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Research Article

DESIGN AND DEVELOPMENT OF METOPROLOL SUCCINATE PULSINCAP TECHNOLOGY CHRONOTHEREPEUTIC SYSTEM USING NATURAL GUM AS A MATERIAL FOR COLON TARGETING

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ABSTRACT

The aim of the present study was to develop modified pulsincap drug delivery system containing Metaprolol Succinate for colon specific drug delivery in the management of Angina Pectoris. The IR spectral studies of"Metoprolol Succinate" and different grades of Gum Kondagogu proved that they were compatible. Upon Formaldehyde treatment the size "2" capsule bodies showed a significant decrease in the length and diameter from 18.3 mm to 17.5mm and 6.3mm to 6.1 mm respectively. The untreated caps disintegrated within 15 minutes in the buffer medias such as 1.2, 6.8, 7.4 where as the treated bodies remained intact for about 24 hours. The coating thickness of the capsules varied from 0.0052 mm to 0.0057 mm between the formulations. The formulations containing Gum Kondagogu as a natural polymeric plug-in material showed better colonic release profiles of 101.72% and 99.98% for grade-III (70mg and 75 mg) at 6hrs and 6.5 hrs respectively observed as per the lag time equated for the drug to reach colon when compared to that of gum Kondagogu grade-II where much of the drug released prior reaching to simulated colonic medium. On contrary, the formulations containing HPMC 3000cps showed delayed release profile for more than 7 hrs deviating from the objective. Further the results suggested that the formulation F8 containing gum Kondagogu grade-III (75 mg) showed optimum drug release when compared to the formulation F7 thus specifically adhering to the objective.

INTRODUCTION

The term chronobascially refers to the observation that every metabolic event undergoes rhythmic changes in time. Chronotherepeutic drug delivery system refers to a treatment method in which in-vivo drug availability is timed to match circadian rhythm of disease in order to optimize therapeutic outcomes and minimize side effects. Several techniques have been developed but not many dosage forms for all the diseases are available in the market. Chronotherepeutic drug delivery systems are gaining importance in the field of pharmaceutical technology as systems reduce dosing frequency, toxicity and deliver the drug that matches the Chronotherepeutic drug delivery systems of that particular disease when the systems are maximum to worst.

Angina pectoris is the medical term for chest pain due to coronary heart disease. Angina is a symptom of a condition called myocardial Ischemia. It occurs when the heart muscle (myocardium) doesn't get as much blood (hence as much oxygen) as it needs. This usually happens because one or more of the heart's arteries (blood vessels that supply blood to the heart muscle) is narrowed or blocked.

Metoprolol Succinate is a beta-adrenergic blocking agent that is used for treating high blood pressure,

heart pain, abnormal rhythms of the heart and some neurological conditions. Metoprolol blocks the action of the sympathetic nervous system, a portion of the involuntary nervous system, by blocking beta receptors on sympathetic nerves. Since the sympathetic nervous system is responsible for increasing the rate with which the heart beats, by blocking the action of theses nerves Metoprolol reduces the heart rate and is useful in treating abnormally rapid rhythms.

An attempt was made to develop a colon targeted drug delivery system of Metoprolol Succinate using pulsing cap technology which helps to release the drug at appropriate time with maximum bioavailability. The developed chronotherepeutic drug delivery system reduces the attack of Angina pectoris generally observed in early hours of morning by releasing the drug at appropriate time in early morning hours preventing the sharp increase of Angina Pectoris.

EXPERIMENTAL

Materials

Capsules were obtained from National scientific source Metoprolol Succinate was gifted from NATCO drugs ltd., Hyderabad. Formaldehyde was procured from Thermo fisher scientific India pvt. Ltd.-Hyderabad. Alcohol was procured from Jiangsu hoax International trade co.Ltd.-China. Potassium permanganate, Isopropyl alcohol was procured from Qualigens Ltd.-Mumbai. Gum kondagogu (3 grades) was procured from Girijan cooperative society-Tirupathi. HPMC (3000 cps, 50cps), Cellulose Acetate Phthalate, Ethyl acetate was procured from Fourrts India laboratories pvt Ltd.-Chennai. Lactose was procured from S.D Fine Chem. Ltd.-Mumbai. PVP K 30 was procured from Loba chemi, Laboratory reagents and fine chemicals-Mumbai.

Methods

CONSTRUCTION OF STANDARD CALIBRATION CURVE FOR METOPROLOL SUCCINATE

Standard calibration curves for Metoprolol Succinate were performed in three different media i.e. in 1.2 pH HCl, 7.4pH Phosphate buffer, 6.8 pH simulated colonic fluid. For this 100mg of drug was accurately weighed and transferred into 100 ml volumetric flask. To it 10 ml of 1.2 pH HCl buffer was added and shaken well to form clear solution. Then finally it was made up to 100ml using 1.2pH HCl buffer. From this aliquot samples were withdrawn and made up until they contained 2, 4, 6, 8, 10 µg/ml of drug. Similar procedure was adopted for other buffers such as 7.4pH phosphate buffer and 6.8 pH simulated colonic fluid. Then the absorbance of these samples containing 2, 4, 6, 8, 10 µg/ml individually were measured using UV- visible spectrophotometer at 275nm. Based on the absorbance values the graph for the individual buffer concentrations was plotted.

