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EFFECT OF SINTERING ON SUSTAINED RELEASE PROFILE OF B-BLOCKER TABLET PREPARED BY DIRECT COMPRESSION METHOD

Pentewar R. S.*, Sayyed Sarfaraz Ali Riyasat Ali, Thonte S. S., Nasheer Shaikh

Department of Pharmaceutics, Channabasweshwar Pharmacy College, Latur, Maharashtra, India.

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***Corresponding Author**
Pentewar R. S.
Department of Pharmaceutics, Channabasweshwar Pharmacy College, Latur, Maharashtra, India.

ABSTRACT

Exploration of sintering concept in the pharmaceutical science is relatively recent. The objective of this study was to investigate the release characteristic of matrix tablet consisting of a different concentration of various retarding polymers and Sotalol Hcl for sustain release formulation using different sintering techniques. The Sotalol tablet was prepared by using different polymers by direct compression method and formulation was sintered at various temperatures and time point. The sintering of tablet is done by using different techniques like thermal sintering and microwave sintering. The sintered tablets were tested for weight variation, hardness, friability, content uniformity and *in-vitro* dissolution study. The sintered tablet showed more strength and drug was also retarded than unsintered tablet. Formulation Fs3 and Fs6 showed 96.31% and 95.41 % release profile in 18 hr when subjected to thermal sintering at 80°C for 5 hr. whereas, Formulation Fm3 and Fm6 provided 97.21 % and 97.68 % release profile in 18 hr when subjected to microwave sintering at 100 watt for 6 min. Sintering *i.e.* Application of heat, causes the bonding of adjacent particle surfaces in a mass of powder or in a compact leading to the retardation of drug release. FT-IR, Differential Scanning Calorimetry studies ruled out the occurrence of drug interaction after sintering condition. The drug release followed Peppas kinetics. The mean diffusional exponent values (n) ranged from 0.2987 to 0.4972 indicating that all these formulations presented a dissolution behavior controlled by Fickian Diffusion. The stability study conducted as per the ICH Guidelines for optimized formulation was found to be stable.

KEYWORDS: Sotalol Hcl, sintering technique, direct compression, Eudragit RS100 sustained release, FTIR.

INTRODUCTION

The oral route of drug administration is the most important method of administering drugs for systemic effects. Oral route is one of the most popular routes of drug delivery due to its ease of administration, patient compliance, least sterility constraints and flexible design of dosage form. At least 90% of all drugs used to produce systemic effects are administered by oral route. Of drugs that are administered orally, solid oral dosage forms represent the preferred class of product.[1-3]

1. Rationale of Sustained and Controlled Drug Delivery

The basic rationale for controlled drug delivery is to alter the pharmacokinetics and pharmacodynamics of pharmacologically active moieties by using novel drug delivery systems or by modifying the molecular structure and pharmacological parameters inherent in the selected route of administration. Thus, design of controlled release systems necessitates a thorough understanding of the pharmacokinetics and pharmacodynamics of the drugs.[2-5]

A. Potential Advantages of Sustained Release Dosage Form [5-16]

- Better patient compliance due to reduced frequency of dosing.
- Uniform level of drug in blood is maintained.
- Quantity of drug required is less.
  - Minimize or eliminate local or systemic side effects.
  - Minimize drug accumulation with chronic dosing.
- Improved efficiency in treatment.
  - Cure or control condition more promptly.
  - Improved control of condition i.e. reduced fluctuation in drug level.
  - Improves bioavailability of some drugs.
- Make use of special effects, e.g. sustained release aspect for relief of arthritis by dosing before bedtime.
- Economic
- Overall, administration of sustained release form enables increase reliability of therapy.

B. Disadvantages of Sustained Release products[2, 6, 7]

- Dose Dumping
- Reduced potential for accurate dose adjustment
- Need for additional patient education
- Increased potential for first pass metabolism
- Possible reduction in systemic availability
- Increased variability among dosage units
- The complexity of sustained release forms may lead to stability problems resulting in either faster or slower drug release than anticipated.

2. Modified Release System[8-9]

To overcome the potential problem associated with conventional drug therapy, modified release systems were developed and may be divided into four categories,

1. Sustained release.
2. Controlled release.
3. Site specific and
4. Receptor release

1. Sustained Release System[6,10]

Sustained release systems are that which achieve slow release of drug over an extended period of time and in this drug is initially made available to the body in amount to cause the desired pharmacological response.

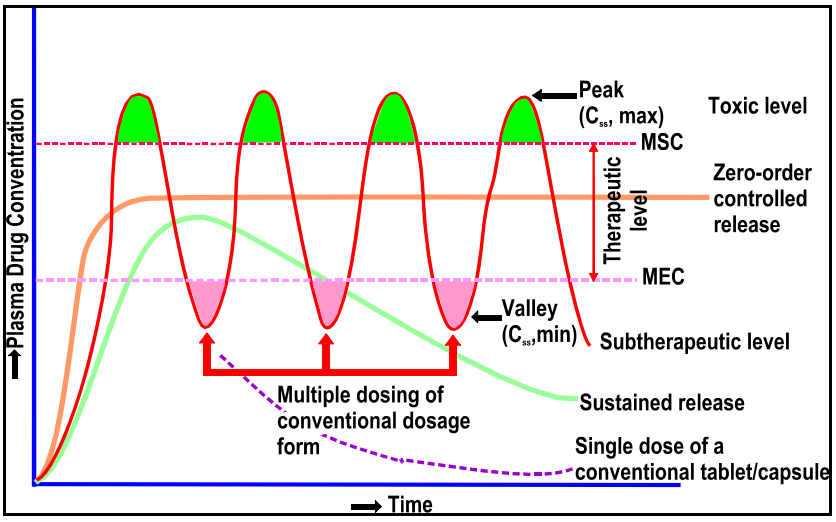

Figure 1. Hypothetical plasma concentration-time profiles from conventional multiple dosing and single doses of sustained and controlled delivery.

