CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.23887635

Available online at: http://www.iajps.com Research Article

FORMULATION AND EVALUATION OF CONTROLLED RELEASE MATRIX TABLETS OF PROPRANOLOL HYDROCHLORIDE FOR HYPERTENSION

Dr. R Sridhar Babu [1], Syed Asimuddin [2], Ameen Fatima[2], Sana Begum[2], Syed sami ahmed [2]

1-Professor and Principal, Department of Pharmaceutics, Shadan College of Pharmacy, Peeramcheru, Hyderabad, Telangana 500086

2- Department of Pharmaceutics, Shadan College of Pharmacy, Peeramcheru, Hyderabad, Telangana 500086

Abstract:

The aim of the present work is to formulate and evaluate sustained release of Propranolol matrix tablets used for treatment of Hypertension. Formulate of CR Propranolol is proposed considering the adverse event profile and high fluctuation index of Propranolol observed with CR dosage forms. Propranolol was subjected to Preformulation studies, based on the results obtained Propranolol controlled release tablets were successfully formulated. Formulations prepared by direct compression technique. Set of trials were formulated for which Propranolol evaluated parameters (bulk density, tapped density, compressibility index, Hausner's ratio, weight, thickness, hardness) were found to lie within the specifications. Dissolution study was performed in USP type II apparatus at 100 RPM in pH 6.8 phosphate buffer. From the results of the in vitro study it appears that the release of the Propranolol was significantly influenced by the characteristics of the polymer used.

Keywords: *Propranolol Hydrochloride, polymers, FTIR studies, Direct compression technique, In vitro drug release studies.*

Corresponding author:

Dr. R Sridhar Babu,

Professor, Department of Pharmaceutics, Shadan college of pharmacy

Peerancheru, Hyderabad - 500086

Mobile:

Email Id:

QR CODE

Please cite this article in press ***R Sridhar Babu*** *et al.,* ***Formulation And Evaluation Of Controlled Release Matrix Tablets Of Propranolol Hydrochloride For Hypertension.,****. Indo Am. J. P. Sci, 2026; 13(11).*

INTRODUCTION:

Oral administration of drugs is the most common and preferred route for delivery of therapeutic agents. The popularity of the oral route is due to patient compliance, ease of administration, accurate dosing, cost-effective manufacturing methods, and generally improved shelf-life of the product. The rationale for development of controlled release formulation of a drug is to enhance its therapeutic benefits, minimizing its side effects. The first commercially developed oral controlled release formulation was the pellet filled capsule called Spansules which was introduced in the year 1950 by Smith, Kline and French. These were formulated by coating a drug onto nonpareil sugar beads and further coating with glyceryl stearate and wax. Since then number of strategies were developed to obtain controlled release of a drug in the body. They vary from simple matrix tablets or pellets to more technologically sophisticated controlled release systems which have been introduced into the marketplace. Successful formulation of a controlled release dosage form usually involves consideration of many factors such as the physicochemical properties of the drug, physiological factors and manufacturing variables.

Advantages

• Reduction in frequency of drug administration
• Improved patient compliance
• Reduction in drug level fluctuation in blood.
• Reduction in total drug usage when compared with conventional therapy.
• Reduction in drug accumulation with chronic therapy.
• Stabilization of medical condition because of more uniform drug levels.
• Improvement in bioavailability of some drugs because of spatial control.
• Economical to the health care providers and the patient.
• Product life-cycle extension.

Limitations

• Delay in onset of drug action.
• Possibility of dose dumping in case of a poor formulation strategy.
• Increased potential for first pass metabolism.
• Greater dependence on GI residence time of dosage form.
• Possibility of less accurate dose adjustment in some cases.
• Cost per unit dose is higher when compared with conventional doses.