PREPARATION OF CROSS LINKED GELATIN CAPSULES

About 100 capsules of size '2' were selected. Their body was separated from cap and placed on a wire mesh. 15% w/v of formaldehyde solution in ethanol was taken in a beaker and kept in an empty glass dessicator. To this 0.25 gms of Potassium permanganate was added to generate formalin vapours. On the top of the beaker a wire mesh containing body of the capsule was kept and immediately the dessicator was closed. The body of capsule was made to react with formaldehyde vapours for a period of 12 hours. Then they were removed and kept on filter paper and dried for 48 hrs at room temperature to ensure the completion of reaction between formaldehyde and gelatin. Afterwards the capsules were kept in open atmosphere to facilitate the removal of residual formaldehyde. These capsule bodies were capped with untreated caps and stored in polythene bag.

FORMULATION OF MODIFIED PULSINCAP DRUG DELIVERY SYSTEMS

It involves five steps,

1. Punching of gum.
2. Preparation of metoprolol succinate granules.
3. Filling of capsule with granules and pluggin material.
4. Sealing of capsule.
5. Enteric coating of capsule.

1. PUNCHING OF GUM

Different grades of Gum Kondagogu with varied concentrations such as 70,75,80 mg were weighed individually and directly compressed using 5mm punch, in 16 station Cadmach punching machine (D- tooting)

2. PREPARATION OF METOPROLOL SUCCINATE GRANULES

Initially the drug (Metoprolol Succinate) was passed through 100 sieve and the excipients were passed through sieve 60. Then the drug was admixed with the other excipients. To this mixture, sufficient quantity of isopropyl alcohol was added to form a damp coherent mass. The obtained

coherent mass was passed through sieve no 16, air dried and further the granules that were retained on sieve no. 20 were collected.

3. FILLING OF CAPSULE WITH GRANULES AND PLUGGIN MATERIAL

100 mg weighed granules equivalent to the dose 50mg of Metoprolol Succinate were placed in the formaldehyde treated body of the capsule and it was locked by hydrogel pluggin material of Gum Kondagogu. Finally non-treated cap of the capsule was placed on it.

4. SEALING OF CAPSULE

Sealing solution of 0.25% ethyl acetate in ethanol was prepared. The cap was sealed with the body using this sealing solution.

5. ENTERIC COATING OF CAPSULE

Enteric coating was done using cellulose acetate phthalate (5%).Capsules were completely coated with 5%CAP to prevent variable gastric emptying. Coating was repeated until an 8-12% increase in weight obtained(5% Coating solution was prepared using CAP in mixture of ethanol and acetone in the ratio of 2:8 and dibutyl phthalate(0.5%)as plasticizer).

EVALUATION OF MODIFIED PULSINCAP

1. Thickness of the cellulose acetate phthalate coating
2. Weight variation
3. *Invitro*-release profile

1. THICKNESS OF THE CELLULOSE ACETATE PHTHALATE COATING

Thickness of the cellulose acetate phthalate coating was measured by using vernier callipers. It was expressed in mm.

2. WEIGHT VARIATION

10 capsules were selected randomly from each formulation and weighed individually for weight variation. The test requirements are met if none of the individual weights are less than or more than ±10% of the average.

3. DRUG CONTENT UNIFORMITY

From each batch of the prepared pulsincaps of Metoprolol Succinate ten pulsincaps were randomly selected and the contents
were removed and powdered. From this sample 100 mg powder was accurately transferred into a 100 ml volumetric flask. To this 10 ml of methanol was added to dissolve Metoprolol Succinate. The solution was made up to volume with 6.8pH simulated colonic fluid. The resulted solution was filtered through 0.45 µm filter paper and suitably diluted and the drug content was estimated spectrophotometrically by measuring the absorbance at 275 nm. The results are shown in Table (6)

4. *Invitro* RELEASE PROFILE

Invitro dissolution profile of each formulation was determined by employing dissolution apparatus by rotating basket method in different media like simulated gastric fluid pH 1.2HCl buffer for 2 hours since the average gastric emptying time was 2 hr, simulated intestinal fluid pH 7.4 buffer for 3 hr (average small intestinal transit time is 3hr) and colonic fluid pH 6.8 Simulated colonic fluid for subsequent hours. The dissolution media was maintained at a temperature 37±5^{0}C at a speed of 100 rpm. Modified pulsincap was placed in a basket in each dissolution vessel. 5 ml of the samples were withdrawn from dissolution media at suitable intervals and the same amount was replaced with same fresh buffer. The absorbance was measured at 275 nm using UV-Visible spectrophotometer.

RESULTS AND DISCUSSION

From the spectra of metoprolol succinate and combination of different grades of gum kondagogu with metoprolol succinate it was observed that all characteristic peaks of metoprolol succinate were present in the combination spectrum , thus indicating the compatibility of drug and the different grades of natural polymer.

In the present study an attempt was made to develop and evaluate modified pulsincap drug delivery system containing metoprolol succinate for colon specific delivery for better treatment of Angina Pectoris. Colon delivery of metoprolol succinate could improve the bioavailability and prevent the unwanted side effects and subsequently a lower dose of the drug may be sufficient to prevent the early morning symptoms in Angina Pectoris.

