablets of osmotic pump tablets were prepared as per the formula shown in the Table 1. Direct compression method was used to prepare the core tablets. An accurately weighed quantity of each ingredient was passed through sieve No. 60 and blended homogeneously through geometric dilution. The powder mixture was then passed through sieve No. 20 and lubricated with talc (1% w/w) and magnesium stearate (1% w/w). The homogenous blend was then compressed into 250 mg, 8 mm biconvex tablets in the single punch tablet machine (Cadmach, Ahmedabad).

Table 1: Formulation containing various concentrations of osmotic agent

Ingredients	Quantity/Tablet (mg)							
	Formulation code							
	F1	F2	F3	F4	F5	F6	F7	F8
Metoprolol succinate 47.5 mg (Equivalent to metoprolol tartrate 50 mg)	47.5	47.5	47.5	47.5	47.5	47.5	47.5	47.5
Lactose	50.0	37.5	25.0	18.5	12.5	6.5	0	0
Fructose	0	12.5	25.0	31.5	37.5	43.5	50.0	0
Dicalcium phosphate	141.0	141.0	141.0	141.0	141.0	141.0	141.0	191.0

Cont…

Ingredients	Quantity/Tablet (mg)							
	Formulation code							
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
PVP K30	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0
Magnesium stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Total	**247.5**	**247.5**	**247.5**	**247.5**	**247.5**	**247.5**	**247.5**	**247.5**

Evaluation of formulations

The prepared granules were evaluated for their flow properties like, compressibility index, angle of repose etc. and the prepared tablets were tested for hardness, thickness, friability, weight variation and drug content. The results are shown in Table 2.

Table 2: Evaluation of uncoated core tablets of metoprolol succinate

Formulation parameters (Average values)	Formulation code							
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
Loose bulk density * (g/mL)	0.4431 ± 0.0076	0.4549 ± 0.0081	0.4733 ± 0.0004	0.5433 ± 0.0113	0.5746 ± 0.0012	0.5166 ± 0.0103	0.5158 ± 0.0010	0.4503 ± 0.0008
Tapped bulk density * (g/mL)	0.5253 ± 0.103	0.5354 ± 0.0113	0.5581 ± 0.0116	0.6383 ± 0.0000	0.6569 ± 0.0168	0.6239 ± 0.0149	0.591 ± 0.0013	0.5298 ± 0.0111
Compressibility index* (%)	15.65 ± 1.57	15.01 ± 0.268	15.20 ± 0.268	14.89 ± 1.772	12.48 ± 2.107	12.86 ± 0.256	12.86 ± 0.259	15.01 ± 0.268
Angle of repose* (θ)	27.87 ± 0.99	29.82 ± 0.4716	26.63 ± 0.9029	29.93 ± 0.2875	29.23 ± 0.942	29.45 ± 0.4665	29.09 ± 0.3064	29.30 ± 0.159
Hardness* (Kg/cm^2)	5.2 ± 0.464	5.3 ± 0.471	6 ± 0.816	5.3 ± 0.471	5.3 ± 0.471	5.3 ± 0.471	5.3 ± 0.471	5.1 ± 0.000
Thickness* (mm)	4.3 ± 0.471	4.3 ± 0.471	4.5 ± 0.081	4.3 ± 0.081	4.4 ± 0.081	4.4 ± 0.081	4.4 ± 0.041	4.4 ± 0.047

Cont…

Formulation parameters (Average values)	Formulation code							
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
Diameter* (mm)	8.0 ± 0.047	8.0 ± 0.000	8.1 ± 0.047	8.0 ± 0.000	8.1 ± 0.047	8.0 ± 0.000	8.0 ± 0.000	8.0 ± 0.047
Friability* (%)	0.693	0.628	0.630	0.669	0.646	0.665	0.647	0.601
Drug content*	99.85 ± 0.4006	100.1 ± 0.4006	99.42 ± 0.2027	99.56 ± 0.1970	99.71 ± 0.5318	99.28 ± 0.2027	99.71 ± 0.5318	99.71 ± 0.5318
Weight variation* (mg)	237.81 ± 0.056	238.67 ± 0.047	245.9 ± 0.081	238.88 ± 0.124	239.83 ± 0.169	240.61 ± 0.163	239.21 ± 0.081	241.03 ± 0.124