2. Controlled Release System

An ideal controlled drug delivery is that which delivers the drug at predetermined rate, locally or systemically for the predetermined period of time.

3. Site Specific Release System

Site specific release system refers to targeting of the drug directly to a certain body location.

4. Receptor Release System

Receptor release system refers to targeting of the drug depending on specific receptor of certain biological location.

3. Recent trends in sustained drug delivery system[9-12]

Sustained release dosage forms are categorized as

1. Single unit dosage form.
2. Multiple unit dosage form.

1. Single Unit Dosage Form: These refer to diffusion systems where the drug is uniformly distributed (dispersed/dissolved) throughout the solid matrix and the release of the drug is controlled or sustained either by incorporating hydrophilic or hydrophobic filler within the matrix or by coating the drug matrix with a swellable or non swellable polymer film.

2. Multiple Unit Dosage Forms

It represents a combination of subunits of the dosage forms, the source of which may either be homogeneous or heterogeneous. It offers the advantages of releasing one of the drug or part of the same drug immediately, while remaining drug or parts of the same can be sustained release. These are useful where drug - excipients and drug-drug interactions are inevitable in a single unit dosage form. The various forms are as

- Micro granules/Spheroids
- Beads
- Pellets
- Microcapsules

4. Sintering Technique[17-21,22-26]

In the pharmaceutical science, sintering has been described as the mechanism for the strengthening of the mechanical properties of consolidated pharmaceutical powders at

elevated temperatures, for solid-bond formation, and for thermal curing of polymer-latex film coatings. The concept of sintering was applied in the investigation of the effect of heating on the mechanical properties of pharmaceutical powders. The formation of solid bonds within a powder bed during tablet compression was also studied in terms of sintering. The changes in the hardness and disintegration time of tablets stored at elevated temperatures were described as a result of sintering. Furthermore, the sintering process has been used for the fabrication of sustained – release matrix tablets and for the stabilization of the drug permeability of film coatings derived from various pharmaceutical lattices. Exploration of the sintering concept in the pharmaceutical sciences is relatively recent, but research interests relating to this process have been growing.

Sintering is defined as the bonding of adjacent particle surfaces in a mass of powder, or in compact, by the application of heat. Conventional sintering technique involves the heating of compact (matrix tablets) at a temperature close to the melting point of retarding material. Variation in this method include heating in the presence of transient or stable liquid phases and/or under pressure (hot-pressing). Plasma activated sintering, microwave sintering and laser sintering are the more recent advances in sintering technologies. Historically, sintering is a process employed to fabricate parts for metals, ceramics and glass.

2. MATERIALS AND METHODS

Sotalol Hcl obtained as gift sample from Bmr Pharma And Chemicals, Hyderabad, Telangana. Eudragit RS 100 obtained from Hi Media Chem. Pvt. Ltd. Mumbai., HPMC K4M Research-lab fine chem. industries, Mumbai, Gum Acacia Ozone International, Mumbai (LR)., Xanthan gum Ozone International, Mumbai(LR). Sodium starch glycolate, Avicel Ph 102, Aerosil 200 are of analytical grades.

Preparation of Sustained Release tablet by Direct Compression Method

Various formulations were prepared using Eudragit RS100, HPMC K4M, Gum Acacia, Xanthan Gum separately and incombination. Sotalol and other ingredients were weighed and the mixture was then blend with lubricant in a polybag and compressed into tablets. All tablets were prepared using single rotatory tablet machine equipped with standard flat punches of 7-mm diameter. Compressed tablets were subjected to sintering for different time points as shown in Tables 2 and 3 at various temperatures using hot air oven and micro wave oven.

3. RESULT AND DISCUSSION

Table 1. Formulation table

Formulations	F1	F2	F3	F4	F5	F6
Sotalol Hcl	40	40	40	40	40	40
Eudragit RS 100	40	60	80	-	-	40
HPMC K4M	-	-	40	40	60	80
Gum Acacia	-	-	-	-	-	-
Xanthan Gum	-	-	-	-	-	-
Avicel Ph 102	112	92	32	112	92	32
Sodium Starch Glycolate	2	2	2	2	2	2
Magnesium stearate	2	2	2	2	2	2
Aerosil 200	4	4	4	4	4	4
Total weight	**200**	**200**	**200**	**200**	**200**	**200**

(All quantities are in mg)

Table 2: Sintering condition for Fs1 to Fs6 formulations by hot air oven.

Formulation (unsintered)	Formulation (sintered)	Sintering Temperature (°C)	Sintering time (hr)
F1	Fs1	80	5
F2	Fs2	80	5
F3	Fs3	80	5
F4	Fs4	80	5
F5	Fs5	80	5
F6	Fs6	80	5

Table 3. Sintering condition for formulations Fm1 to Fm6 (Microwave).

Formulation (unsintered)	Formulation (sintered)	Sintering Temperature (Watt)	Sintering time (min)
F1	Fm1	100	6
F2	Fm2	100	6
F3	Fm3	100	6
F4	Fm4	100	6
F5	Fm5	100	6
F6	Fm6	100	6

Evaluation of Mixture for Precompressional Parameters: Bulk density obtained for all formulations was in the range of 0.3053±0.07 to 0.3625±0.01 that shows good powder / granules flowability. Carr's index between 5-15% shows excellent flow properties but readings above 40% shows extremely poor flowability. In above formulations Carr's index ranged from 15.29±0.03 to 21.46±0.11 showing good to fair flowability. Hausner's ratio ranged from 1.11±0.09 to 1.29±0.06.

