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FORMULATION AND EVALUATION OF CONTROLLED POROSITY OSMOTIC TABLET OF METOPROLOL SUCCINATE

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ABSTRACT

Objectives: Metoprolol Succinate is mainly used to treat hypertension. It has a short elimination half- life and rapidly absorbed in GIT. Conventional tablets of Metoprolol succinate require multiple dosing with resulting inconvenience to the hypertensive patient and the possibility of reduced patient compliance. **Experimental Work:** Core tablets for drug were prepared by direct compression technique using mannitol, fructose, KCl as osmogens and Avicel PH101 as direct compressible diluents. The prepared core tablets were coated by coating agent cellulose acetate (2%w/v) with PEG400 and PEG 6000as water soluble pore former and dibutyl-pthalate as plasticizer. The formulations were evaluated for their pre compression and post compression characterizations. **Results and discussion:** The present study confirmed that the drug release depends on the % weight gain of tablet and it is inversely proportional to membrane weight gain. The combination of two osmogens shows better drug release as compared to individual.

KEYWORDS: Metoprolol succinate, Hypertension, controlled porosity, Osmogen.

INTRODUCTION[1-10]

Oral controlled release systems continue to be the most popular amongst all the drug delivery systems because pharmaceutical agents can be delivered in a controlled pattern over a long period by osmotic pressure, there has been increasing interest in the development of osmotic devices over the past 2 decades. Drug release from oral controlled release dosage forms may be affected by pH, GI motility and presence of food in the GI tract**.** Metoprolol succinate is very high soluble drug, so complete drug release obtained very fast. It is difficult to formulate osmotic tablet of Metoprolol succinate which gives drug release up to 24 hr at zero order. But drug release from osmotic drug delivery system is not affected by physiological factors Metoprolol succinate {2-hydroxy-3-[4-(2-methoxyethyl) phenoxy] propyl} (propan-2-yl) amine Metoprolol is a cardioselective β1-adrenergic blocking agentused for acute myocardial infarction and mild to moderate hypertension. Metoprolol Succinate is a white crystalline solid with a molecular weight of 267.363. Metoprolol Succinate is having high solubility and high permeability (BCS Class-I). Metoprolol succinate has short elimination half life (3-7 hours) and a potent drug. Drugs utilized for long duration of action in hypertension. The rationale for this approach is that the presence of water in gastrointestinal tract is relatively constant, at least in terms of the amount required for activation and controlling osmotically base technologies.

MATERIALS AND METHODS

Metoprolol Succinate was provided as a gift sample from (Ranbaxy Lab Ltd, Gurgaon, India); Potassium chloride and Fructose as a gift sample from (SD Fine Chemicals, Mumbai, India); Talc and Magnesium stearate as a gift sample from (Elegant Drugs Pvt Ltd) Following chemicals were purchased from commercial sources and used as such: Poly Ethylene Glycol 400 and Poly Ethylene Glycol 6000 from (Ranbaxy Lab Ltd, Gurgaon, India); Avicel PH101, Cellulose Acetate, Dibutyl pthalate (Thomas Baker Chemicals Pvt Ltd, Mumbai, India) All other reagents and solvents used were of analytical grade.

Preparation of Core tablets[11]

The core osmotic tablets were prepared by direct compression technique and preparation of osmotically controlled tablets, drug was mixed with osmotic agents in different concentration and Avicel PH 101 were sifted together through 40# sieve and blended for 15 minutes. The blend was again passed through 40 # sieve and lubricated with Talc and Magnesium Stearate (previously Sifted through 60 # sieve) for 5 minute. The blend was compressed into tablets using multi station rotary tablet punching machine (Krishna Engineering, India) of keeping round standard concave punch of 9.5 mm. The compositions of different core tablets are shown in Table no. 1.

Table 1: Formulation of Core Tablets of Metoprolol Succinate

Ingredients (mg)	F1	F2	F3	F4	F5
Metoprolol Succinate	100	100	100	100	100
Mannitol	125	-	-	-	75
Fructose	-	125	-	50	-
Potassium Chloride	-	-	125	75	50
Avicel PH 101	170	170	170	170	170
Mg. Stearate	3	3	3	3	3
Talc	2	2	2	2	2
Total Weight (mg)	**400**	**400**	**400**	**400**	**400**

Preparation of Coating Solution

Coating process was started with rotation speed of 4 to 5 rpm. The spray rate and atomizing air pressure were 4 to 6 ml/min and 17.5 kg/cm^2, respectively Inlet and outlet air temperatures were 60°C±10°C and 45°C, respectively. Coated tablets were dried at 50°C for 12 hours and the percentage weight gain of the coating membrane was measured. The detailed compositions of coating solution are shown in Table no. 2.

