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FORMULATION AND EVALUATION OF SUSTAINED RELEASE TABLETS OF PROPRANOLOL HYDROCHLORIDE

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ABSTRACT

The main aim of proposed work was to develop propranolol hydrochloride matrix tablets, sustained release dosage form, for the treatment of hypertension. Sustained release formulation is the drug delivery system that designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of single dose. The matrix tablets were prepared by direct compression method using hydroxypropymethylcelluose (HPMC K4M), Avicel pH 102**,** magnesium stearate and talc. In the formulation HPMC K4M and magnesium stearate used in varying ratios. Tablets blends were evaluated for loose bilk density, tapped density, compressibility index and angle of repose shows satisfactory results. The compressed tablets were then evaluated for various physical tests like diameter, thickness, uniformity of weight, hardness, friability and drug content. The results of all these tests were found to be satisfactory. The in vitro dissolution study was carried out for 12 hours using paddle method in phosphate buffer (pH6.8) as dissolution media. Formulation F6 shows – of drug release at the end of 12 hours.

KEYWORD: HPMC K4M, Propranolol hydrochloride, matrix tablets.

INTRODUTION

Oral route of drug delivery is the most preferred route of the various drug molecules among, all other routes of drug delivery because of ease of administration, patient compliance and flexible design of dosage form.[1] Sustained release formulation maintains a uniform blood level of drug with better patient compliance as well as increased efficacy of drug. Sustained release tablets are generally taken once or twice a day during a course of treatment whereas in

conventional dosage forms there is need to take 3-4 times dosage in a day to achieve the same therapeutic action.[1,2]

Propranolol hydrochloride, a non-selective beta –adrenergic blocker, has been widely used in the treatment of hypertension, angina pectoris, and pheochromocytoma and cardiac arrhythmias.[3] Because of its relatively short plasma half-life, patients are routinely asked to take propranolol hydrochloride in divided daily dose, once every 6-8 hr. such frequent drug administration may reduce patient compliance and therapeutic efficacy.[4] In recent years, slow or sustained release formulation of propranolol hydrochloride have become available with claims that these formulation maintain beta adrenoreceptor blockade throughout a 24 h period and enable the drug to be given once daily.[4,14] The half-life of propranolol hydrochloride is 3to 5 h. the daily dose of propranolol is 40 mg daily given in divided dose. Therefore, to improve patient compliance and to decrease the incidence of adverse effects and side effects, propranolol is formulated as a sustained release table using hydroxypropymethylcelluose. Then the prepared tablets were evaluated for appearance, weight variation, diameter, thickness, hardness, friability, drug content and in vitro drug release.

MATERIALS AND METHODS

Materials

Propranolol hydrochloride was obtained as a gift sample Sai supreme chemicals Tamilnadu and otheringredients like HPMC K4M and Avicel pH 102 and magnesium stearate were gifted by SD Fine chem. Mumbai.

Method

Sustained release tablets of propranolol were prepared by developing the formulate using variable concentration of polymer like HPMC K4M as shown in table no 1 the concentration of propranolol was kept constant for all batches of formulation. Proparnolol and all excipients were weighed accurately except talc and magnesium stearate, after that blended in mortar with the help of pestle for 5-10 min. after the mixing of drug with excipient, required amount of talc and magnesium stearate were added and further mixing was done for 4-5 min. the gross weight of each formulation was kept 300 mg.

Table no.1: Formulation of sustained release tablets of propranolol.

Ingredients	F-I	F-II	F-III	F-IV	F-V	F-VI
Propranolol hydrochloride	20	20	20	20	20	20
HPMC K4M	150	155	160	165	170	175
Avicel pH 102	100	95	90	85	80	75
Magnesium stearate	20	20	20	20	20	20
Talc	10	10	10	10	10	10
Total weight	300	300	300	300	300	300

Evaluation of Powder Blends

IR spectral analysis[7,11,13]

Compatibility of drug with excipients was carried out using I.R. spectroscopy. Infrared spectra of formulation were recorded by KBr method using Fourier Transform Infrared Spectrophotometer (Iraffinity1®Shimadzu, Japan.). A baseline correction was made by using dried potassium bromide. Scanning was done from 450to 4000cm^{-1}.