*n = 3

Preparation of elementary osmotic pump tablet (EOP)[9]

EOP tablets were prepared by coating the core tablets with cellulose acetate (4% w/w) in acetone and IPA (80 : 20) by pan coating method. Diethyl phthalate (30% w/w) was used as plasticizer. Then, delivery orifice of 0.4 mm was drilled on one side of the tablet surface manually. Later, from the release studies, suitable formulation was selected for the preparation of controlled porosity osmotic pump tablets.

Preparation of controlled porosity osmotic pump (CPOP) tablets[10]

The selected formulation is coated with coating solution containing pore forming substances and the components are shown in Table 3. The tablets were coated with cellulose

Table 3: Various pore formers used in coatings on formulation

Ingredients	Coating code				
	Quantity/Tablet (mg)				
	C1	**C2**	**C3**	**C4**	**C5**
Cellulose acetate (% w/v)	4	4	4	4	4
PEG 400 (% w/w)	10	20	-	-	-
Dibutyl phthalate (% w/w)	-	-	10	20	-

acetate (4% w/v) in acetone and IPA (80 : 20) along with suitable pore forming agents i.e PEG400, DBP. Talc and titanium dioxide were used as anti-adherent and opacifier. The

tablets were coated by pan coating method having pan diameter of about 30 cm at a rotational speed of 25 rpm, and the coating solution was sprayed using automizer spray gun at a rate of 5 mL/min. The tablets were coated to a target thickness of about 0.2 mm.

Estimation of drug content

Metoprolol succinate content of the tablet was estimated by an UV-Visible spectrophotometer based on the measurement of absorbance at 222 nm in phosphate buffer pH 7.4. No interference from the excipients used, was observed.

In vitro release studies of osmotic pump tablets[11]

In vitro release studies of EOP tablets was carried out in the USP XXI Type II (paddle) dissolution apparatus (Disso 2000 Lab India) at 37 ± 1°C and 100 ± 1 rpm in 900 mL of dissolution medium for about 10 hrs. The dissolution medium was simulated intestinal fluid (SIF pH 7.4 buffer). Samples (5 mL) were withdrawn periodically and the same volume was replaced to maintain the volume of dissolution medium at 900 mL. The drug release was estimated by measuring the absorbance of the samples at 222 nm using UV-Visible spectrophotometer. The release rates are shown in Fig. 1.

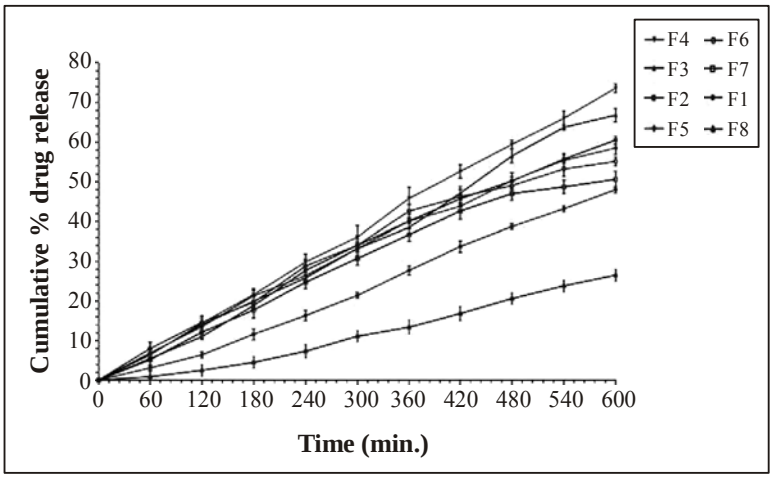


Fig. 1: Comparison of *In vitro* release profile of metoprolol succinate & various concentration of osmogens

Evaluation of CPOP tablets

The evaluation parameters like general appearance, hardness, thickness, diameter, friability, weight variation and analysis of drug content were performed for the CPOP and the results are shown in Table 4.