MATERIALS:

Propranolol Hydrochloride was procured from Synpharma Research Lab, Hyd, Eudragit RS 100, Ethyl cellulose, Micro crystalline cellulose , Magnesium Stearate and Talc were obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

METHODOLOGY:

Table-1: Formulation table of Propranolol Hydrochloride controlled release tablets

S.NO.	INGREDIENTS	F1	F2	F3	F4
1	Propranolol Hydrochloride	40	40	40	40
2	Ethyl cellulose	50	100	-	-
3	Eudragit RS 100	-	-	50	100
4	Microcrystalline Cellulose	305	255	305	255
5	Magnesium stearate	3	3	3	3
6	Talc	2	2	2	2
7	Total weight	400	400	400	400

Preparation method:

Tablets of Propranolol Hydrochloride were prepared by direct compression method as per the formulae given in Table. All the materials required as per the formulae were blended in a closed polyethylene bag. The blends were compressed into tablets on a tablet punching machine to a hardness of 6 kg/cm ^{2} using 8 mm concave punches.

EVALUATION STUDIES

Bulk Density

The powder were precisely weighed from all trials and was slightly shaken to breakdown any agglomerates formed. Then it was kept in the measuring cylinder of required quantity. The volume engaged by the granules was calculated. The bulk density of granules was calculated by the formula.

Bulk density = weight of sample taken /volume noted

Tap density

The granules were precisely weighed from all trials. It was slightly shaken to breakdown any agglomerates formed. Then it was kept in the measurable cylinder of required quantity. Then the measuring cylinder was tapped until there is no further variation in volume. This is the tapped volume. The tapped density of granules was calculated as given below.

Tapped density = weight of sample taken / tapped volume

Where,

V_o = initial volume

V_f = final volume.

Compressibility index

Carr's index also known as compressibility index is the index which determines the flow property with small quantity. Carr's indexes of the granules was calculated as given below,

Carr's index (%) = [(TBD-LBD)/ TBD] x100

Hausner's ratio

It is used to predict the flow property and this is underarticulate friction. Hausner's ratio was calculated as given below,

Hauser's Ratio = Tapped bulk density / Loose bulk density

The value of Hauser's ratio less than 1.25 directs good flow while higher than 1.5 directs poor flow.

Angle of repose

Angle of Repose It can be determined by using classic funnel method. The prepared granules which the flow property need to be analyzed was weighed accurately. The funnel height was accustomed in the way that the lowest just touched the top of heap of granules. Granules was permitted to freely flow through the funnel orifice to the surface. The radius of heap formed was measured. The angle of repose was determined using the equation.

$$\theta = \tan^{-1} h/r$$

Where

h = height of pile

r = radius of the base of the pile

θ = angle of repose

Evaluation Of Tablet

Weight Variation

Weight variation is one of the official quality control tests for tablets. This is important because it directly relates with drug content. To do this test, minimum 20 tablets were weighed separately and average weight was calculated and compared with individual weight. The deviation gives the report of the weight variation. Usually it is expressed in percentage. Weight variation should be done in process checking and for finished products.

Thickness

The dimensions like thickness and diameter of the tablets may have important effect in the drug content and other parameters. Hence it is required to maintain the thickness and diameter in the optimum acceptable range. This can be done by means of Vernier caliper. 10 tablets prepared from each trial were used. The average values were noted.

Tablet Hardness

Monsanto hardness tester was utilized to find the tablet hardness. In each formulation, 10 tablets were taken and the hardness was measured. The tablet was kept in the perfect position in the axis in the two jaws of instrument. The measurement should be zero kg/cm^2 at this stage. The knob is rotated to apply force to the tablet, the force is continued until there is fracture in the tablet. The point at which tablet breaks is break point and it was noted in kg/cm^2.

