ISSN: 0975-766X
Available Online through
www.ijptonline.com
Research Article

PREPARATION AND EVALUATION OF TWICE DAILY MATRIX TABLETS OF TRAMADOL HCL USING ISPAGULA HUSK POWDER

K.V.Ramana Murthy*, S.Nyamathulla, D.Thahera Parveen, G.S.V.Subramanyam and S.Ganapaty
Pharmaceutical Technology Division, Andhra University College of Pharmaceutical sciences,
Andhra University, Visakhapatnam-530 003, A.P., INDIA.
Email: drkvrmurthy@rediffmail.com

Received on 17-09-2010 *Accepted on 10-10-2010*

ABSTRACT

The present work was aimed to prepare and evaluate controlled release matrix tablets of Tramadol HCL which can release the drug for 12 hrs to act as twice daily formulations using Ispagula husk powder at different concentrations. Controlled release polymer, HPMC (K4M) was used in the ratio of 3:1 to the drug. High concentration of the polymer is intentionally used keeping the swelling power and disintegrating ability of the Ispagula husk powder. Matrix tablets, TI-1 to TI-6 were prepared using wet granulation technique with 5% corn starch as granulating agent and 0, 5%, 10%, 15%, 20% and 25% of Ispagula husk powder to the drug. The prepared tablets were evaluated for tabletting characteristics like weight variation, hardness, friability and drug content uniformity; found that they were within the compendial limits. *In vitro* dissolution studies were carried using USP-II (Paddle) apparatus at 50 rpm; the absorbance was measured at 270 nm. As the objective of the work is to prepare a formulation for 12 hrs, TI-4 was found to be the optimized formulation which has a release of more than 95% in 12 hrs. In conclusion it is found that the gelling and swelling combination of HPMC and the Ispagula husk powder effectively controlled the release of drug to formulate twice daily formulations.

Key words: Tramadol HCL, Ispagula husk powder, Controlled release, HPMC, matrix tablets.

1. INTRODUCTION

The controlled release technology is an effective way by which patient compliance and life cycle of drug can be extended. Polymers show a very simple and logical approach in controlling the drug release by forming a gelling layer across which the drug is released slowly over a period of time either by diffusion or by erosion. This leads to reduced peaks and valleys associated with immediate release dosage forms. Among different techniques of controlled release technology matrix systems are popular, simple and effective in controlling the drug. Another advantage is initial burst release of drug may occur due to surface leaching when a matrix containing a polymer comes in contact with an aqueous medium.

Excipients are frequently used to exhibit defined technical roles in dosage forms. They can increase solubility or bioavailability, can increase stability, maintain pH or osmolarity etc. Since introduction of a new excipient is regulated by several stringent procedures given by regulatory authorities, search for new uses for existing excipients is gaining much attention and is a way of reducing time and establishing multiple uses of existing ones.

Tramadol HCL is a white or almost white, crystalline powder, freely soluble in water and in methanol, very slightly soluble in acetone. It is a centrally-acting analgesic[1-7], used for treating moderate to moderately severe pain. The drug has a wide range of applications, including treatment for restless leg syndrome, acid reflux, and fiber myosis. Tramadol HCL is used as drug of choice in this study because of its high solubility and less Biological half life. The drug is taken 4-6 times a day depending on requirement and hence it is felt appropriate and reasonable to prepare and evaluate twice daily formulations of the drug.

Ispagula husk powder is obtained from the dried seeds of *Plantago ovata*[8], plantaginaceae and it is the outer epidermis of the seed coat having high swelling ability due to mucilage.

The present investigation was carried out to prepare controlled release matrix tablets of Tramadol HCL using HPMC K4M and Ispagula husk powder to extend the drug release up to 12 hrs, to evaluate and optimize the

formulations to get the desired release and to compare the optimized formulation with existing commercial formulations.

2. MATERIALS AND METHOD

Materials

Tramadol HCL was procured as a gift sample from Tini Pharmaceuticals Ltd, Tirupati, India. Ispagula husk powder was purchased from Yucca enterprises, Mumbai, India. HPMC K4M was supplied by Loba chemie, Mumbai, India. Magnesium stearate and talc were of S.D fine chemicals LTD, Mumbai, India and they are of laboratory grade.