Table 4: Evaluation of coated CPOP tablets

Formulation parameters (Average values)	Formulation coated code				
	C1	**C2**	**C3**	**C4**	**C5**
Hardness* (kg/cm^2)	6.5 ± 0.461	6.3 ± 0.373	6.1 ± 0.470	6.1 ± 0.081	6.2 ± 0.912
Diameter* (mm)	8.0 ± 0.047	8.1 ± 0.000	8.0 ± 0.047	8.0 ± 0.047	8.0 ± 0.047
Thickness* (mm)	4.5 ± 0.165	4.7 ± 0.124	4.6 ± 0.169	4.6 ± 0.081	4.5 ± 0.124
Weight variation* (mg)	242.56 ± 0.046	243.67 ± 0.091	244.62 ± 0.167	244.23 ± 0.124	245.90 ± 0.169
Drug content* (%)	99.86 ± 0.400	99.84 ± 0.197	99.83 ± 0.197	99.84 ± 0.202	99.84 ± 0.531
Friability* (%)	0.694	0.630	0.665	0.685	0.681

Drug release study of CPOP tablet

In vitro dissolution studies of CPOP metoprolol succinate tablets were performed in the USP XXI Type II (paddle) dissolution apparatus (Disso 2000 Lab India) at 37 ± 1°C and 100 ± 1 rpm in 900 mL of dissolution medium for about 12 hrs. The dissolution medium was simulated gastric fluid (pH 1.2) for first two hours and for the remaining ten hours; simulated intestinal fluid (pH 7.4) phosphate buffer was used as the dissolution medium. Aliquots of samples were withdrawn periodically to estimate the drug release at 222 nm in UV-Visible spectrophotometer (Shimadzu 1700, Japan). *In vitro* drug release characters are shown in Fig. 2.

Release kinetics of CPOP

Release data were fit into zero order, first order, Higuchi, Hixson Crowell and Peppas models to assess the drug release kinetics and the results are shown in Table 5.

FTIR studies[12]

FTIR (Shimadzu 8400S) studies are carried out for pure drug and other excipients to find out any interaction between drug and excipients.

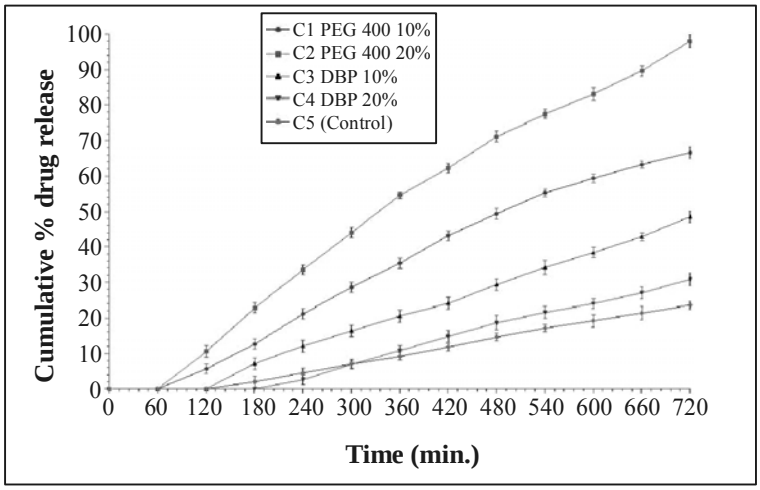


Fig. 2: Comparison of *in vitro* drug release profile of different pore forming agents

Table 5: Kinetics of *in vitro* drug release from different batches of coated tablets