Values of angle of repose upto 20 shows excellent flow properties whereas angle of repose $\geq 40^{o}$ shows very poor flow. Values of angle of repose of all formulations ranged from

22.5±0.06 to 29.75±0.05 i.e. granules were of good flow property.

All the pre-compressional parameters comply with the standard values and are shown in table no 4.

Table 4: Precompressional parameters of all the batches prepared

Batch	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Carr's index IC	Hausner's ratio HR	Angle of repose (Θ)
F1	0.3261±0.04	0.3626±0.01	17.25±0.10	1.15±0.04	26.51±0.04
F2	0.3625±0.01	0.3850±0.02	19.32±0.11	1.29±0.06	22.34±0.12
F3	0.3156±0.06	0.3458±0.05	15.29±0.03	1.11±0.09	27.20±0.09
F4	0.3243±0.04	0.4035±0.04	21.46±0.11	1.20±0.10	23.19±0.08
F5	0.3053±0.07	0.4145±0.07	16.27±0.07	1.13±0.11	29.75±0.05
F6	0.3278±0.06	0.3745±0.03	19.55±0.11	1.24±0.08	22.58±0.04

All values are expressed as mean ± SD. n=3, F=Batch code

Evaluation parameters for tablets of final batches: Formulation F1 to F6 were subjected to the quality control test as per IP such as hardness, thickness, weight variation, friability and drug content before and after sintering were evaluated.

Hardness: Hardness of tablets of each formulation was measured and was found in the range of 5-8 kg/cm^2. Hardness of sintered tablets was improved as compared to unsintered tablets. Each sample was analyzed in triplicate.

Friability: Compressed tablets should not lose more than 1% of their weight. Percentage weight loss of the tablets of each formulation was measured and was found to be less than 1% for all the formulations.

Weight variation test: Tablets from each batch showed uniformity of weight as per I. P. limits. Average weight of the tablet was found to be 200 ± 3 mg for all formulations.

Tablet thickness and size: Diameter of formulations was found to be 6 ± 0.05 mm. Thickness was found to be 3 ± 0.2 mm for all the formulations. Every measurement was made in triplicate.

Content uniformity: The content uniformity for all tablet formulations was found to be 99.0% to 101% for Sotalol Hcl. All the above mentioned parameters have been summarized in Table 5.

Table 5. Evaluation parameters of sintered and unsintered tablets

Formulation	Tablet Hardness (kg/cm^2)*	Tablet thickness (mm)*	Weight variation (mg)*	Friability (%)*	Drug content (%)*
F1	6-7	3.0±0.10	200 ±2	0.50 ±0.02	99.20±0.20
Fs1	7-8	3.2±0.10	200 ±2	0.30 ±0.02	99.66±0.20
Fm1	7-8	3.0±0.10	200 ±2	0.20 ±0.02	99.45±0.20
F2	7-8	3.0±0.10	200 ±2	0.40 ±0.02	99.20±0.20
Fs2	7-8	3.0±0.10	200 ±2	0.20 ±0.02	99.22±0.20
Fm2	6-7	3.2±0.10	200 ±2	0.20 ±0.02	100.2±0.20
F3	5-6	3.2±0.10	200 ±2	0.60 ±0.02	99.88±0.20
Fs3	6-7	3.1±0.10	200 ±2	0.40 ±0.02	99.45±0.20
Fm3	7-8	3.2±0.10	200 ±2	0.40 ±0.02	100.90±0.20
F4	5-6	3.3±0.10	200 ±2	0.40 ±0.02	100.40±0.20
Fs4	7-8	3.4±0.10	200 ±2	0.20 ±0.02	99.20±0.20
Fm4	6-7	3.5±0.10	200 ±2	0.20 ±0.02	99.88±0.20
F5	5-6	3.2±0.10	200 ±2	0.50 ±0.02	99.78±0.20
Fs5	7-8	3.4±0.10	200 ±2	0.20 ±0.02	99.56±0.20
Fm5	7-8	3.4±0.10	200 ±2	0.30 ±0.02	99.78±0.20
F6	5-6	3.6±0.10	200 ±2	0.40 ±0.02	99.78±0.20
Fs6	7-8	3.6±0.10	200 ±2	0.20 ±0.02	100.20±0.20
Fm6	7-8	3.6±0.10	200 ±2	0.30 ±0.02	99.40±0.20

**Average of three determinants*

Curve Fitting Analysis of Different Formulations

The kinetic data of Sotalol Hcl tablets were given in table no.6.

The correlation coefficient values of zero order of all the formulations were in the range of 0.8459 to 0.9763 and first order r values were from 0.8253 to 0.9756.

The results suggest that, the drug release followed Peppas kinetics. To ascertain, the drug release mechanism in vitro release data were also subjected to Higuchi's diffusion plot and Peppa's plot and the correlation coefficient values were in the range of 0.9457 to 0.9934 and 0.9758 to 0.9965 respectively. So it confirms that, the calculated r values for Peppa's plot was nearer to one (1) in all the cases suggesting that drug released by diffusion mechanism.

The mean diffusional exponent values (n) ranged from 0.2987 to 0.4972 indicating that all these formulations presented a dissolution behavior controlled by Fickian Diffusion (when n tends toward ≥ 0.5).