On formaldehyde treatment the 2 size capsule bodies showed a significant decrease in the length and diameter. When the capsules were subjected in different buffers the untreated caps disintegrated within 15 minutes in all the buffer medias where as the treated bodies remained intact for about 24 hours. The thickness of the coating was found to be uniform with less deviations indicating that most of the capsules were filled uniformly. The filled capsules complied

with the weight variation limits indicating that most of the capsules were of uniform weight.

During dissolution study, it was observed that the enteric coat of the CAP was intact for 2 hr in pH 1.2 HCl buffer thus indicating the efficiency of 5%CAP for enteric coating ,but dissolved in pH 7.4 Phosphate buffer leaving the soluble cap of the capsule which also dissolved in pH 7.4.Then the exposed polymeric plug absorbed the surrounding intestinal fluid, swelled and released the drug negligibly through the swollen matrix except in the formulations containing gum kondagogu grade-I and HPMC 50cps where the drug released significantly in 7.4pH itself. The formulations containing gum kondagogu as a natural polymeric pluggin material showed the better colonic release profiles 101.72% and 99.98% for grade-III 70mg and 75 mg at 6 and 6.5 hrs respectively observed as per the lag time equated for the drug to reach colon when compared to that of gum kondagogu grade-II where much of the drug released prior reaching to simulated colonic medium. On contrary, the formulations containing HPMC 3000cps showed the delayed release profile for more than 7 hr deviating from the objective. Further the results suggested that the formulation F8 containing gum kondagogu grade-III 75 mg showed the optimum drug release when compared to the other formulation F7.

Table 1: FORMULATIONS WITH DIFFERENT CONCENTRATIONS OF GUM KONDAGOGU GRADE 1

INGREDIENTS (mg/ capsule)	F1	F2	F3
METOPROLOL SUCCINATE(DRUG)	50	50	50
GUM KONDAGOGU (GRADE 1)	70	75	80
PVP-30	5	5	5
LACTOSE	45	45	45
TOTAL	100	100	100

Table 2: FORMULATIONS WITH DIFFERENT CONCENTRATIONS OF GUM KONDAGOGU GRADE 2

INGREDIENTS (mg/capsule)	F4	F5	F6
METOPROLOL SUCCINATE (DRUG)	50	50	50
GUM KONDAGOGU(GRADE 2)	70	75	80
PVP-K 30	5	5	5
LACTOSE	45	45	45
TOTAL	100	100	100

Table 3: FORMULATIONS WITH DIFFERENT CONCENTRATIONS OF GUM KONDAGOGU GRADE 3

INGREDIENTS (mg/capsule)	F7	F8	F9
METOPROLOL SUCCINATE (DRUG)	50	50	50
GUM KONDAGOGU(GRADE 3)	70	75	80
PVP-K 30	5	5	5
LACTOSE	45	45	45
TOTAL	100	100	100

Table 4: FORMULATIONS WITH DIFFERENT CONCENTRATIONS OF HPMC 3000cps

INGREDIENTS (mg/ capsule)	F10	F11	F12
METOPROLOL SUCCINATE (DRUG)	50	50	50
HPMC (3000 CPS)	70	75	80
PVP-K 30	5	5	5
LACTOSE	45	45	45
TOTAL	100	100	100

Table 5: FORMULATIONS WITH DIFFERENT CONCENTRATIONS OF HPMC 50cps

INGREDIENTS(mg/capsule)	F13	F14	F15
METOPROLOL SUCCINATE(DRUG)	50	50	50
HPMC (50 CPS)	70	75	80
PVP-30	5	5	5
LACTOSE	45	45	45
TOTAL	100	100	100

Table 6: DETERMINATION OF DRUG CONTENT

FORMULATIONS	DRUG CONTENT (PERCENT)
F1	99.75
F2	99.63
F3	100.11
F4	101.75
F5	98.52
F6	99.74
F7	99.92
F8	100.03
F9	97.58
F10	99.02
F11	98.92
F12	101.45
F13	98.05
F14	99.57
F15	101.41

Table 7: COATING THICKNESS

Formulation	Thickness of coating in mm
F1	0.0052
F2	0.0053
F3	0.0052
F4	0.0054
F5	0.0056
F6	0.0053
F7	0.0054
F8	0.0056
F9	0.0057
F10	0.0051
F11	0.0056
F12	0.0053
F13	0.0054
F14	0.0052
F15	0.0057

DISSOLUTION STUDIES

Table 8: RELEASE PROFILE OF CAPSULES FORMULATED WITH GUM KONDAGOGU OF GRADE -1 (F1)

TIME (hrs)	Percent drug release (1.2pH HCl BUFFER)
0	0.00
0.5	0.01 ± 0.002
1.0	0.01 ± 0.004
1.5	0.01 ± 0.003
2.0	0.01 ± 0.002
7.4 pH phosphate buffer	
2.5	9.17± 0.03
3.0	11.46± 0.05
3.5	20.82± 0.3
4.0	82.24± 0.08
4.5	102.17± 0.07

Table 9: RELEASE PROFILE OF CAPSULES FORMULATED WITH GUM KONDAGOGU OF GRADE -1 (F2)

TIME(hrs)	Percent drug release (1.2pH HCl BUFFER)
0	0.00
0.5	0.01 ± 0.001
1.0	0.01 ± 0.003
1.5	0.01 ± 0.003
2.0	0.01 ± 0.004
7.4 pH phosphate buffer	
2.5	11.17± 0.03
3.0	14.45± 0.08
3.5	17.76± 0.09
4.0	22.12± 0.03
4.5	83.54± 0.3
5.0	99.00± 0.09