Formulation	Regression co-efficient (R^2)									
	Zero order		First order		Higuchi		Hixson crowell		Korsemeyer peppas	
	R^2	K_0	R^2	K_1	R^2	K_H	R^2	K_{HC}	R^2	n
C1	0.9992	6.6378	0.9861	0.0316	0.9973	6.3448	0.9845	0.0428	0.9346	0.1294
C2	0.9931	8.7871	0.9867	0.0452	0.9841	8.7871	0.9739	0.0944	0.9656	0.1281
C3	0.9937	4.5129	0.9732	0.1137	0.9925	4.5129	0.9930	0.2403	0.9854	0.1448
C4	0.9824	3.1122	0.9715	0.1731	0.9641	3.1122	0.9512	0.3851	0.9471	0.1575
C5	0.9783	2.3154	0.9672	0.1285	0.9632	2.3154	0.9341	0.2857	0.9325	0.1327

Differential scanning calorimetry (DSC) study[14]

The differential scanning calorimetry (Perkin Elmer STA 6000) thermogram studies are carried out for pure drug and other excipients to find out any interaction between drug and excipients.

Scanning electron microscope (SEM) studies

Surface morphology of coating membrane was examined under Scanning Electron Microscope both; before and after dissolution of the osmotic tablets. The tablet (before

dissolution) was placed as such on specimen stub and examined under SEM Model HITACHI S-3000H, Japan. Similarly, the dried sample of osmotic tablets after dissolution was used as specimen for scanning the nature of the coating material and the results are shown in Fig. 5, Fig. 5(a), Fig. 6 and Fig. 6(a).

Stability studies[13]

Short term stability studies are carried out at 40°C ± 2°C/75% RH ± 5% as per modified ICH guidelines to find out any physico-chemical changes of CPOP formulations.

RESULTS AND DISCUSSION

Pre-formulation characters of EOP and CPOP tablets

The pre-formulation characters of both; EOP and CPOP tablets are shown in Table 2 and Table 4. The angle of repose valued between 26º63-29º93 and the percentage compressibility valued in the range of 12.86-15.65%. The bulk density and tapped density were in the range of 0.44-0.57 g/mL and 0.52-0.65 g/mL, respectively. These values indicated that the granules of all the formulations had good flow properties. The drug content of the granules was found in the range of 99.28% to 100.1% indicating the uniform distribution of drug in all the formulations (Table 3).

Post-compression parameters

The post-compression parameters, hardness, thickness, diameter and friability of all the tablet formulations were observed and were found in the range of 5.1-6.0 kg/cm^2, 4.5-4.7 mm, 8 mm, 0.630% - 0.694%, respectively.

The weight variation ranges from 242.56-250.81 mg and passed the I. P limits. The drug content of the tablet was found in the range of 99.28% to 100.2% explaining again the uniform distribution of the drugs in the coated tablets (Table 4).

In vitro release studies of elementary osmotic pump tablets

Effect of osmogens

The *in vitro* release profile of metoprolol succinate showing effects of different osmotic agents are shown in Fig. 1. From this, it has been observed that the formulation contain no osmogen (F8) released 26.5% of drug at the end of 10 hrs whereas the formulations containing osmogen release 48.0% (F1), 60.5% (F2), 66.8% (F3), 73.6% (F4), 58.5% (F5), 55.1% (F6) and 50.6% (F7) after 10 hrs. This clearly indicates that the presence of osmogens improve the drug release from the formulations. But, in this study, osmogens

have been used separately and in mixtures (in different ratio) while formulating the tablets, also, have an impact in controlling the drug release. From the release studies, it has been observed, that the formulation F4 contains the mixture of lactose and fructose (F4) (1 : 2) showed 73.6% of drug release in 10 hours whereas the formulation contains lactose (F1) showed 48.0% of drug release and the formulation contains fructose (F7) showed 50.6% of drug release at the end of the 10 hours dissolution study. Hence, it may be concluded that, the increase in the drug release may be due to the synergistic effect of mixture of osmogens present in the formulation than the formulation containing single osmogen. Since, the formulation F1 showed better controlled drug release (48.0% in 10 hrs), it has been considered and preferred for further development of CPOP tablets.