Table 2: Composition of Coating Solution.

Ingredients (mg)	C1	C2	C3	C4
Cellulose Acetate (gm)	2	2	2	2
PEG 400 (% w/w)	20	20	-	-
PEG 6000 (% w/w)	-	-	20	20
Dibutyl Pthalate % (w/w)	10	10	10	10
Weight gain	4%	8%	4%	8%
Coating Solvent : (Acetone : Methanol) in 9:1				

Evaluation of Osmotic Tablets[12-19]

All the Metoprolol succinate osmotic tablets were evaluated for pre compression as well as their post compression parameters like flow behaviours, hardness, friability, thickness, drug content and weight variation.

***In Vitro* drug release studies[20-24]**

Dissolution of formulated osmotic tablets were carried out in USP type-II paddle apparatus (Veego, Mumbai, India) at 37 ± 0.5° C in 900 ml of 1.2 pH buffer with a speed of 100 rpm. After 2 hrs pH 1.2 buffer medium was replaced by pH6.8 phosphate buffer and dissolution was carried out for next 10 hrs. 5ml was withdrawn at 1 hour time intervals over a period of 12 hour and every time medium was replenished with fresh dissolution fluid to maintain sink condition. Samples were measured using a UV spectrophotometer at a wavelength of 274nm.

RESULTS

Pre Compression Parameters of Metoprolol Succinate Mixture

Metoprolol Succinate drug powder were evaluated for bulk density, tapped density, Carr's index, angle of repose, Hausner ratio as shown in Table no. 3.

Table 3: Pre Compression Parameters.

Formulation Code	Bulk Density(g/cm^3) (n=3)	Tapped Density(g/cm^3) (n=3)	Carr's Index (%) (n=3)	Hausner Ratio (n=3)	Angle of Repose (Θ) (n=3)
F1	0.47±0.04	0.54±0.02	12.96±1.02	1.14±0.06	25.17
F2	0.48±0.07	0.56±0.02	14.28±1.15	1.16±0.05	26.22
F3	0.45±0.08	0.59±0.04	23.72±1.25	1.31±0.03	27.78
F4	0.48±0.03	0.57±0.07	15.78±1.13	1.18±0.08	25.33
F5	0.46±0.05	0.56±0.05	17.85±1.19	1.21±0.09	25.23

Post compression parameters evaluation of Metoprolol succinate tablets

All prepared osmotic tablets were evaluated for weight variation and drug content, thickness, hardness and friability as shown in Table no. 4.

Table 4: Post Compression Parameters

Formulation Code	Wt. Variation n=20 (±SD)	% Friability	Hardness n=3 (±SD)	Thickness n=3 (±SD)	Drug Content n=10 (±SD)
F1C1	400±0.12	0.14	6.8±0.32	4.34±0.024	98.10±0.12
F2C1	400±0.16	0.23	7.0±0.18	4.76±0.023	97.89±0.19
F3C1	399±1.21	0.17	6.6±0.11	4.76±0.034	99.89±0.33
F4C1	398±1.09	0.12	6.5±0.16	4.57±0.023	99.12±0.21
F5C1	400±0.05	0.21	7.0±0.18	4.65±0.024	98.45±0.67
F1C2	399±1.31	0.16	6.9±0.12	4.76±0.021	98.23±0.46

F2C2	400±0.73	0.12	7.0±0.16	4.45±0.020	99.37±0.97
F3C2	400±1.23	0.17	7.0±0.17	4.46±0.034	98.67±0.54
F4C2	400±1.32	0.21	6.9±0.18	4.65±0.032	99.56±0.56
F5C2	401±1.32	0.18	6.9±0.32	4.72±0.025	99.56±0.56
F1C3	400±0.65	0.21	7.0±0.92	4.56±0.029	98.82±0.35
F2C3	400±0.87	0.20	6.8±0.32	4.76±0.018	98.82±0.35
F3C3	399±1.31	0.17	6.9±0.23	4.64±0.017	97.69±0.14
F4C3	400±1.43	0.16	6.9±0.65	4.86±0.019	99.78±0.72
F5C3	399±1.21	0.19	6.6±0.35	4.62±0.027	98.45±0.24
F1C4	400±0.98	0.18	6.8±0.45	4.58±0.035	99.56±0.58
F2C4	400±1.01	0.17	6.9±0.34	4.86±0.045	98.32±0.51
F3C4	399±1.07	0.19	7.0±0.76	4.63±0.023	98.67±0.48
F4C4	400±0.87	0.21	6.9±0.54	4.56±0.076	99.43±0.29
F5C4	400±0.54	0.20	7.0±0.46	4.69±0.065	99.59±0.23

