Design and characterization of matrix tablet of Prazosin HCl

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Abstract : The main objective of present investigation was to formulate and evaluate sustained release matrix tablets of Prazosin Hydrochloride to improve patient compliance by reducing dosing frequency.Sustained release matrix tablets of Prazosin Hydrochloride was prepared by wet granulation method. Natural polymers like Xanthan Gum and Sodium Alginate was used as release controlling polymers. Povidone used as a binder. Lactose and Microcrystalline cellulose were used as a glidant. Magnesium stearate was used as lubricant. Formulation optimization was done using 3^2full factorial design by taking xanthan gum and PVP K30 as independent variable. Initially trial batches F1 to F7 were taken for Sustained release matrix tablets of Prazosin Hydrochloride by using Xanthan Gum and Sodium Alginate as a polymer. Optimization was done from the overlay contour plot and final batch P12 was prepared and evaluated, found satisfactory. One-month stability study was found satisfactory.Sustained release matrix tablets of Prazosin Hydrochloride was successfully formulated using Xanthan gum as natural gum for release controlling polymer which gives sustained effect up to 12 hours and reduced dosing frequency which ultimately improves patient compliance.

Key Words: Prazosin Hydrochloride, Matrix Tablets, Sustained Release, Xanthan Gum, Sodium alginate

I. INTRODUCTION

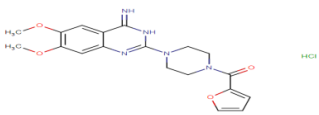
INTRODUCTION

Introduction of Sustained release drug delivery system[(1 to 16)]

The delivery of accurate drug concentration to the site of action in order to achieve appropriate therapeutic effect or response in the body is the key objective of the drug delivery systems. There are two types of delivery systems which are generally used. Modified release drug delivery systems are the other type. In order to achieve definite therapeutic responses, there is an alteration in the rate, site and kinetic performance of the API released inside the body in these types of drug delivery systems. These include: Targeted drug delivery systems, delay or repeated drug delivery systems and prolonged or extended drug delivery systems (Controlled release, Sustained release and long-acting dosage forms). In this review article, we selected sustained release drug delivery matrix system, hence only this topic will be focused in detail.

Sustained release tablets and capsules are commonly taken only once or twice daily, as compared with counterpart conventional forms that may have to be taken three or four times daily to attain the same therapeutic effect. Sustained-release formulations provide an immediate release of drug that produces the desired therapeutic effect, followed by a gradual release of additional amounts of drug to maintain this effect over a predetermined period. There is a growing interest in the pharmaceutical industry for sustained release oral drug delivery systems. In addition, there is a high interest for design a dosage product that allows high drug loading, particularly for drugs with high water solubility. The oral administration is the most popular route used for sustained release delivery due to ease of administration, convenience, greater flexibility in dosage form design, ease of production and low cost of production of such a system. Solid dosage forms are the most of the sustained release delivery systems for oral use and based on diffusion, dissolution or a combination of both mechanisms for the control of drug release.

Matrix tablets can be defined as the oral solid dosage forms in which the drug is homogeneously dispersed or dissolved within the hydrophilic or hydrophobic polymeric matrices. The preparation of sustained release matrix tablets involves the direct compression of blend powder mixture of drug, retardant material and other additives to formulate a tablet in which the drug is dispersed in a matrix of the retardant. Alternatively, drug, retardant blend and other additives may be granulated prior to compression. These systems release the drug in a continuous manner by dissolution-controlled and diffusion-controlled mechanisms. Prazosin is a selective α-1-adrenergic receptor antagonist used to treat hypertension. It has also been used to decrease urinary obstruction and relieve symptoms associated with symptomatic benign prostatic hyperplasia.



Materials and Methods Prazosin Hydrochloride was obtained from Zydus Research Centre, Ahmedabad,Sodium Alginate Polymer, Xanthan Gum Polymer, PVPK-30, Lactose MCC, Colloidal Silicone dioxide Talc, Magnesium Stearate were obtained ACS Chemicals, Ahmedabad.

Drug Excipient Compatibility Study

The Results of compatibility study were given in below table. There is no any change observed in initial and physical mixture sample.