Friability

Tablet strength can be measured by using friabilator. This is performed to know the impact of shock abrasion on tablets when on travelling and handling. The test involves keeping the tablets in a plastic chamber and allowing it to revolve at 25rpm for 4 minutes that is equivalent to 100 rotations. In this test the tablets are subjected to drop at heights of 6 inches in each revolution. The initial weight and final weight of the tablets after dedusting were noted. The limit acceptable is less than 1% weight variation. It was calculated as follows. The percentage friability was measured using the formula,

$$\% F = \{1-(Wo/W)\} \times 100$$

Where,

% F = friability in percentage

W o = Initial weight of tablet

W = weight of tablets after revolution

Drug Content

The drug content directly relates to the pharmacological efficacy, so it is mandatory to do the drug content test. It is an official quality control test. The drug content in all formulations were analyzed by triturating 20 tablets in mortar and pestle, then from the powder 75 mg equivalent of Propranolol Hydrochloride was taken and transferred to 100ml standard volumetric flask. Then the volume was prepared to 50ml with pH 6.8 phosphate buffer. This was shaken for 15 min to mix. Then the volume was prepared to 100ml with phosphate buffer. The solution was strained by using whatmann filter paper and then it is diluted and absorbance was determined by using UV-Visible spectrophotometer at 246 nm using pH 6.8 phosphate buffer as blank.

In vitro release studies
This in vitro release can be done by using USP dissolution apparatus I. The test is performed at 50 rpm. The media used were pH 1.2 buffer for initial 2 h, followed by 8 h in pH 6.8 phosphate buffer. The temperature was maintained at 37 ± 0.5°C. The samples were taken at predetermined time and the dissolution basket is replenished with the buffer. The taken samples were filtered through filtered through a 0.45 membrane filter. The absorbance was measured at 246 nm.

Stability studies:
The stability studies are performed to analyze the quality of drug and drug product with exposure to different temperature and humidity conditions on estimated time. General conditions like light, environment and other general parameters are maintained and the general evaluation tests were performed at different time interval periods. It is undesirable and time consuming to do full shelf life period study. To avoid this accelerated stability studies has been adopted.

RESULTS AND DISCUSSION:

Pre compression Parameters

a) **Bulk Density:** The bulk density for the formulated blend was carried out for all formulation and found in the range of 0.612-0.622.

b) **Tapped density:** The tapped density for the formulated blend was carried out for all formulation and found in the range of 0.710-0.720.

c) **Angle of repose:** The angle of repose for the formulated blend was carried out. It concludes that all the formulations blend was found to be in the range of 28 to 30^0

d) **Compressibility index:** Compressibility index was carried out, it found between10% to 14.23 % indicating the powder blend have the required flow property for compression.

Table-2: Results of Pre-compression parameters

F. No	Bulk density	Tapped density	Compressibility index	Hausner ratio	Angle of repose(0)
F1	0.620	0.710	13.15	1.14	28^0
F2	0.612	0.718	14.23	1.17	29^0
F3	0.622	0.719	13.46	1.14	30^0
F4	0.619	0.720	13.89	1.17	29^0

Post compression parameters
Weight variation:
All the formulated (F1 to F4) tablets passed weight variation test as the % weight variation was within the pharmacopoeia limits of ±7.5% of the weight. The weights of all the tablets were found to be uniform with low standard deviation values.

Thickness:
Tablets mean thickness were uniform in F1 to F4 formulations and were found to be in the range of 3.26 mm to 3.69 mm.

Hardness:
The measured hardness of tablets of each batch ranged between 4.79 to 5.01 kg/cm^2. This ensures good handling characteristics of all batches.

Friability:
The % Friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable.

Content Uniformity:
The percentage of drug content for F1 to F4 was found to be between 90.59 % and 94.25 % of Propranolol Hydrochloride it complies with official specifications.