Table 6: Curve Fitting Analysis of Different Formulations

Formulation code	Zero order (R)	First order (R)	Higuchi's (R)	Peppa's	
				R	N
Fs1	0.8694	0.8253	0.9842	0.9895	0.3852
Fs2	0.9512	0.8944	0.9457	0.9756	0.2987
Fs3	0.8763	0.8818	0.9671	0.9745	0.4685
Fs4	0.8459	0.9637	0.9813	0.9884	0.3496
Fs5	0.9365	0.8483	0.9758	0.9852	0.4262
Fs6	0.8944	0.9756	0.9795	0.9845	0.3941

Excipients compatibility study

FTIR Study

FTIR studies were conducted and the spectrum was recorded in the range of 4000-400 cm^{-1}. No significant interaction between the drug and excipients was observed. All the spectrum i.e. drug and excipients were concordant with that of the standard IR spectra of pure drug sotalol.

Table 7: Interpretation of IR

STANDARD	OBSERVED	GROUP
1260-1350	1392	CH_3 stretch
1180-1140	1149	-S=O(Sulphonamide)
1200-1105	1224	N-H
770-735	773.46	C_6H_6
1180-1140	1149	-Sec-OH
1360-1392	1392	C-H

In vitro dissolution studies

The *in vitro* dissolution studies were performed using USP type-II dissolution apparatus at 50 rpm. The dissolution medium consisted of .1N Hcl and phosphate buffer pH 7.4 for 18 hours (900 ml), maintained at 37°C ± 0.5°C. An aliquot (10 ml) was withdrawn at specific time intervals and drug content was determined by UV-visible spectrophotometer at 229 nm. At each time of withdrawal, 10 ml of fresh corresponding dissolution medium was replaced into the dissolution flask. The release studies were conducted in triplicate. In vitro dissolution studies were carried out for the F1-F6 Formulations for 18 hr. Dissolution profile was checked for unsintered tablets and sintered tablets and results have been summarized in Table 8.

Table 8: *In-vitro* dissolution study of unsintered formulation F1-F6.

Time (hrs)	% Drug release					
	F1	F2	F3	F4	F5	F6
1	11.67	9.31	8.99	11.17	9.78	9.57
2	23.13	20.19	19.40	24.16	19.33	20.45
3	29.74	26.09	25.19	28.25	26.86	26.39
4	36.58	33.54	32.31	37.64	33.98	34.30
5	44.29	39.89	38.75	46.25	42.35	39.55
6	57.33	44.87	45.32	58.31	51.05	45.94
7	69.43	54.74	52.97	70.12	66.23	53.11
8	77.35	65.51	60.87	79.65	72.80	59.31
9	85.17	76.32	69.22	88.24	81.38	66.86
10	97.31	87.66	76.29	98.38	87.12	74.55
11		96.08	85.19		96.86	82.27
12			98.45			97.38

All values are expressed as mean ± SD. n=3, F=Batch code

Table 9: *In-vitro* dissolution study of sintered formulation Fs1-Fs6 using hot air oven

Time (hrs)	% Drug release					
	Fs1	Fs2	Fs3	Fs4	Fs5	Fs6
1	10.31	8.52	6.13	9.41	8.25	6.15
2	19.26	17.26	14.08	20.65	18.35	15.53
3	25.87	24.69	19.31	28.43	25.92	20.09
4	30.71	29.42	24.87	33.45	32.76	25.66
5	35.63	34.18	29.54	38.63	37.52	30.52
6	40.79	39.15	34.32	44.75	43.18	35.53
7	46.18	45.56	39.27	52.25	50.64	41.67
8	51.36	50.89	44.35	57.61	54.29	46.71
9	57.17	56.38	51.27	63.56	59.2	50.08
10	64.87	63.74	57.28	69.35	65.16	56.13
11	71.23	70.5	64.55	74.32	70.84	62.8
12	77.4	75.5	69.22	80.1	76.4	70.3
13	83.68	81.57	75.88	83.38	79.35	76.58
14	90.12	88.82	79.18	89.9	84.31	80.12
15	94.73	92.18	85.61	92.15	89.48	83.02
16	98.39	97.13	89.34	99.38	94.16	88.53
17			93.59		98.65	92.32
18			96.31			95.41

All values are expressed as mean ± SD. n=3, F=Batch code

Excipients compatibility study

FTIR Study: FTIR studies were conducted and the spectrum was recorded in the range of 4000-400 cm^{-1}. No significant interaction between the drug and excipients was observed. All the spectrum i.e. drug and excipients were concordant with that of the standard IR spectra of pure drug sotalol. The spectral data is given in Table. In FTIR spectrum of sotalol, polymer

and physical mixture of drug and polymer all the peaks corresponding to the functional groups were present.

Table 10: *In-vitro* dissolution study of sintered formulation Fm1-Fm6 using microwave oven

Time (hrs)	% Drug release					
	Fm1	Fm2	Fm3	Fm4	Fm5	Fm6
1	7.31	7.1	6.24	8.36	7.2	6.25
2	19.45	16.85	13.09	15.98	14.56	12.83
3	23.48	21.56	19.49	20.57	19.46	18.43
4	28.13	26.35	24.96	26.89	25.4	24.4
5	35.78	33.41	28.7	31.08	30.2	29.56
6	40.52	38.45	35.54	36.11	35.01	34.23
7	48.23	44.51	39.51	44.19	39.93	42.27
8	52.81	50.33	46.21	50.38	45.9	49.65
9	61.25	58.83	49.32	56.73	50.35	54.21
10	65.73	62.55	55.74	61.17	56.37	60.25
11	70.21	69.38	61.74	66.28	60.15	64.13
12	75.08	76.81	69.74	70.63	69.35	68.22
13	82.18	80.23	75.91	77.05	76.49	75.54
14	89.24	85.19	82.11	83.4	82.69	80.51
15	93.39	90.48	86.32	89.6	87.13	85.4
16	99.43	96.5	91.08	94.74	93.41	90.72
17			94.26	98.72	97.08	93.13
18			97.21			97.80