Method: ***Preparation of Matrix tablets[9] of Tramadol HCL:***

All the ingredients were initially passed through sieve no.100 then weighed using Shimadzu analytical balance a quantity equivalent for a batch of 100 tablets according to the formulas shown in Table 1 were geometrically mixed until a homogenous blend was achieved. 5% corn starch was used as granulating agent in the preparation of granules. The granules were initially passed through sieve no. 10, dried below 50^{o} C and then sieved through Sieve no. 24, magnesium stearate and talc were added as required. Final blend was then compressed into tablets on a 16-station rotary tablet punching machine (M/s. Cadmach Machinery Co. Pvt. Ltd., India) using 9 mm round concave punches appropriately at the hardness of around 5 to 6 Kg/cm².

Table 1: Composition of matrix tablets of Tramadol HCL

Ingredients (mg per tablet)	Formula code					
	TI-1	TI-2	TI-3	TI-4	TI-5	TI-6
TRAMADOL HCL	50	50	50	50	50	50
Ispagula husk	0	2.5	5	7.5	10	12.5
5% Corn starch	05	05	05	05	05	05
equivalent to HPMC K4M	150	150	150	150	150	150
Magnesium stearate	7	7	7	7	7	7
Talc	3	3	3	3	3	3
Tablet weight (mg)	**215**	**217.5**	**220**	**222.5**	**225**	**227.5**

Evaluation of prepared matrix tablets:

All the prepared formulations were evaluated for Hardness, Weight variation, Friability and Drug content uniformity, all the prepared tablets were found to be within the compendial limits and the results are as given in Table 2.

Dissolution test was carried out using USP type-II (Paddle) dissolution test apparatus of Model DISSO 2000 of M/s. Lab India at a stirring rate of 50 rpm. 900ml of distilled water is used dissolution medium maintained at 37 ± 0.5^{o} C. 5 ml of sample volume was withdrawn periodically, appropriately diluted and analyzed using Systronics UV-Visible Spectrophometer (117) at 270 nm. The 5 ml of volume maintained at the temperature of the dissolution basket was replaced after each sampling. The calibration curve shown in Fig. 1 was used for all calculations. Cumulative % drug released of all the formulations TI-1 to TI-6 was as shown in Fig. 2. The comparative cumulative % of the TI-4 and commercial was given in Fig. 3.

Table 2: Tabletting characteristics matrix tablets of Tramadol HCL (n=3).

Formulation	Weight[a] (mg)	Drug content[b] (%)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)
TI-1	215.2 ± 1.32	99.8 ± 0.83	5-6	1.3	0.64
TI-2	217.4 ± 2.11	98.12 ± 1.58	5-6	1.5	0.28
TI-3	220.6 ± 1.64	99.1 ± 1.34	5-6	1.7	0.44
TI-4	222.4 ± 2.04	99.62 ± 1.27	5-6	2.1	0.46
TI-5	225.7 ± 1.12	98.44 ± 1.7	5-6	2.2	0.52
TI-6	227.9 ± 1.08	99.77 ± 1.06	5-6	2.3	0.66