Table-3: Results of Evaluation parameters of tablets

F. No.	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
F1	400	3.26	5.01	0.35	92.19
F2	400	3.29	4.79	0.40	94.25
F3	399	3.58	4.96	0.39	93.16
F4	400	3.69	4.82	0.42	90.59

In-vitro Dissolution Study

Table-4: In vitro release data of tablet F_1 to F_4

Time (hrs)	F_1	F_2	F_3	F_4
0	0	0	0	0
1	17.26	18.10	16.59	18.10
2	27.98	29.13	25.18	22.39
3	38.10	37.46	38.43	37.43
4	50.13	52.13	51.16	52.31
5	62.49	63.49	63.91	61.19
6	72.19	75.46	71.80	70.20
7	83.26	85.56	81.92	84.13
8	93.25	96.39	95.43	94.51

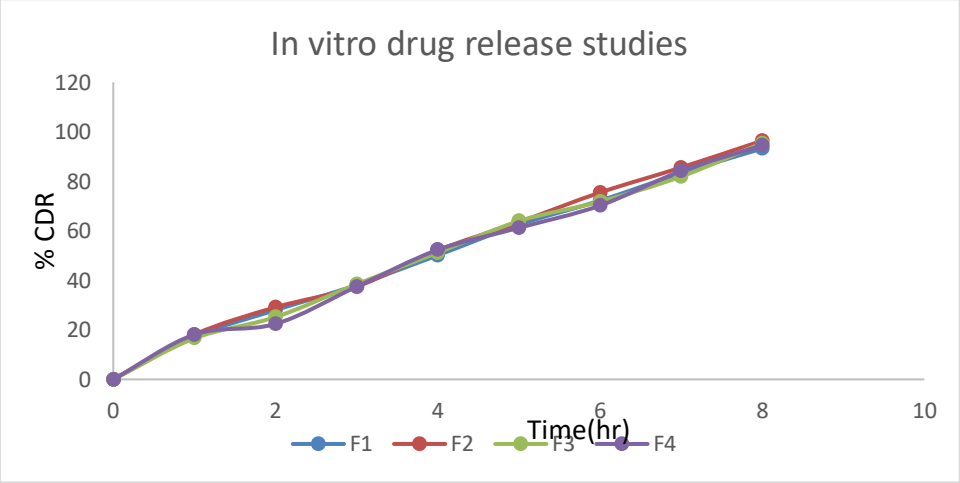


Fig-1: In vitro drug release studies of F1-F4 formulations

Stability studies

There was no significant change in physical and chemical properties of the tablets of formulation F-2 after 3 months. Parameters quantified at various time intervals were shown.

Table-5: Results of stability studies of optimized formulation F2

Formulation Code	Parameters	Initial	1st Month	2nd	3rd	Limits as per Specifications
F-2	**25^{0}C/60%RH**	96.39	95.42	94.68	93.67	**Not less than 85%**
F-2	**30^{0}C/75% RH**	96.39	95.10	94.32	93.49	**Not less than 85%**
F-2	**40^{0}C/75% RH**	96.39	95.02	94.23	93.25	**Not less than85%**

SUMMARY AND CONCLUSION:

Oral route has been the predominantly adopted due to its convenience for drug delivery. This route is considered significantly in the pharmaceutical field, due to its flexibility in formulating the dosage form than other routes. This route of delivery depends on factors such delivery system type, the disease, the patient and the duration of therapy and the characteristic property of the drug. Almost all the oral controlled drug delivery systems follow diffusion or dissolution mechanism of drug release in the GIT.

In the present study, an effort was initiated to prepare the oral CR matrix tablets of Propranolol Hydrochloride to provide a dosage form for prolonged period of time, in order to improve pharmacologic efficacy, reduce the total dose frequency and improved patient compliance. Infrared spectroscopy analysis established the absence of any drug polymer interaction. The CR matrix tablets were prepared by the direct compression method using different polymers as release retardant polymers. The powder was evaluated for angle of repose, bulk density, compressibility index and Hauser's ratio. All the tests revealed that granules showed excellent flow properties.

The resulting tablets were evaluated for official and unofficial tests like diameter, thickness, weight variation, hardness, friability and drug content. All the prepared tablet trials showed acceptable pharmaco technical properties and passes the official pharmacopoeia standards. The in vitro release profiles were applied on various kinetic models. The release studies revealed that the release rate was decreased with increase in polymer proportion. From the results of present study, it appears that the release of Propranolol Hydrochloride was significantly influenced by the characteristics of polymer and excipients used. In-vitro release from the formulation F2 with the hardness of 5.01 kg/cm^2. Higher hardness tablets contain a compact mass of polymer with relatively less pore, resulting in slower release. All other tested parameters of F2 formulation were in the acceptable limits. So, formulation F2 was found to be better than other batch of formulations.