Formulation of SR Tablet of Prazosin HCl[17]

Suatained Release Matrix Tablet formulation of Prazosin HCl using natural polymers like Xanthan Gum & Sodium alginate. PVP K30 was used as a binder. Formulation table for trial batches F1-F7

Tablets formulations were prepared by wet granulation method. All the powders were passed through 60 mesh sieve. Required quantity of drug, and lactose were mixed thoroughly. Then, polymer dissolve in granulating agent (isopropyl alcohol) was added slowly with uniform mixing the get a wet mass. The wet mass was passed through sieve no 10 to obtain wet granules. The granules were dried at 50ºC for 5 to 6 hrs in try dryer. The dried granules were passed through sieve.no.22, after blending with lubricants were compresses into tablet compression machine using tablet compression machine. Each tablet contained 3 mg of Prazosin HCl and other pharmaceutical ingredients as listed in below Table.

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7
Prazosin HCl	3	3	3	3	3	3	3
Microcrystalline Cellulose (Avicel pH 102)	77	57	37	77	57	37	37
Lactose (DCL 11)	80	80	80	80	80	80	80
PVPK30	10	10	10	10	10	10	10
Xanthan Gum	20	40	60	-	-	-	30
Sodium Alginate	-	-	-	20	40	60	30
Colloidal silicon dioxide	4	4	4	4	4	4	4
Magnesium Stearate	4	4	4	4	4	4	4
Talc	2	2	2	2	2	2	2
Isopropyl Alcohol	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Total	200	200	200	200	200	200	200

Physical characteristics of prepared blend of Prazosin HCl

Preliminary trial of Prazosin HCl Matrix tablets

Batch	Bulk density (gm/ml) (n=3)	Tapped Density (gm/ml) (n=3)	Carr's Index (%) (n=3)	Hausner's Ratio (n=3)	Angle of Repose (ϕ) (n=3)
F1	0.44 ± 0.12	0.57 ± 0.16	22.80 ± 0.09	1.29 ± 0.02	30.50 ± 0.08
F2	0.43 ± 0.08	0.56 ± 0.14	23.21 ± 0.08	1.30 ± 0.05	31.57 ± 0.09
F3	0.41 ± 0.10	0.52 ± 0.10	21.11 ± 0.10	1.26 ± 0.06	29.37 ± 0.08
F4	0.45 ± 0.06	0.59 ± 0.08	23.72 ± 0.13	1.31 ± 0.01	30.62 ± 0.06
F5	0.40 ± 0.08	0.51 ± 0.06	21.56 ± 0.15	1.27 ± 0.08	29.77 ± 0.09
F6	0.42 ± 0.05	0.55 ± 0.12	23.63 ± 0.11	1.31 ± 0.09	31.58 ± 0.07
F7	0.45 ± 0.10	0.59 ± 0.10	23.72 ± 0.10	1.31 ± 0.04	30.00 ± 0.08

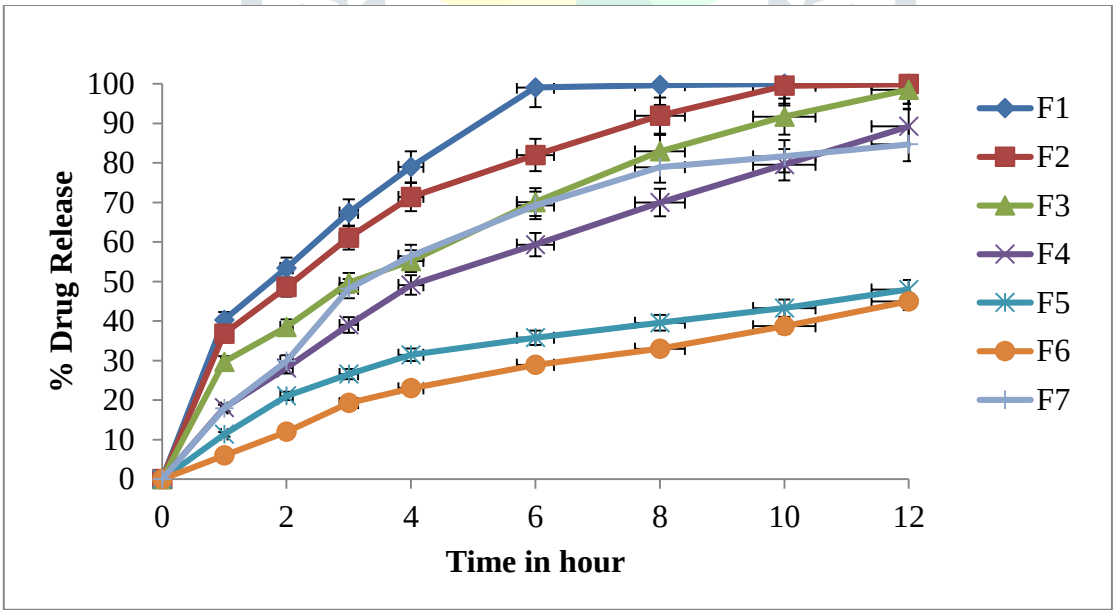
From the above table results it was concluded that the prepared blend has satisfactory flow property. So the selection of wet granulation method was useful.