Drug release study of CPOP tablet

From the release studies of elementary osmotic pump tablets, the formulation F1 containing lactose as osmogen has been selected for the development of controlled porosity osmotic pump tablets.

These tablets are coated with coating solution (cellulose acetate 4% w/w), which contains different pore forming agents as per the composition shown in Table 3. Two types of pore forming agents PEG 400 (10% and 20%) (Hydrophilic) and DBP (10% and 20%) (Hydrophobic) were used to make the pores during dissolution process and they are helpful to release the drugs through leaching process. Also, a batch of tablets was coated with material without pore forming agents and the release was compared with other formulations containing pore forming agents. The tablets are coated by pan coating technique and they were easy to prepare. Further they were evaluated for post-compression parameters and the results are shown in the Table 4. All these parameters are within the acceptable limits, which confirms that the tablets had uniform distribution of drug and they were intact and had enough mechanical strength enable to withstand any type of physical disturbances. Further, there was no visible change in the thickness and the weight gain was about 2% w/w.

In vitro release studies of CPOP tablets were conducted for a period of 12 hrs and the results are shown in the Fig 2. The dissolution was conducted for in acid dissolution medium of pH 1.2 for first 2 hours and for the remaining 10 hours, the dissolution study was conducted at pH 7.4 (Phosphate buffer).

Effect of pore forming agents

From the results, it has been observed that the formulations were able to release 66.7% (C1), 98.0% (C2), 48.5% (C3), 30.8% (C4) and 23.6% (C5), respectively at the end of 12 hours dissolution study (Fig 2). Further, it has been noticed that the coated

formulations without pore forming agents released only 23.6% (C5) of drug whereas the other formulations containing pore forming agents released more amount of drug at the end of 12 hrs release study. This indicates that the pore forming agents have major role in releasing the drug from the formulations by leaching principle where the pore forming agents dissolve preferentially in the dissolution medium and makes pores to increase the permeability of membrane. This is further confirmed that the formulation C5 had the lag time of 3 hrs whereas the formulations have pore forming agents have less lag time of 1 hr (C1 and C2) and 2 hrd. (C3 and C4) to release the drug.

Furthermore, the formulations had 1 hour lag time contains PEG 400 as pore forming agent whereas the formulation had 2 hrs. lag time contains dibutyl phthalate (DBP) as pore forming agents. The difference in the lag time may be due to the differences in the solubility of pore forming agents in the dissolution medium. PEG 400 being hydrophilic gets easily dissolved in the dissolution medium and thus increases the permeability of coating membrane and hence, had less lag time. Since, DBP is hydrophobic, it may have less solubility in the dissolution medium to make the membrane less permeable, and so, it had lag time of 2 hours. Further, increase in the concentration of pore forming agents increases the drug release i.e., coating containing PEG 400 (20%) released 98% of after 12 hrs. and only 66.7% of drug release was achieved with PEG 400 (10%). The same results were observed with hydrophobic pore forming agents i.e., DBP. Both the formulations showed lag time before the drug release when compared to marketed controlled release tablets. But, CPOP containing PEG 400 showed lag time of 1 hour whereas CPOP containing DBP showed lag time of maximum of 4 hrs. Hence, it can be concluded that dibutyl phthalate acts as a barrier for permeation of dissolution medium and increases hydrophobic nature of coating membrane. As the concentration of dibutyl phthalate increases, hydrophobicity of the coating membrane also increases. This acts as a barrier for permeation of dissolution medium inside the tablet core. The results showed that the formulation C1 have good micro porous behaviors and sustained release profile.

FT-IR studies

FT-IR studies showed that there was no interaction between the drug and other excipients in the formulation. The results are shown in Fig. 3.