***In Vitro* drug release study**

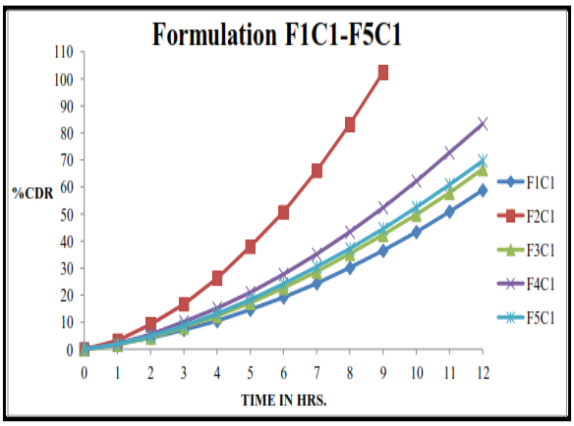

Fig: 1 Dissolution profile comparison of F1C1-F5C1

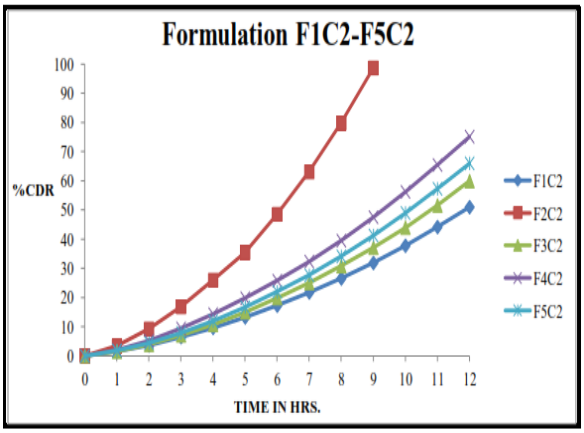

Fig 2 Dissolution Profile comparison of F1C2-F5C2

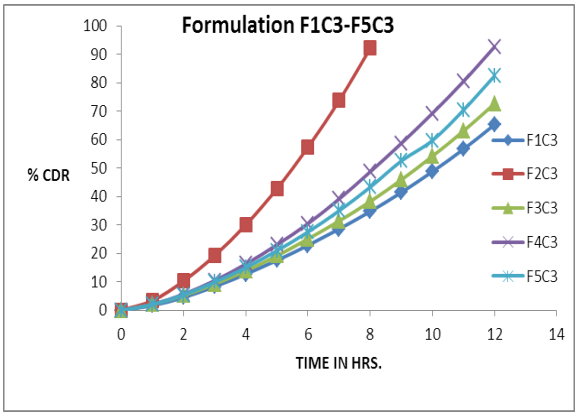

Fig 3 Dissolution Profile comparison of F1C3-F5C3

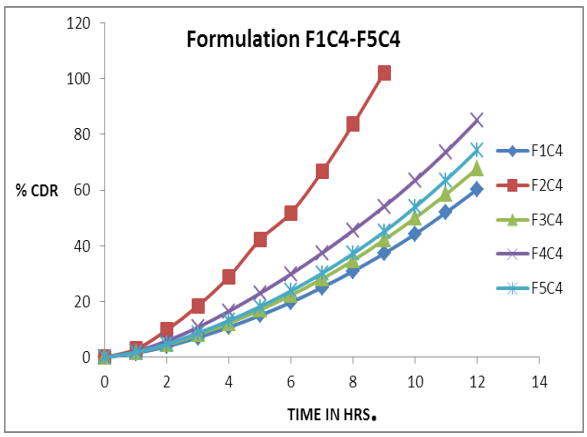

Fig 4 Dissolution Profile comparison of F1C4-F5C4

CONCLUSION

All the formulations show the acceptable pre compression and post compression parameters. Formulation F4C3 shows highest amount of drug release (92.65%) in dissolution media and releases the drug for longer period of time up to 12 hrs. From the evaluation study of coating solution, batch C-3 containing PEG 6000 had film lighter in weight than PEG 400 and also showed a better drug release in 12 hrs than any other batches. From dissolution study of different batches, we can conclude that increasing in % weight gain % drug release was decreased.

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