Evaluation parameters of Prazosin HCl SR matrix tablet

Batch code	Weight Variation (mg) (n=10)	Thickness (mm) (n=3)	Hardness (kg/cm^2) (n=3)	%Friability	% Drug Content (n=3)
F1	201±2.3	3.62± 0.09	6.7± 1.5	0.63	98.9 ± 1.3
F2	200±1.6	3.71± 0.06	7.0± 1.9	0.59	99.1 ± 2.7
F3	198±2.0	3.73± 0.08	7.1± 1.5	0.54	99.5 ± 1.3
F4	200±1.9	3.81± 0.09	7.4± 1.2	0.49	99.7 ± 0.9
F5	200±2.7	3.84± 0.06	8.2± 1.3	0.43	98.1 ± 1.4
F6	198±1.9	3.81± 0.05	7.5± 1.7	0.47	98.6 ± 2.5
F7	202±2.2	3.87± 0.09	8.4± 1.3	0.38	99.2 ± 1.8

From the above results of table it concluded that all the batches pass the weight variation test.
Weight variation observed within acceptable range and no any major deviation found.Also batch F1-F7 have uniform **thickness** value from 3.62 to 3.87 mm.
Hardness was found good enough. F1-F7hardness value found in range between 6.7 to 8.4kg/cm^2.
Friability found below 1 % for all batches. It means all batches have good mechanical strength.
Drug Content found within acceptable limit.
% Drug release study of trials batches F1-F7 performed and results recorded in From the results it assumes that amount of Xanthan Gum increases the drug release for long period of time. In contrast less amount of Sodium Alginate helps in drug release. Batch F3 gives good results compare to others.

Table Cumulative % drug release of batches F1 to F7



Cumulative % drug release of batches F1 to F7

Based on the drug release data of F3, Factorial design applied to optimize the polymer concentration and to check the binder impact on tablets.

6.1 Analysis of factorial batches

Based on trial batches results, 3^2 factorial design is applied to optimize the polymer and binder concentration. Formulation P1-P9 prepared by taking Xanthan Gum and Sodium alginate as independent factors. The results of P1-P9 batches given below;

Precompression parameters of batches P1 to P9

Batch	Bulk Density (gm/ml) (n=3)	Tapped Density (gm/ml) (n=3)	Carr's Index (%) (n=3)	Hausner's Ratio (n=3)	Angle of Repose (ϕ) (n=3)
P1	0.43±0.04	0.49±0.06	12.24±0.02	1.14±0.06	33.50±0.05
P2	0.42±0.03	0.47±0.05	10.64±0.05	1.11±0.03	34.12±0.03
P3	0.40±0.05	0.51±0.03	21.57±0.04	1.28±0.06	42.33±0.02
P4	0.41±0.02	0.50±0.06	18.00±0.05	1.22±0.05	39.41±0.05
P5	0.43±0.04	0.49±0.03	12.24±0.02	1.14±0.07	33.92±0.04
P6	0.42±0.05	0.49±0.06	14.29±0.05	1.17±0.06	38.63±0.07
P7	0.40±0.03	0.53±0.05	24.53±0.06	1.33±0.04	41.52±0.04
P8	0.41±0.03	0.48±0.02	14.58±0.04	1.17±0.02	37.61±0.05
P9	0.43±0.01	0.50±0.04	14.00±0.05	1.16±0.05	38.43±0.06

Factorial batches P1-P9 evaluated for Precompression parameters before compression. Blend was analyzed for various flow propertied characters. The results were showed in above tables and the inference for the same also listed in table. Most of the batches have a good to passable flow in nature. Additionally, the flow of all batches blend was enough for compression operation. By changing binder and polymer concentration, no major difference observed in bulk density and tapped density parameters.