All values are expressed as mean ± SD. n=3, F=Batch code

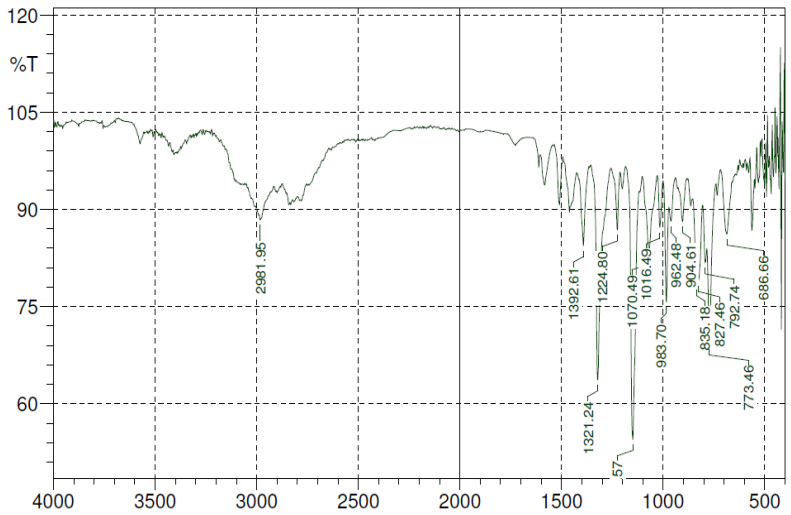

Figure 2. IR spectrum of pure Sotalol

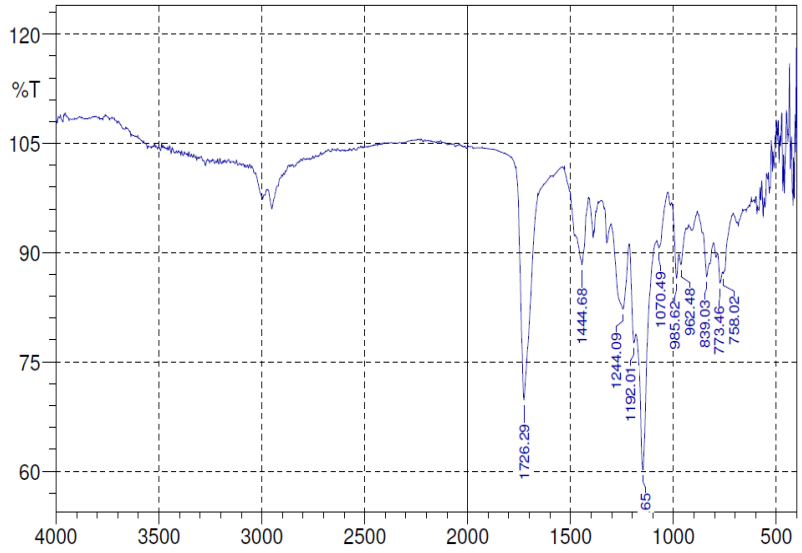

Figure 3. IR spectrum of physical mixture of Eudragit Rs 100 And Drug.

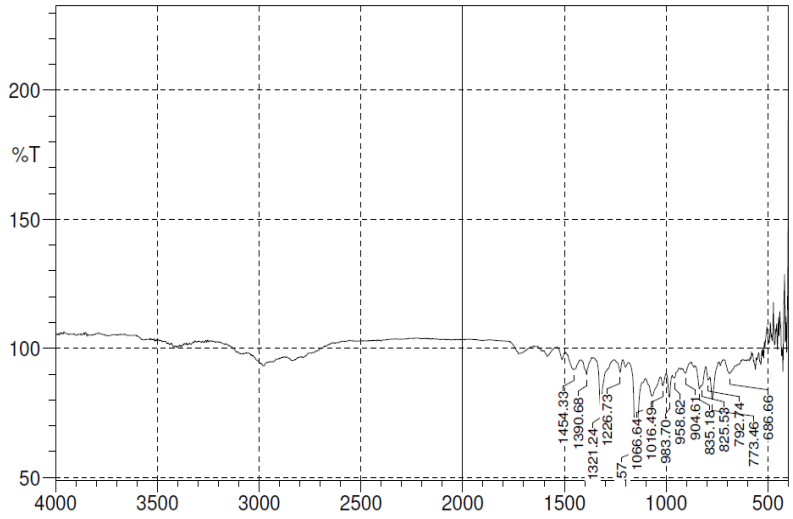

Figure 4. IR spectrum of physical mixture of Hpmc K4 M And Drug.

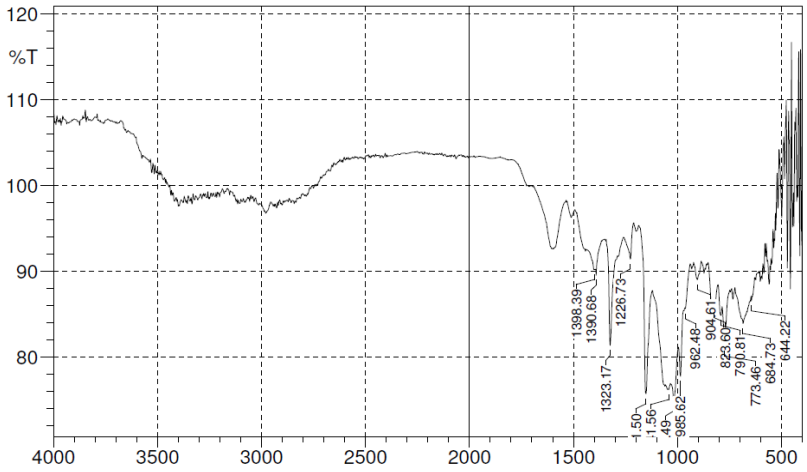

Figure 5. IR spectrum of physical mixture of Xanthan Gum And Drug.