Angle of repose[6,7]

The angle of repose of tablet blends was determined by the funnel method. The blends were allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

Tan θ = h / r

Where; θ= angle of repose

r=radius of the base

h=height from tip of funnel to the surface of graph paper.

Bulk density[6,7]

Apparent bulk density was determined by pouring a weighed quantity of tablet blends into graduated cylinder and measuring the volume and weight.

$$\text{Bulk density} = \frac{\text{mass of powder}}{\text{bulk volume of the powder}}$$

Tapped density[6,7]

Accurately weighed quantity of powder was carefully poured in to graduated 100 mL measuring cylinder through large funnel. The cylinder was then tapped 100 times from a constant height and the tapped volume was read. This is expressed in gm / mL and determined by the following formula.

Tapped density = Weight of the powder / tapped volume.

Car's index[6,7]

It is also one of the simple method to evaluate flow property of a powder by comparing the bulk density and tapped density. Carr's index is an indication of the compressibility of a powder. It is expressed in percentage and determined by the following formula;

% Car's consolidation index = Tapped density – Bulk density / Tapped density x 100

Hausner's ratio[6,7]

A small index like percentage compressibility index has been defined by Hausner's. Values less than <1.25 indicates good flow, whereas greater than 1.25 indicates poor flow. Added glidant normally improves flow of the material under study. Hausner's ratio can be calculated by; **Hausner's ratio = Tapped density / Bulk density x 100**

Evaluation of tablets

Thickness Test[5,6,9,10,12]

The thickness of the tablet is mostly related to the tablet hardness can be uses as starting parameter is to be selection of tablets were randomly and then from each tablet thickness was determined using a Vernier calliper and the reading was recorded in millimeters.

Hardness[5,6,9,10,12]

Hardness (diametric crushing strength) is a force required to break a tablet cross the diameter. The hardness of a tablet is an indication of its strength. The tablet should be stable to mechanical stress during handling and transportation. The degree ofhardness varies with the different manufactures and with the different types of tablets. The hardness was tested by using Monsanto hardness tester.

Thickness[5,6,9,10,12]

Three tablets from each batch of formulation were collected and the thickness of the tablets was measuredwith the help of venires caliper. The average thickness was calculated.

Friability[5,6,9,10,12]

Roche friability test apparatus was used to determine the friability of the tablets. Twenty pre-weighedtablets were placed in the apparatus and operated for 100 revolutions and then the tablets were reweighed. The percentage friability was calculated according to the following formula.

%Friability=initial weight- final weight/initial weight x100

Weight variation[5,6,9,10,12]: The weight of tablet is measured to ensure that a tablet contain the proper amount of drug. Randomly selected twenty tablets form each batch were subjected to weight variation test as per Indian Pharmacopoeia 2007. Not more than two individual weight deviate from the average weight by more than 5% percentage deviation.

Uniformity of Content[5,6,12]: Drug content uniformity was determined by dissolving the tablets in ethyl alcohol and filtering with whattman filter paper. The filtrate was evaporated and drug residue dissolved in 100ml phosphate buffer pH 6.8. The 5 ml solution was then diluted with phosphate buffer pH 6.8 to 20ml, filtered through whattman filter paper, and analyzed at 289 nm using UV double beam spectrophotometer.

In –vitro drug release studies[5,8]: In vitro release of propranolol hydrochloride from extended release tablets were determined using USP II dissolution apparatus in 900 mL of phosphate buffer pH(6.8) at constant temperature of 37°c ± 5°c at 50 rpm. Aliquots (5mL) of the solutions were withdrawn from the dissolution medium to maintain the sink condition. These aliquots were filtered and the absorbance of these solutions was measured by using double beam ultra-violet spectrophotometer at 289 nm against fresh phosphate buffer solution as blank.