Differential scanning calorimetry (DSC) study

Fig. 7 depicts the DSC thermograms of metoprolol succinate and formulation. No changes in the endotherms were observed as the drug exhibited a sharp melting endotherm in the osmogen and coated formulation. From the thermograms, it was cleared that no

specific interactions between the drug and excipients used in present formulation (Perkin Elmer STA 6000 made in USA).

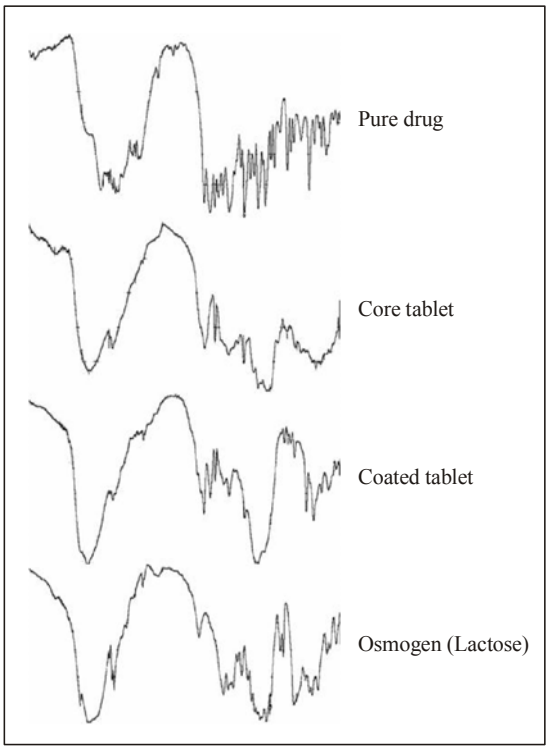


Fig. 3: FTIR studies

Scanning electron microscope studies[8]

To investigate the change in the membrane structure, surface of coated tablets (both before and after dissolution studies) was studied using scanning electron microscopy microphotographs [Fig. 5, 5(a) & 6, 6(a)]. The membrane structure of the coating before dissolution was smooth initially before coming into contact with aqueous environment and coats appeared without any defects [Fig. 5, 5(a)]. A porous structure was observed in the membrane after dissolution [Fig. 6, 6 (a)] may be due to leaching of water-soluble additive i.e. PEG 400 during dissolution through which drug release takes place.

Stability studies

The results of short term stability studies for the formulation (F1) showed no significant change in the physical appearance and drug content (99.28% -100.1%) after storing them at 40°C ± 2°C/75% RH ± 5% and hence, it may be concluded that the

formulation may have the stability during its shelf life period.

Comparison of marketed product

From the release studies, it has been observed that the formulated tablets showed similar release profile as that of the marketed tablet. It was further confirmed from the similarity factor (f_2) 55.37% and it is shown in the Fig. 4**.** Hence, it may be concluded that the release of drug was controlled by the pores formed due to the dissolution of pore forming agents in the surrounding medium.