After completion of Precompression parameters evaluation, batches P1-P9 compressed as per required weigh (200.0 mg) and post compression parameters were evaluated for all batches. During compression no any critical observation listed with respect to flow property. The results of post compression parameters were recorded in below table.

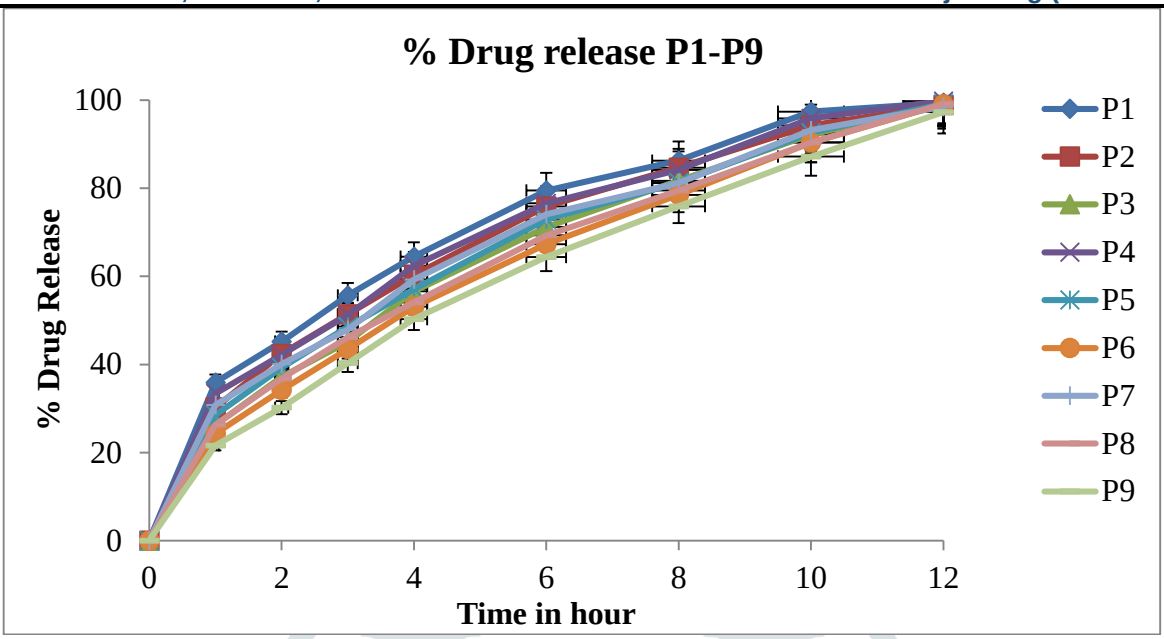
Post compression parameters of batches P1 to P9

Batch code	Weight Variation (mg) (n=10)	Thickness (mm) (n=3)	Hardness (kg/cm^2) (n=3)	%Friability	% Drug Content (n=3)
P1	198± 2.4	3.51± 0.16	7.5 ± 1.20	0.55	99.4±1.8
P2	201± 1.9	3.44± 0.34	8.0± 0.89	0.43	98.5±2.5
P3	199±2.6	3.48± 0.47	7.8± 0.55	0.52	99.3±1.6
P4	198± 2.6	3.54± 0.31	7.3± 0.89	0.57	97.8±1.9
P5	201± 1.5	3.63± 0.18	7.1± 1.20	0.59	98.7±2.1
P6	198± 1.7	3.36± 0.37	8.5± 0.98	0.39	99.3±2.6
P7	201± 2.2	3.84± 0.34	6.9± 1.20	0.52	98.8±2.4
P8	202± 1.8	3.38± 0.15	8.6± 0.98	0.36	97.4±1.9
P9	201± 2.4	3.46± 0.25	7.9 ± 0.98	0.47	98.2±2.4

Based on above table of post compression parameters, it seems that the weight variation in all batches found well within acceptable limit. The weight variation is within 3% range which was more stringent than the acceptable range. Further the thickness found within range as per desired parameters. Hardness was good enough to give a proper mechanical strength to tablets and hence the friability wasobserved below 1 %.

Drug release study of factorial batches P1-P9 performed as per method describe in section 5. The data of drug release tabulated below.