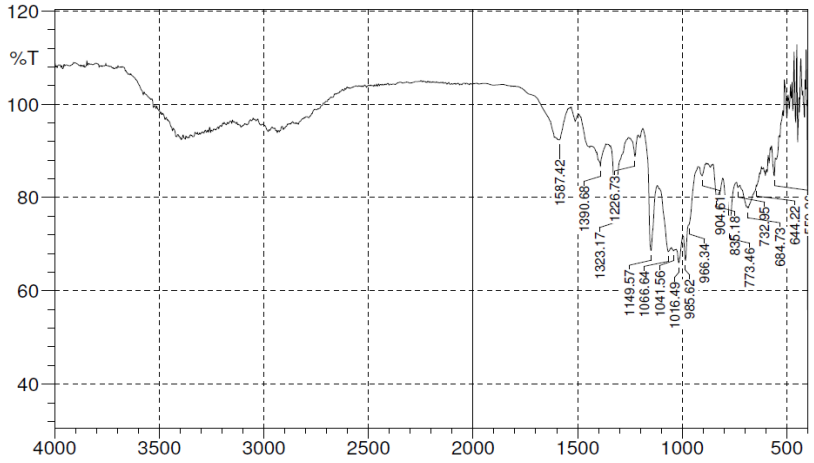

Figure 6. IR spectrum of physical mixture of Gum Acacia And Drug.

Differential scanning calorimetry studies: DSC was used to examine thermal behavior of unsintered and sintered formulations. DSC studies of formulations mentioned below realized that, during the process of formulation chemical reaction is not taken place and the drug has remained in the Free State to show its desired effects in controlled manner.

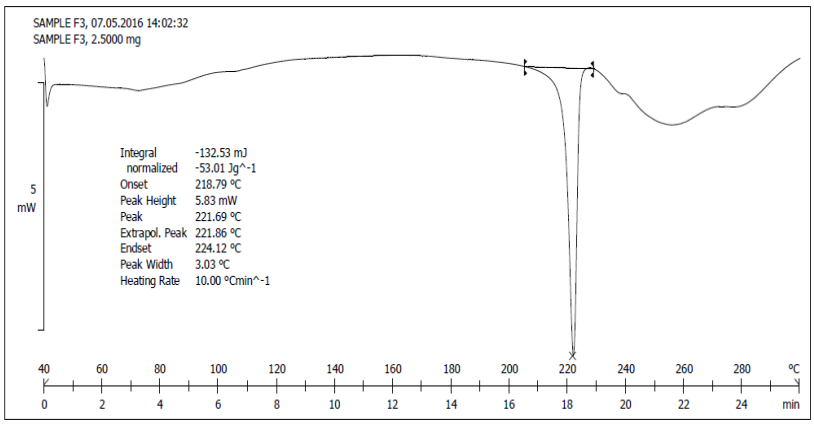

Figure 7. DSC thermogram of Fs3 formulation

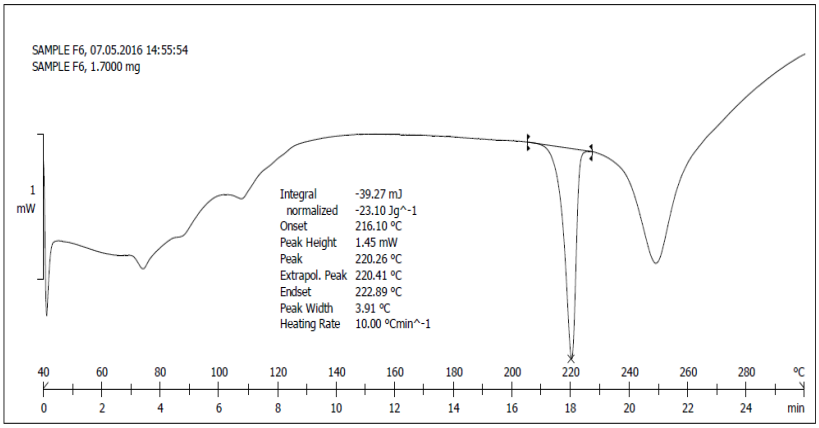

Figure 8. DSC thermogram of Fs6 formulation

Therefore there is no evidence of drug interaction or complexation during manufacturing process and on sintering.

In-vitro dissolution study: In vitro dissolution studies were carried out for 18 hr. Dissolution profile was checked for unsintered tablets and sintered tablets.