In the current research work, matrix formulation F2 containing Eudragit RS 100 were perhaps show maximum delay of drug release as optimum formulation among all formulations

Stability study was carried out with F2 formulation as per ICH guidelines and found to be stable both in accelerated and long-term stability conditions.

REFERENCES:

1. Diclofenac controlled release tablets employing olibanum resin, IJPSR, 2012; Vol. 3(4): 1090-1095
2. Dwarakanadha Reddy peram, Surya prakash,A, Swarnalatha.D, Usha Sree , Formulation and Evaluation of Ethyl Cellulose Coated Microcapsules of Glibenclamide for Controlled Release, Asian Journal of Chemistry; Vol. 26, No. 3 (2014), 770-772
3. Sujata D. Bansode, Veena S. Kasture, Sarita S. Pawar, Sanjay B. Kasture, Formulation and evaluation of telmisartan microspheres by emulsion solvent evaporation technique, Journal of Applied Pharmaceutical Science Vol. 2 (10), pp. 113-116, October, 2012.
4. GR. Girish Reddy, Design and Evaluation of Sustained Release Capsule of Telmisartan, international journal of advances in pharmacy, biology and chemistry, Vol. 1(3), Jul- Sep, 2012.
5. Avachat, A., and V., Kotwal, 2007 Design and evaluation of matrix-based controlled release tablets of diclofenac sodium and chondroitin sulphate. AAPS PharmSciTech. 8(4):E88. [PMID: 18181548]
6. Kulkarni G.T, Gowthamarajan K, Suresh B. stability testing of pharmaceutical product: an overview. Indian J Phar Edu. 2004, 38(4): p.no.194-202
7. 71) Kanvide S A, Kulkarni M S, Stability of oral solid dosage form: A global perspective. Pharma Time 2005,37(5):p.no. 9-15
8. 72) Mohrle R. Effervescent tablets in Liberman HA, Lachman L, editor. Pharmaceutical dosage form –Tablet, Marcel Dekker Inc, New York:1980, p.no. -232-246(vol-1)
9. 73) Khan G.M., Zhu J.B, "Studies on drug release kinetics from ibuprofun carbomer hydrophilic matrix tablets**"** J. Cont. Rel.,1999, 57, p.no.197-203.
10. 74) Hoyashi T, Kanbe H, Okado M. Suzuki M, Sonobe T. "formulation study and drug release mechanism of a new theophylline Sustained Release preparation" Int. J. Pharm**,** 2005,304, p.no. 91-101.
11. 75) Solinis M.A, Cruz Y. De, Gascon A, Calvo B, Pedraz J. L "Release of Ketoprofen enantiomeres from HPMC K100M matrices – Diffusion studies" Int. J. Pharm., 2002,239, p.no. 61-68.
12. 76)Qiu Y. Chidambaram N, Porter W. Flood K., "Formulation and characterization of new diffusional matrices for Zero – order sustained release" J. Cont. Rel**.,** 1998,52, p.no.149-158.
13. Leon Shargel, Susanna Pong, Andrew B.C., Applied Biopharmaceutics and Pharmacokinetics, Modified-Release Drug Products, Pg 515 Fifth Edition, 2004
14. Chien Y.W., Controlled- and modulated-release drug-delivery systems. Encyclopedia of pharmaceutical technology. New York, Dekker, pgs 281-313, 1992.

15. J. R. Robinson, S. P. Eriksen**,** Theoretical formulation of sustained-release dosage forms.*J Pharm Sci*. 1966.

16. Gilbert S. Banker, Christopher T. Rhodes, Modern Pharmaceutics, Sustained - and Controlled -release drug-delivery systems, Pg 505 Fourth Edition, 2002