Table 10: RELEASE PROFILE OF CAPSULES FORMULATED WITH GUM KONDAGOGU OF GRADE -1 (F3)

TIME(hrs)	Percent drug release (1.2pH HCl BUFFER)
0	0.00
0.5	0.01 ± 0.002
1.0	0.01 ± 0.004
1.5	0.01 ± 0.003
2.0	0.01 ± 0.004
7.4 pH phosphate buffer	
2.5	8.17± 0.08
3.0	12.45± 0.09
3.5	15.75± 0.3
4.0	19.09± 0.1
4.5	81.40± 0.2
5.0	93.81± 0.09

Table 11: RELEASE PROFILE OF CAPSULES FORMULATED WITH GUM KONDAGOGU OF GRADE -2 (F4)

TIME(hrs)	Percent drug release (1.2pH HCl BUFFER)
0	0.00
0.5	0.01 ± 0.003
1.0	0.01 ± 0.004
1.5	0.01 ± 0.002
2.0	0.01 ± 0.004
7.4 pH phosphate buffer	
2.5	10.55± 0.3
3.0	13.03± 0.4
3.5	17.40± 0.09
4.0	21.78± 0.1
4.5	83.20± 0.3
5.0	95.66± 0.5

Table 12: RELEASE PROFILE OF CAPSULES FORMULATED WITH GUM KONDAGOGU OF GRADE -2 (F5)

TIME(hrs)	Percent drug release (1.2pH HCl BUFFER)
0	0.00
0.5	0.01 ± 0.001
1.0	0.01 ± 0.003
1.5	0.01 ± 0.003
2.0	0.01 ± 0.004
7.4 pH phosphate buffer	
2.5	9.94± 0.5
3.0	12.22± 0.3
3.5	15.11± 0.05
4.0	19.47± 0.08
4.5	84.84± 0.5
5.0	92.24± 0.3

Table 13: RELEASE PROFILE OF CAPSULES FORMULATED WITH GUM KONDAGOGU OF GRADE -2 (F6)

TIME(hrs)	Percent drug release (1.2pH HCl BUFFER)
0	0.00
0.5	0.01 ± 0.002
1.0	0.01 ± 0.004
1.5	0.01 ± 0.003
2.0	0.01 ± 0.004
7.4 pH phosphate buffer	
2.5	8.14± 0.09
3.0	14.42± 0.3
3.5	17.91± 0.06
4.0	21.44± 0.08
4.5	24.77± 0.09
5.0	91.16± 0.5
6.8 pH simulated colonic fluid	
5.5	100.36± 0.1

Table 14: RELEASE PROFILE OF CAPSULES FORMULATED WITH GUM KONDAGOGU OF GRADE -3 (F7)

TIME(hrs)	Percent drug release (1.2pH HCl BUFFER)
0	0.00
0.5	0.01 ± 0.003
1.0	0.01 ± 0.003
1.5	0.01 ± 0.002
2.0	0.01 ± 0.004
7.4 pH Phosphate buffer	
2.5	7.54± 0.5
3.0	10.61± 0.4
3.5	15.50± 0.5
4.0	19.20± 0.06
4.5	23.51± 0.08
5.0	26.04± 0.5
6.8 pH Simulated colonic fluid	
5.5	89.74± 0.5
6.0	101.72± 0.1

Table 15: RELEASE PROFILE OF CAPSULES FORMULATED WITH GUM KONDAGOGU OF GRADE -3 (F8)

TIME(hrs)	Percent drug release (1.2pH HCl BUFFER)
0	0.00
0.5	0.01 ± 0.001
1.0	0.01 ± 0.003
1.5	0.01 ± 0.003
2.0	0.01 ± 0.004
7.4 pH phosphate buffer	
2.5	8.54± 0.06
3.0	11.42± 0.4
3.5	17.33± 0.4
4.0	21.67± 0.5
4.5	24.05± 0.06
5.0	27.05± 0.09
6.8 pH simulated colonic fluid	
5.5	30.16± 0.3
6.0	87.58± 0.5
6.5	99.98±0.2

Table 16: RELEASE PROFILE OF CAPSULES FORMULATED WITH GUM KONDAGOGU OF GRADE - 3 (F9)

TIME(hrs)	Percent drug release (1.2pH HCl BUFFER)
0	0.00
0.5	0.01 ± 0.001
1.0	0.01 ± 0.003
1.5	0.01 ± 0.003
2.0	0.01 ± 0.004
7.4 pH phosphate buffer	
2.5	9.54± 0.06
3.0	10.39± 0.08
3.5	12.86± 0.2
4.0	14.94± 0.1
4.5	17.83± 0.3
5.0	21.94± 0.5
6.8 pH simulated colonic fluid	
5.5	27.44± 0.2
6.0	31.65± 0.02
6.5	83.18± 0.06
7.0	92.15± 0.5
7.5	101.4± 0.09

Table 17: RELEASE PROFILE OF CAPSULES FORMULATED WITH SYNTHETIC POLYMER HPMC 3000 cps- (F10)