RESULTS AND DISCUSSION

Performulation studies: Drug excipients compatibility studies were performed by force degradation and Fourier transform infrared spectroscopy. Results obtained from (figure no 1&2) showed that drug and excipients were compatible with each other.

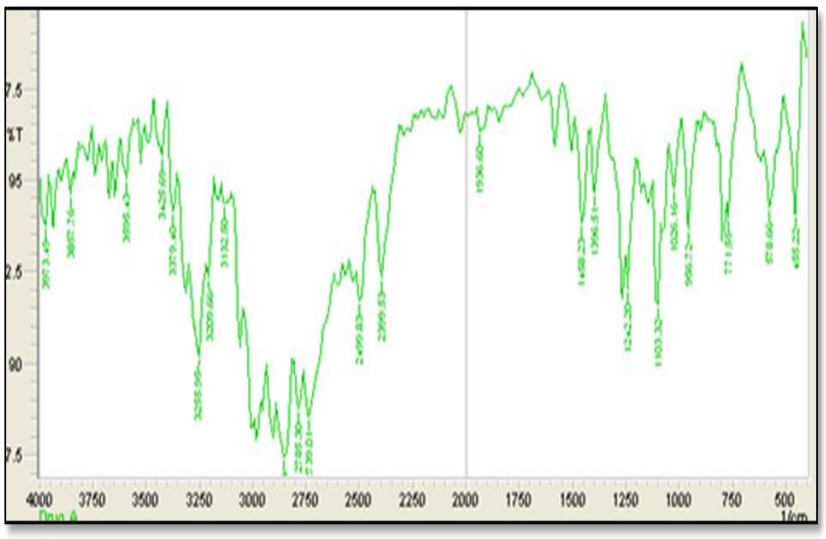

Fig. no. 1: FTIR spectrum of pure drug.

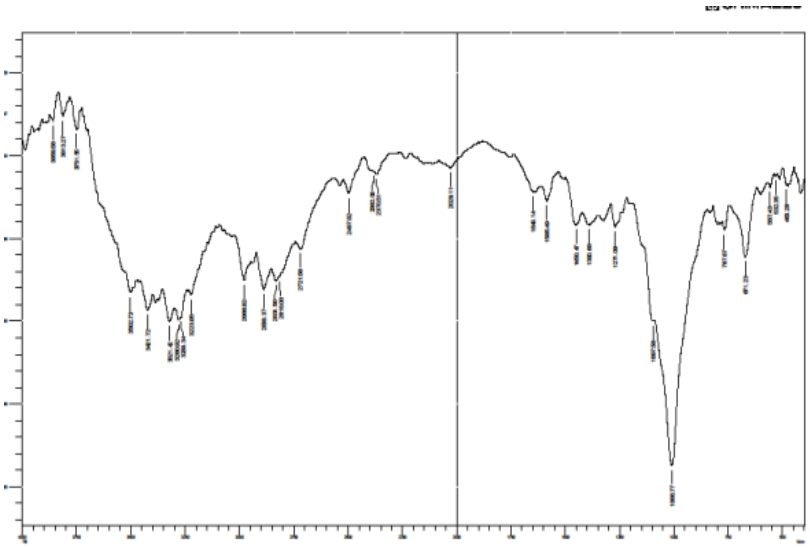

Fig. no. 2: FTIR spectrum of tablet.

Evaluation of pre-compression parameters

Table no. 2: Evaluation Pre-compression parameters of powder blend.

Formulation code	Bulk density (gm/cc)	Tapped density (gm/cc)	Hausner's ratio	Compressibility index	Angle of repose (º)
F1	0.32	0.38	1.1	15.78	25.23
F2	0.34	0.39	1.1	12.82	21.20
F3	0.29	0.33	1.1	12.12	19.24
F4	0.31	0.35	1.1	11.42	18.20
F5	0.33	0.36	1.0	8.33	16.23
F6	0.31	0.34	1.0	8.82	16.10

Evaluation post compression parameters

Table no.3: Evaluation post compression parameters of Propranolol tablets.