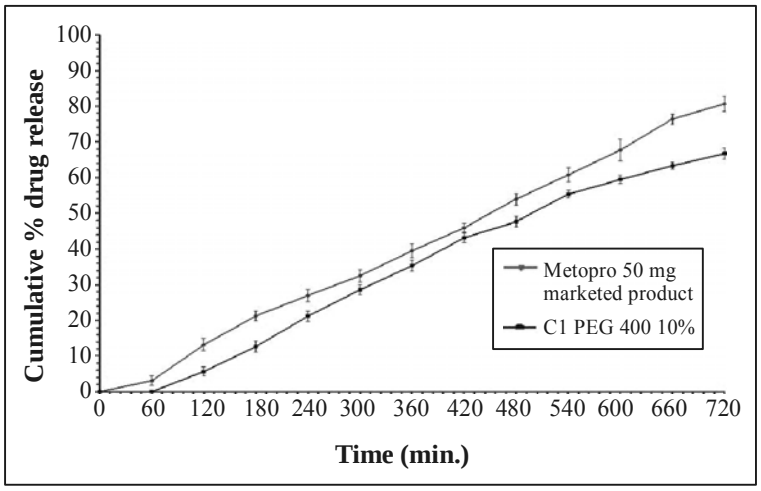


Fig. 4: Comparison of marketed product

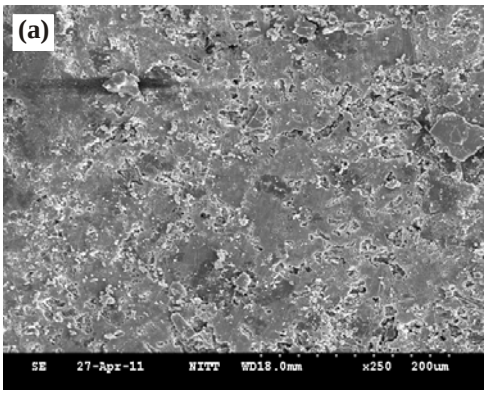


Fig. 5(a): SEM Microphotograph (at 500X magnification) of osmotic tablet before dissolution

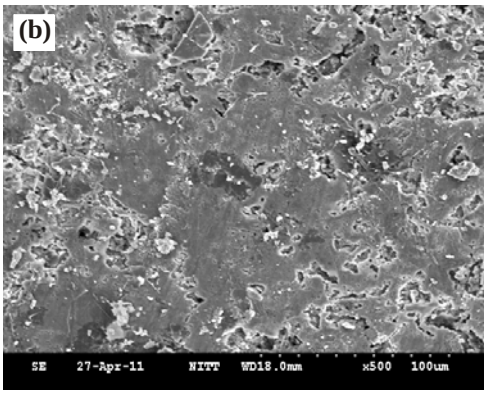


Fig. 5(b): SEM Microphotograph (at 250X magnification) of osmotic tablet before dissolution

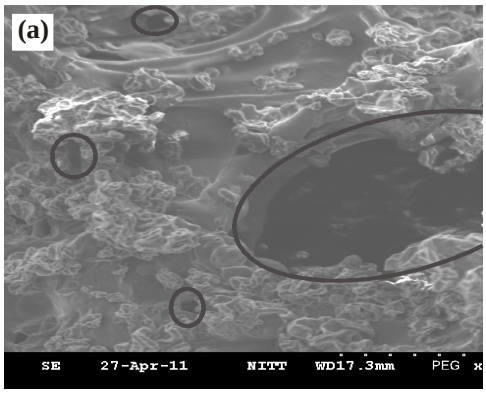


Fig. 6(a): SEM Microphotograph (at 500X magnification) of osmotic tablet after dissolution, showing formation of pores