TIME(hrs)	Percent drug release (1.2pH HCl BUFFER)
0	0.00
0.5	0.01 ± 0.003
1.0	0.01 ± 0.003
1.5	0.01 ± 0.002
2.0	0.01 ± 0.004
7.4 pH phosphate buffer	
2.5	10.67± 0.05
3.0	15.90± 0.1
3.5	18.22± 0.02
4.0	21.80± 0.09
4.5	24.99± 0.3
5.0	26.97± 0.5
6.8 pH Simulated colonic fluid	
5.5	29.45± 01
6.0	32.7± 0.2
7.0	92.64± 0.5
7.5	104.56± 0.5

Table 18: RELEASE PROFILE OF CAPSULES FORMULATED WITH SYNTHETIC POLYMER HPMC 3000 cps- (F11)

TIME(hrs)	Percent drug release (1.2pH HCl BUFFER)
0	0.00
0.5	0.01 ± 0.001
1.0	0.01 ± 0.003
1.5	0.01 ± 0.003
2.0	0.01 ± 0.004
7.4 pH phosphate buffer	
2.5	9.99± 0.1
3.0	11.34± 0.5
3.5	16.92± 0.1
4.0	19.77± 0.2
4.5	21.33± 0.05
5.0	23.32± 0.06
6.8 pH simulated colonic fluid	
5.5	25.53± 0.2
6.0	28.33± 0.3
6.5	31.34± 0.1
7.0	34.22±0.1
7.5	87.33± 0.3
8.0	99.34±0.1

Table 19: RELEASE PROFILE OF CAPSULES FORMULATED WITH SYNTHETIC POLYMER HPMC 3000 cps- (F12)

TIME(hrs)	Percent drug release (1.2pH HCl BUFFER)
0	0.00
0.5	0.01 ± 0.001
1.0	0.01 ± 0.003
1.5	0.01 ± 0.003
2.0	0.01 ± 0.004
7.4 pH phosphate buffer	
2.5	11.76± 0.04
3.0	13.56± 0.04
3.5	15.99± 0.09
4.0	18.31± 0.2
4.5	20.92± 0.3
5.0	23.66± 0.1
6.8 pH simulated colonic fluid	
5.5	25.54± 0.5
6.0	28.12± 0.2
6.5	31.57± 0.1
7.0	35.54±0.1
7.5	86.33±0.2
8.0	97.57±0.1

Table 20: RELEASE PROFILE OF CAPSULES FORMULATED WITH SYNTHETIC POLYMER HPMC 50 cps- (F13)

TIME(hrs)	Percent drug release (1.2pH HCl BUFFER)
0	0.00
0.5	0.01 ± 0.001
1.0	0.01 ± 0.003
1.5	0.01 ± 0.003
2.0	0.01 ± 0.004
7.4 pH phosphate buffer	
3.0	12.42± 0.2
3.5	85.83± 0.3
4.0	102.91± 0.2

Table 21: RELEASE PROFILE OF CAPSULES FORMULATED WITH SYNTHETIC POLYMER HPMC 50 cps- (F14)

TIME(hrs)	Percent drug release (1.2pH HCl BUFFER)
0	0.00
0.5	0.01 ± 0.003
1.0	0.01 ± 0.003
1.5	0.01 ± 0.002
2.0	0.01 ± 0.004
7.4 pH phosphate buffer	
2.5	10.66± 0.5
3.0	15.97± 0.2
3.5	17.88± 0.3
4.0	87.41± 0.2
4.5	98.44± 0.09

Table 22: RELEASE PROFILE OF CAPSULES FORMULATED WITH SYNTHETIC POLYMER HPMC 50 cps- (F15)

TIME(hrs)	Percent drug release (1.2pH HCl BUFFER)
0	0.00
0.5	0.01 ± 0.002
1.0	0.01 ± 0.004
1.5	0.01 ± 0.003
2.0	0.01 ± 0.004
7.4 pH phosphate buffer	
2.5	14.88± 0.2
3.0	17.88± 0.3
3.5	25.76± 0.5
4.0	85.32± 0.1
4.5	94.33± 0.2