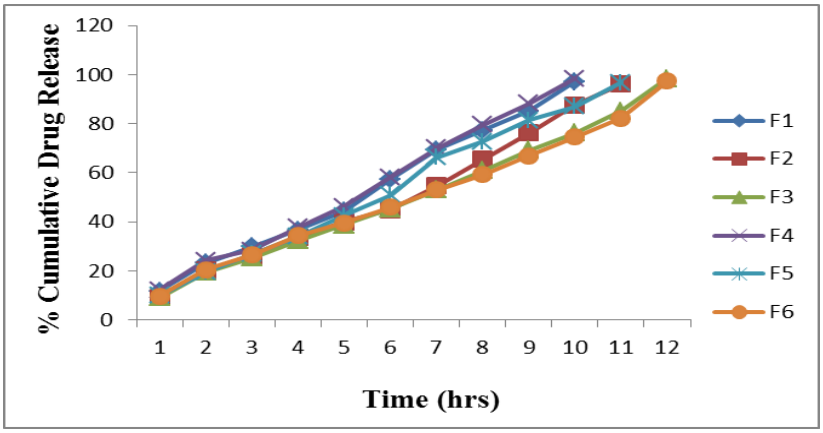

Fig. 9: Percentage drug released vs time plots of unsintered formulations F1-F6

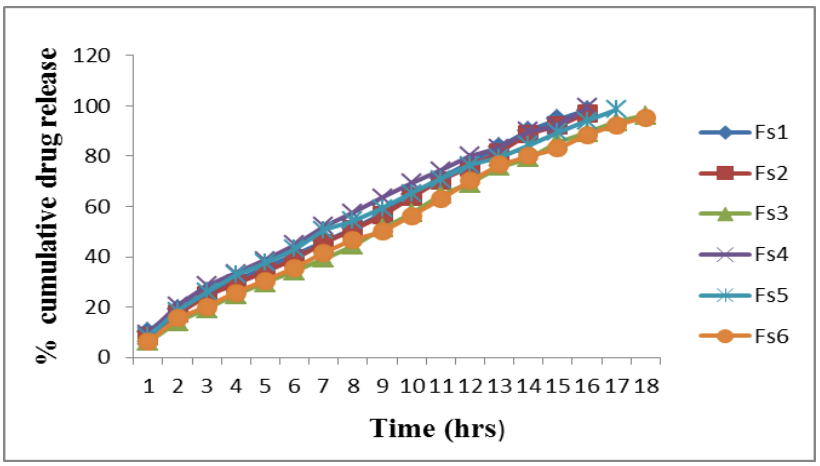

Fig. 10: Percentage drug released vs time plots of sintered formulations Fs1-Fs6

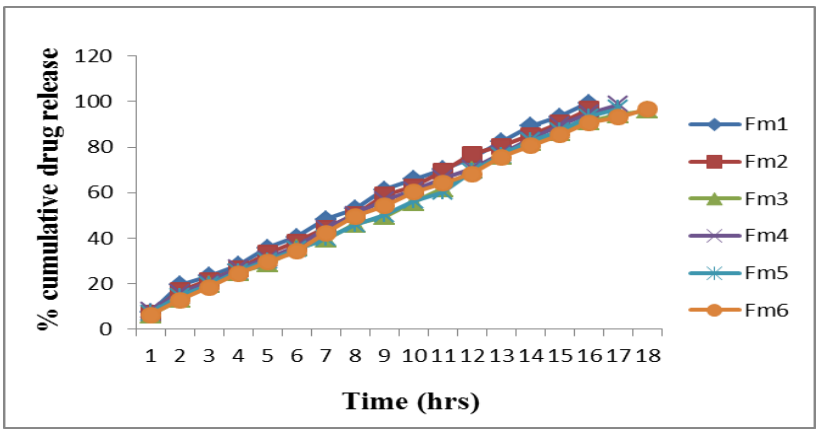

Fig. 11: Percentage drug released vs time plots of sintered formulations Fm1-Fm6

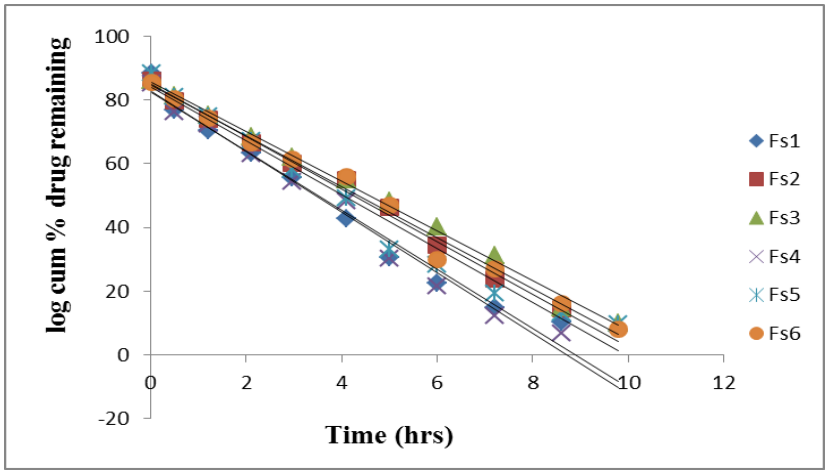

Fig. 12: Log cumulative percent drug remaining vs time plots (first order) of formulations Fs1-Fs6

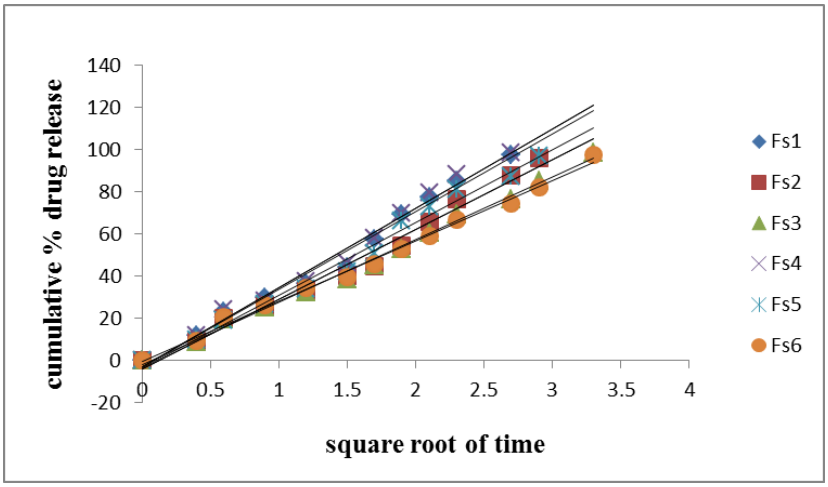

Fig. 13: Cumulative percent drug relased vs square root of time (higuchi's plots) of formulations Fs1-Fs6.