Formulation no	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	%Friability	%Drug content
F1	296	5.3	4.2	0.49	93.01
F2	293	5.4	4.5	0.44	94.30
F3	295	5.7	4.5	0.46	91.43
F4	297	5.9	4.1	0.43	92.04
F5	295	5.3	4.4	0.47	92.84
F6	296	5.8	4.3	0.56	96.19

Table no.4: In -Vitro Dissolution Profile of Formulation F1 –F6.

Time (Hr.)	F 1	F 2	F 3	F 4	F 5	F 6
0	0	0	0	0	0	0
1	8.18	6.13	8.80	8.79	9.01	10. 27
2	16.36	1.88	16.36	14.31	14.31	22.5
3	20.45	20.45	22.5	24.54	28.63	30.68
4	28.63	30.68	30.68	30.68	34.77	34.77
5	36.81	40.90	38.86	40.90	45.00	42.95
6	42.95	51.13	47.04	51.13	55.22	53.18
7	51.13	57.27	55.22	61.36	63.40	61.36
8	55.22	61.36	63.40	65.45	69.54	65.45
9	59.31	63.40	67.5	69.54	75.68	79.77
10				71.59	77.72	83.86
11					79.77	87.95
12						96.13

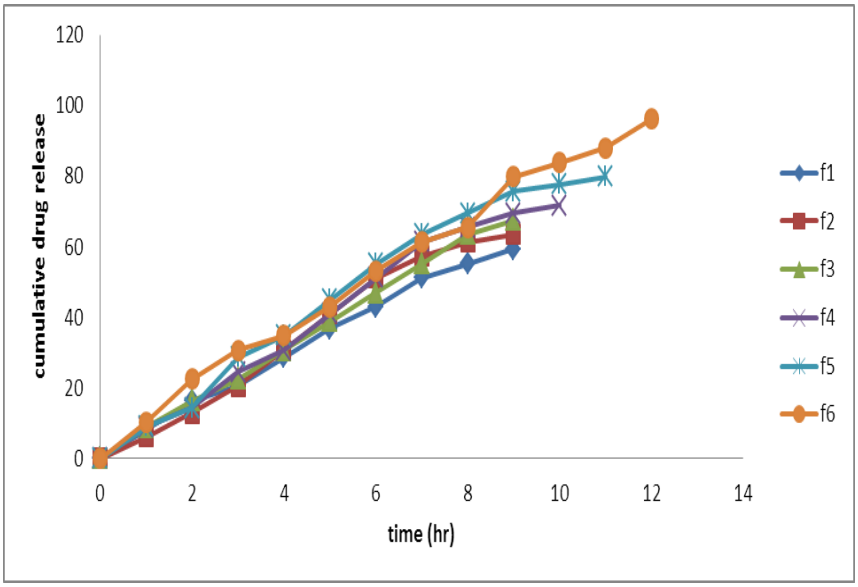

Fig no. 3: dissolution profile of various formulations (F1-F6) of propranolol hydrochloride The present investigation was undertaken to formulate and evaluate propranolol hydrochloride matrix tablet for extended release dosage form. All tablets formulations were subjected to various evaluation parameters and the results obtained were within range.

The results of the pre –compression parameters evaluation suggested that all the formulation exhibited the good flow properties. The weight variation test was in range 293mg-297mg.The hardness of tablets was range of 5.3 to 5.9 kg /cm^2. The thickness of the tablets was in the range of 4.1 to4.5 mm, which shows uniform thickness of the tablets. The friability was in the range of 0.43% to 0.56 %. The percentage drug content for different tablets formulation varied from 91.43 to 96.19% was found to be within the limit. The % drug release of different

formulation was ranged in 59.31% to 96.13% was extended for 9 to 12 hrs. F-6 formulation showed 96.13% drug release in 12 hrs.

CONCLUSION

Form the above results, it can be concluded that formulation F-6 has achieved the objective of prolonged drug release and thus improve the patient convenience by reducing dosing frequency. It was promised extended release tablets of propranolol hydrochloride and appears to be further by conducing bioavailability studies in human volunteers and long term testing stability testing.

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