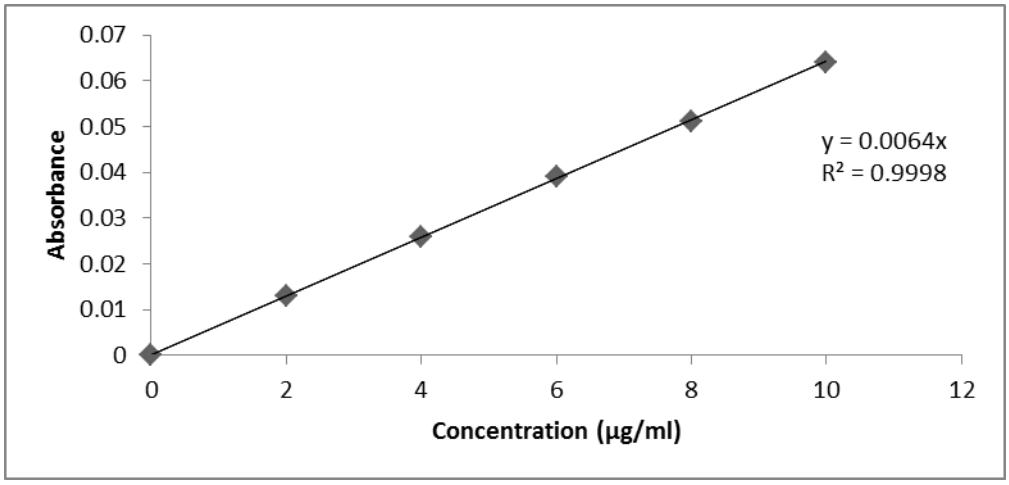

Fig. 1: Standard calibration curve of Metoprolol succinate in pH 1.2 HCl buffer

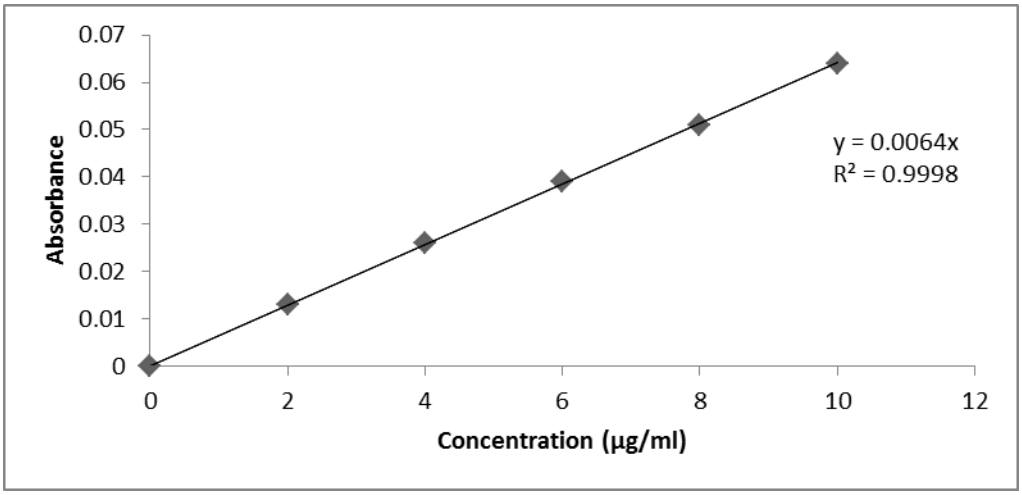

Fig. 2: Standard calibration curve of Metoprolol succinate in pH 7.4 pH phosphate buffer

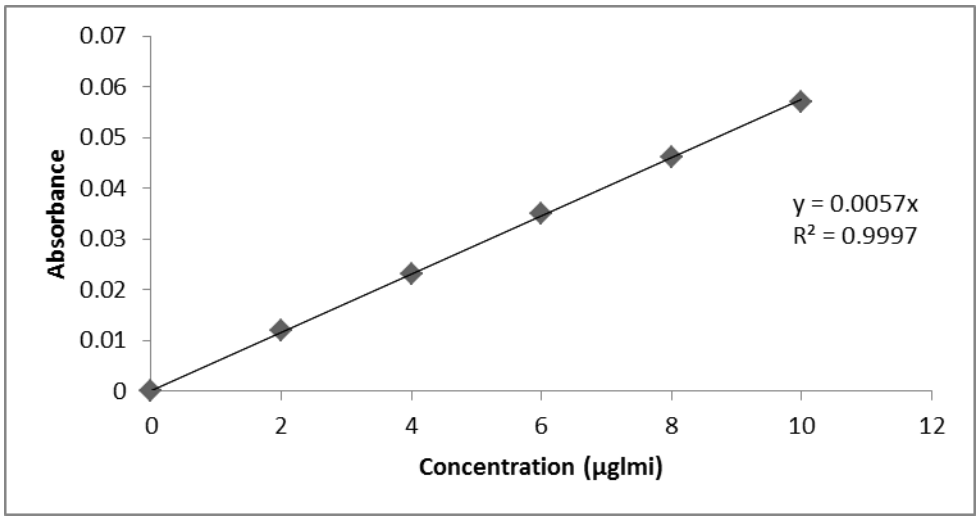

Fig. 3: Standard calibration curve of Metoprolol succinate in pH 6.8 pH colonic fluid