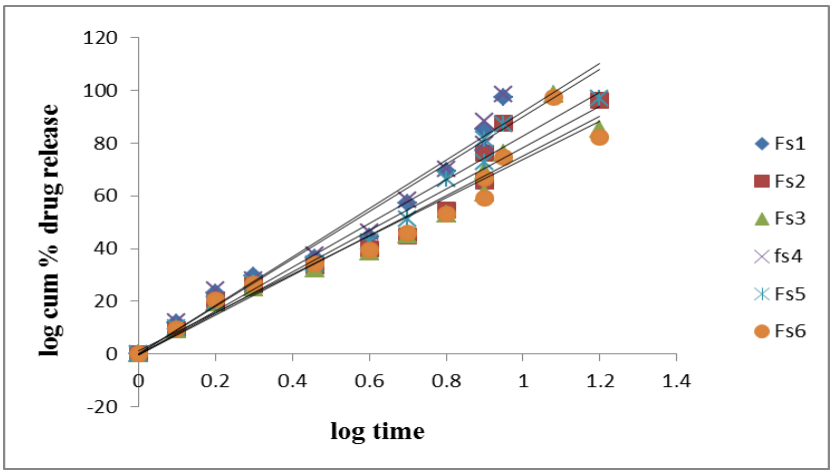

Fig. 14: Log cumulative percent drug released vs log time (peppa's plots) of formulations Fs1-Fs6

Stability studies

Short term stability studies were performed over a period of 3 weeks (21 days) on the optimized tablet formulation Fs6. Sufficient number of tablets (25) were packed in HDPE container and kept in Stability Chamber maintained at 45°±1 ° C. and 75% RH for 3 weeks (21 days) samples were taken on 21st day for evaluation of hardness, friability, drug content estimation which were found to be within range and *in-vitro* studies were performed to determine the drug release profile.

Appearance: Tablets kept for stability studies were examined. The colour of all the formulation was similar before and after stability studies.

The estimation of hardness, friability, wt variation and drug content and data of dissolution and *in-vitro* studies are shown in tables no 24 and 25 respectively.

Table 24: Evaluation data of stability formulation Fs6

Formulation	Tablet Hardness (kg/cm^2)*	Tablet thickness (mm)*	Weight variation (mg)*	Friability (%)*	Drug content (%)*
Fs6	7-8	3.6±0.10	200 ±2	0.20 ±0.02	99.87±0.20

All values are expressed as mean ± SD, n=3, F=formulation code.

Table 25: *In-Vitro* release data of stability formulation Fs6

Sr. no.	Time (hrs)	Cum% drug released	
		1st day	21st day
1	1	7.15±0.35	6.85±0.11
2	2	15.53±0.21	15.20±0.48
3	3	20.09±0.73	19.54±0.56
4	4	25.66±0.28	25.47±0.84
5	5	30.52±0.17	30.12±0.75
6	6	35.53±0.44	34.83±0.11
7	7	40.67±0.48	41.07±0.48
8	8	45.71±0.56	44.81±0.56
9	9	51.08±0.32	51.48±0.75
10	10	56.13±0.77	55.38±0.55
11	11	62.80±0.11	62.47±0.36
12	12	69.30±0.48	68.90±0.69
123	123	75.58±0.56	75.38±0.56
14	14	79.18±0.75	78.18±1.75
15	15	83.02±0.77	82.62±0.31
16	16	88.53±0.56	88.74±0.65
17	17	92.32±0.75	92.45±0.85
18	18	95.87±0.78	94.58±0.15

All values are expressed as mean ± SD, n=3, F=formulation cod

CONCLUSION

At the end, from the experiments carried out and results obtained, it can be concluded that the developed formulations achieved the objective of the investigation. The data obtained from the study of "Effect of Sintering on Sustained Release profile of β-Blocker tablet prepared by Direct Compression Method." FTIR, DSC, Hardness, Friability, % drug content, % drug release, weight variation test of all the formulations were within its range. During sintering, the formulations did not undergo any degradation or complexation by which its release could be retarded. The various time points and temperature alongwith the concentration and type of polymer influences the release and compression characteristics of the sustained release tablets. The dissolution study shows that the formulation Fs3 containing Eudragit RS 100 and HPMC K4 M (2:1) In combination shows 96.31% release profile in 18 hr when subjected to thermal sintering at 80°C for 5 hr. whereas, the formulation Fs6 containing Eudragit RS 100 and HPMC K4 M (1:2) in combination shows 95.41 % release profile in 18 hr when subjected to thermal sintering at 80°C for 5 hr.

Formulation Fm3 containing Eudragit RS 100 and HPMC K4 M (2:1) and Fm6 containing Eudragit RS 100 and HPMC K4 M (1:2) provided 97.21 % and 97.68 % release profile in 18 hr when subjected to microwave sintering at 100 watt for 6 min.

Sintering *i.e.* Application of heat, causes the bonding of adjacent particle surfaces in a mass of powder or in a compact leading to the retardation of drug release. The sintered tablets showed more strength than unsintered tablet and sintered tablet show less drug release than the unsintered tablet. FT-IR, Differential Scanning Calorimetry studies ruled out the occurrence of drug interaction after sintering condition. The stability study conducted as per the ICH Guidelines for optimized formulation was found to be stable.

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