Drug release study shows the impact of Xanthan Gum in formulation. Higher the amount of Xanthan Gum retards the drug release and vice versa. It also seems that the amount of PVPK30 which was used as binder also impact on drug release. The actual impacts of both factors analyzed by using factorial design regression study.



Drug release study of factorial batches P1 to P9

7 CONCLUSION

The aim of present investigation was formulation and development of Prazosin HCl Sustained Release Matrix Tablets using natural polymers. Study started withPreformulation study of the drug. Drug having good solubility in physiological range. The flow of API was found poor hence wet granulation method was selected for tablet preparation. While studying IR spectrum, it was found that there is no interaction between drug and other excipients. Initially feasibility trials were taken using two natural polymers Xanthan Gum and Sodium Alginate. Tablets were found acceptable in physical parameters evaluation. During drug release evaluation amount of Xanthan Gum increases the drug release for long period of time. In contrast less amount of Sodium Alginate helps in drug release.So, role of polymer concentration is very important in this formulation. Based on trial batches results, F3 batch found satisfactory and considering for further factorial screening. 3^2 factorial design applied by taking Xanthan Gum and PVPK30 as independent factors. Drug release at 2 hours and 4 hours considered the dependent factors. Factorial batch P1-P9 prepared by wet granulation method and evaluation was done. Drug release study for P1-P9 batch shows the significant impact of both factors. Xanthan Gum and PVPK30 significantly impact on Drug release and hence the model found significant. Validation of design was done and fond satisfactory. Finally, the optimized batch P12 taken based on Contour plot and complete evaluation was done. Batch P12 loaded for stability study for 1 month and found stable.

Reference

1. Pundir S, Badola A, Sharma D,"Sustained release matrix technology and recent advance in matrix drug delivery system: a review."*International Journal of drug research and technology*.,**2017**, *3(1)*, 8-17.
2. Songire P, Aher S, Saudagar R,"Recent research on matrix tablets for controlled release-a review."*Asian J Pharm Technol.*, **2015**, *5*, 214-221.
3. Rathore A, Jat R, Sharma N, Tiwari R. "An Overview: Matrix tablet as controlled drug delivery system."*Int J Res Dev Pharm Life Sci.*, **2013,***2*, 482-492.
4. Kumar V, Prajapati S, Soni G, Singh M, Kumar N,"Sustained release matrix type drug delivery system: a review."*World journal of pharmacy and pharmaceutical sciences*,**2012**, *1(3)*, 934-960.
5. Chugh I, Seth N, Rana A, Gupta S,"Oral sustained release drug delivery system: An overview."*Int Res J Pharm*, **2012**, *3*, 57-62.
6. Jaimini M, Kothari A,"Sustained release matrix type drug delivery system: a review."*Journal of Drug Delivery and Therapeutics*. **2012**, *2(6)*, 1-8.
7. Dixit N, Maurya S, Sagar B,"Sustained release drug delivery system." *Indian Journal of Research in Pharmacy and Biotechnology*,**2013**, *1*, 305-310.
8. Nisargi S, Chintan O, Shital T, Nihar S, Shreeraj S, "Review on Sustained Release Matrix Tablets: An Approach to Prolong the Release of Drug", *JPSBR*, **2015**, *5(3)*, 315-321.
9. Patel H, Panchal D, Patel U, Tushar, Brahmbhatt MS. "Matrix type drug delivery system: A review." *J Pharm Sci Biosci Res.*, **2011**, *1*, 143- 151.
10. Ghori M, Conway B,"Hydrophilic matrixes for oral control drug delivery."*Am J Pharmacol Sci.*, **2015**, *3*, 103-109.
11. Wani M,"Controlled Release system-A Review."*Pharmaceutical Reviews*. **2008**,*6(1)*, 41-46.
12. Hypertension, September 2015:-https://www.medicalnewstoday.com/articles/159283.php
13. Drug Information, September 2015:-https://www.drugbank.ca/drugs/DB00457
14. Drug Information, September 2015:-https://pubchem.ncbi.nlm.nih.gov/compound/Prazosin_ hydrochloride.
15. Drug Information, September 2015:-https://www.drugs.com/mmx/prazosin-hydrochloride.html
16. Raymond C, Paul J, Marian E, Handbook of Pharamaceutical excipients, 6th Edn, 2009.

Prasanna K, Vaishnavi G, Divya K, Lakshmi U, "An Overview on Preformulation Studies", *IAJPS*, **2015**, *2(10)*, 1399-1407.