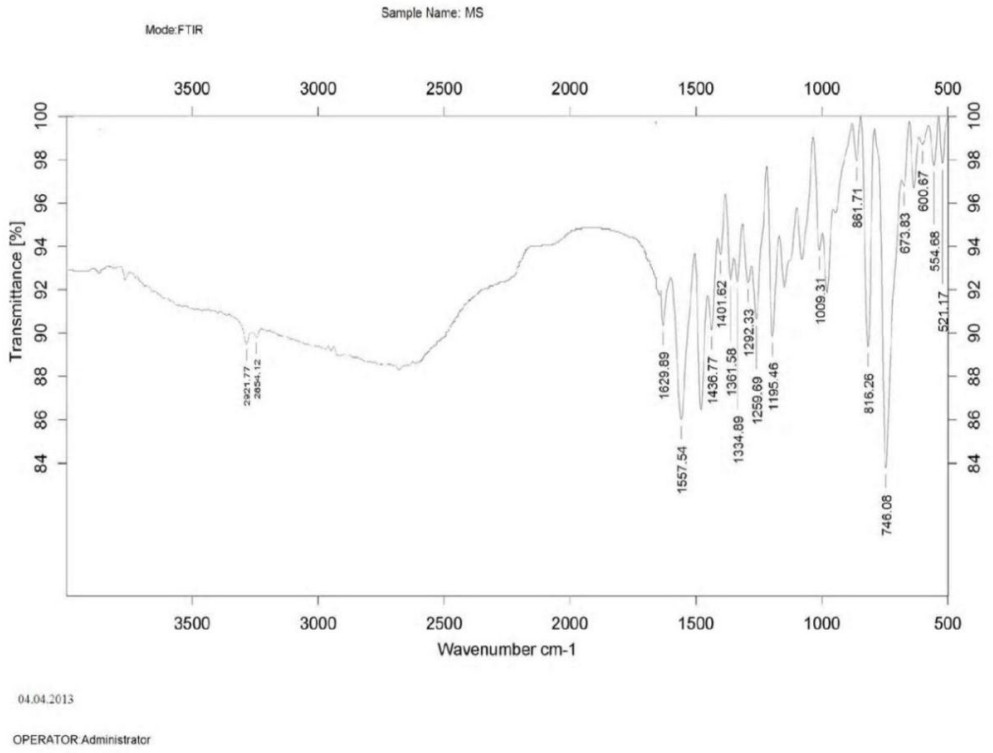

Fig. 4: FTIR gragh for Metoprolol Succinate pure drug

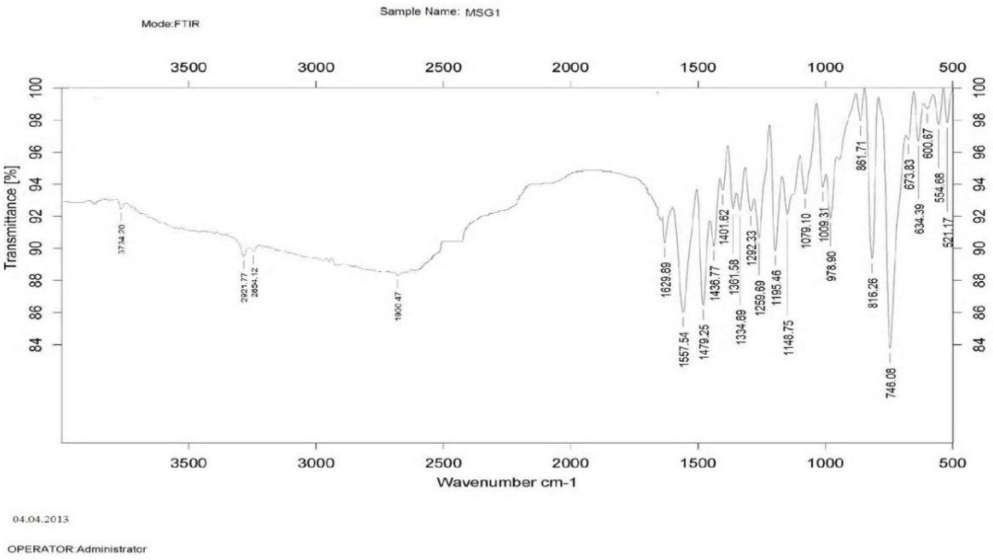

Fig. 5: FTIR gragh for Metoprolol Succinate and gum Kondagogu grade

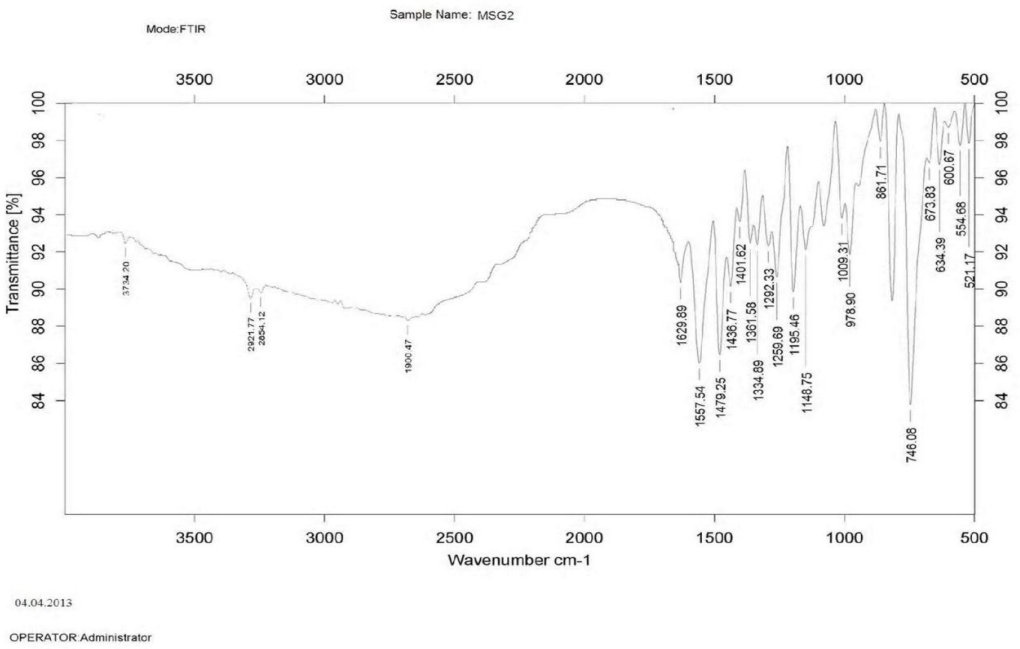

Fig. 6: FTIR gragh for Metoprolol Succinate and gum Kondagogu grade 2

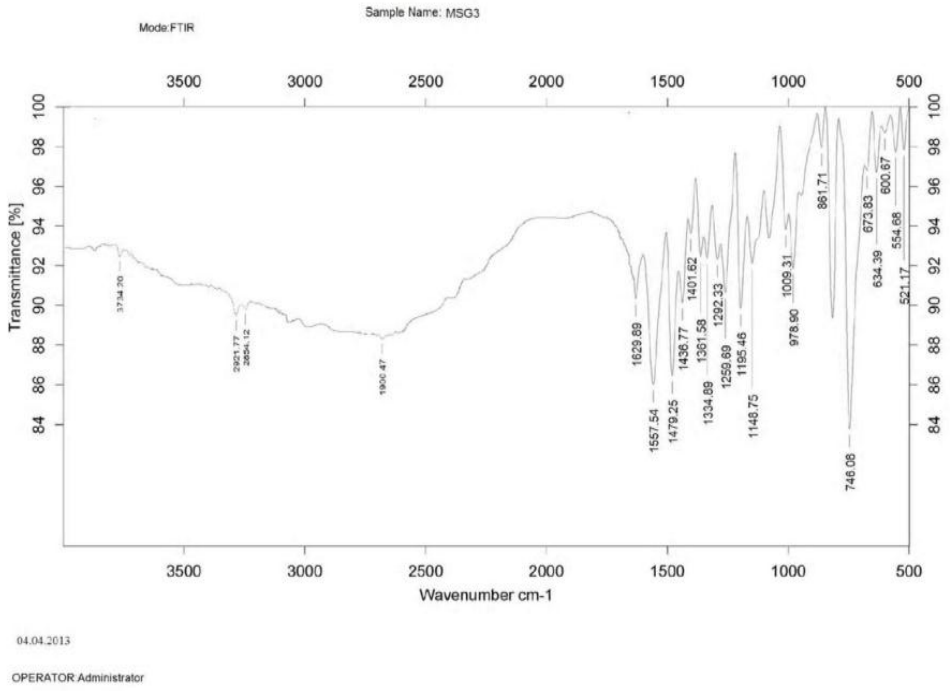

Fig. 7: FTIR gragh for Metoprolol Succinate and gum Kondagogu grade 3

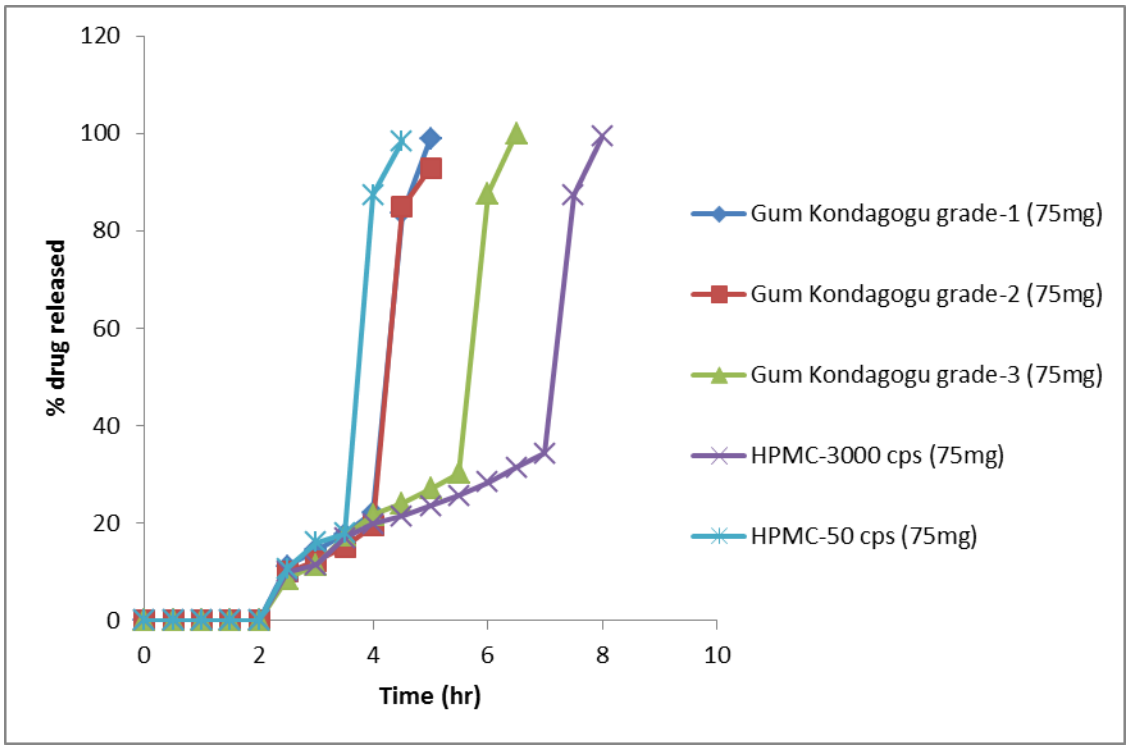

Fig. 8: Cumulative drug release profiles of Metoprolol succinate

CONCLUSION

In conclusion the modified pulsincap technology can be utilized with the lag time equated for the drug to reach colon and thus this system can be considered as one of the promising formulation technique for preparing colon specific drug delivery systems and hence in the chronotherapeutic management of Angina Pectoris.

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