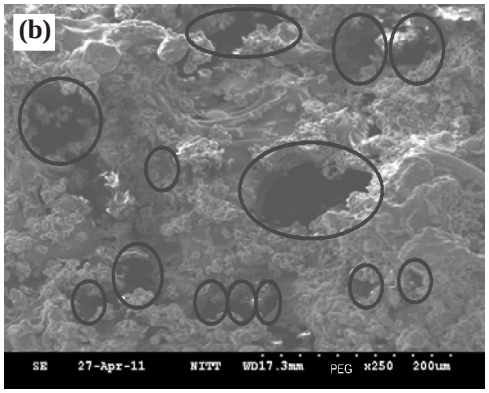
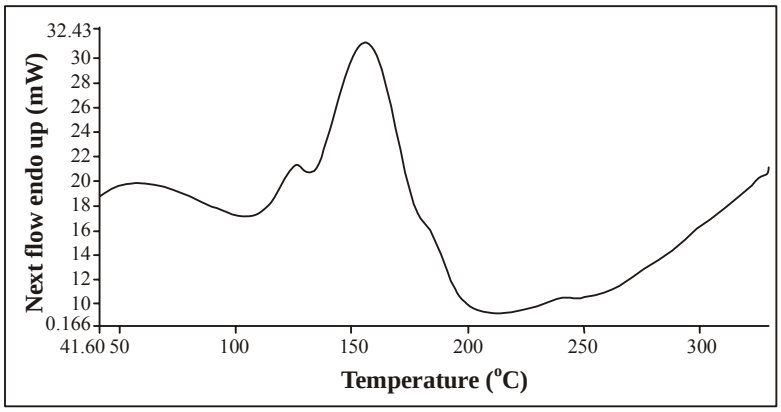
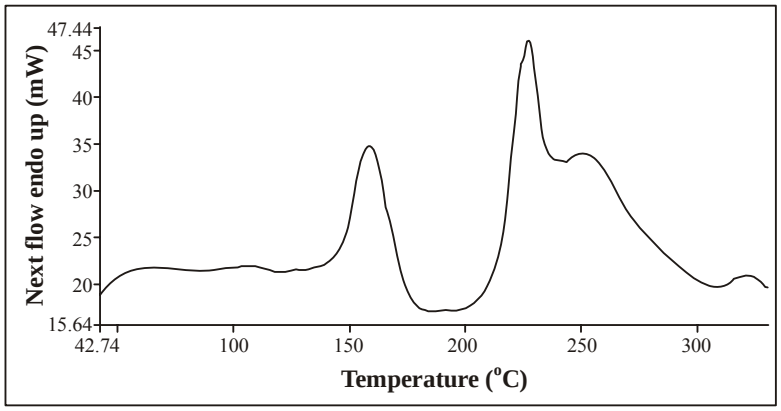


Fig. 6(b): SEM Microphotograph (at 250X magnification) of osmotic tablet after dissolution, showing formation of pores





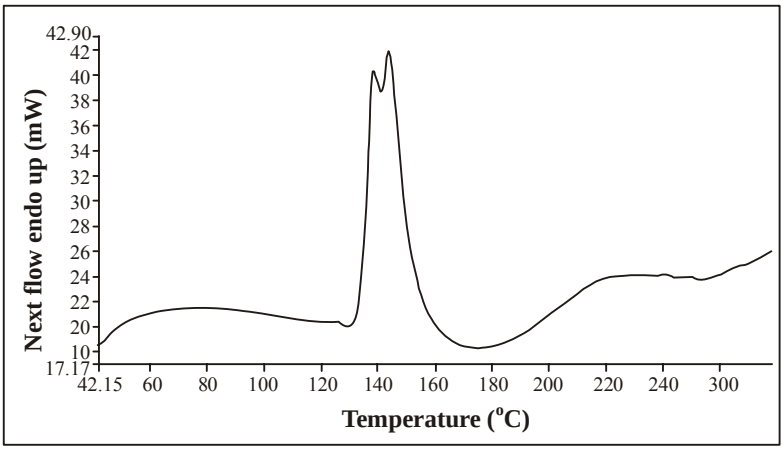


Fig. 7: DSC studies

Kinetics of drug release

Data for release kinetics reveals that the all the prepared tablets follow zero order kinetics and Higuchi as it had high correlation value for zero order kinetics equation and it is shown in the Table 5.

CONCLUSION

A osmotic pump containing controlled porosity drug delivery system was designed for controlled release of drug metoprolol succinate. It is evident from the results that the rate of drug release can be controlled through osmotic pressure of the core, level of pore forming agent and nature of pore forming agent with release to be fairly independent of pH and hydrodynamic condition of the body. The present study is to analyze the feasibility of considering metoprolol succinate in the form of porous osmotic drug delivery system to have better control in the drug release for prolonged period to improve the patient compliance. Further, this type of formulation may be administered safely for the treatment of anti-hypertension with improved therapeutic efficacy. Osmotically controlled oral delivery system can be used as once–a–day controlled release formulation; thus, improved patient adherence.

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