a: Mean ± s.d., n = 20 tablets; b: Mean ± s.d., n = 10 tablets

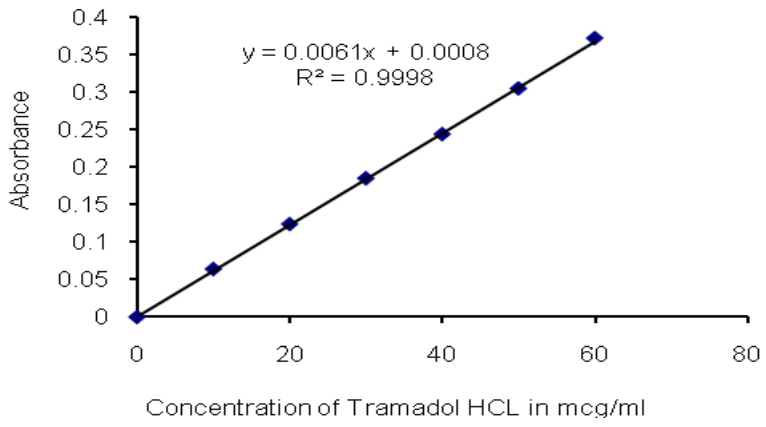

Fig. 1: Calibration curve of Tramadol HCL used in the present study

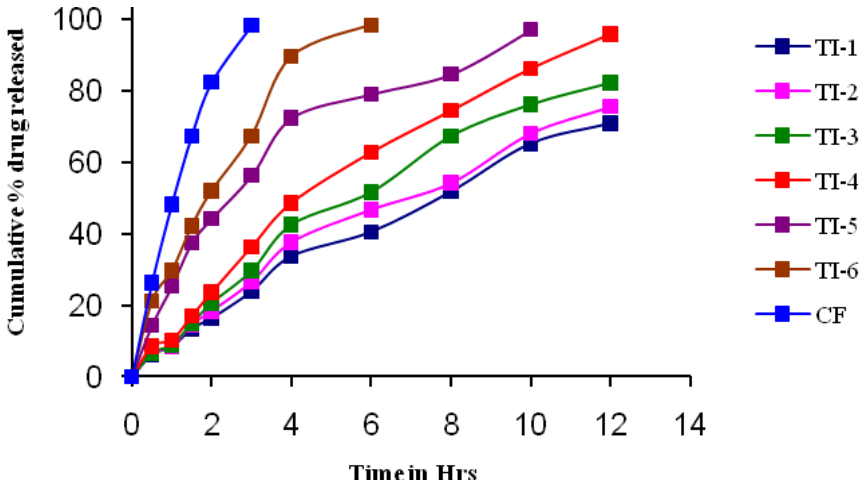

Fig. 2: Cumulative % drug release in all the prepared formulations

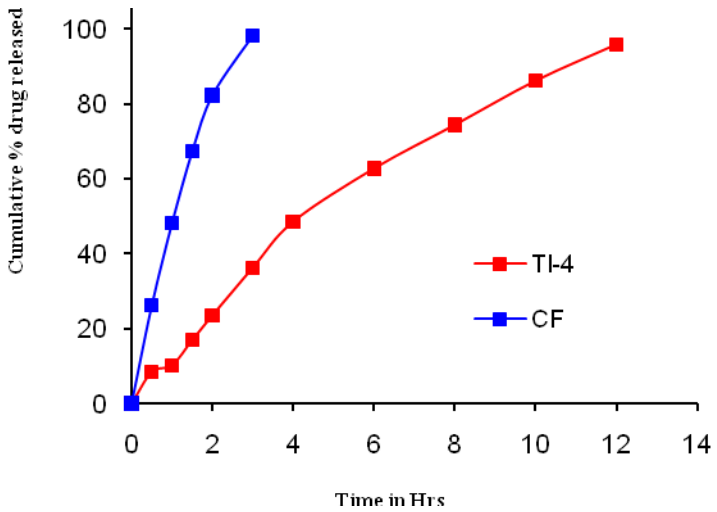

Fig. 3: Comparative cumulative % drug release of optimized formulation TI-4 and Commercial formulation

3. RESULTS AND DISCUSSION

The prepared matrix tablets of Tramadol HCL using Ispagula husk powder complied with the official IP limits. The hardness which is tested using Monsanto Hardness tester was in the range of 5-6 Kg cm^{-1}. The friability values were in the range of 0.28 – 0.66, which is in acceptance with the required 1% limit. All the formulations were satisfied in drug content and low standard deviation indicate uniformity of drug distribution. All the formulations thus are with enough ability to withstand the pressure, stress, friction during the transportation.

Formulations TI-1 to TI-6 were prepared using 0, 5%, 10%, 15%, 20% and 25% Ispagula husk powder respectively. Among all the prepared formulations the formulation TI-I is without Ispagula husk powder and it is clearly observed in its profile the dominance of HPMC K4M used in the matrix system. It is known that the quick hydration and immediate gel formation are two important steps in the mechanism of a successful polymer. The controlled release polymer used in these formulations prevented the diffusion of drug from the core of the tablet due to thick gel and hence by the end of 12 hrs could only release 70.92% of the drug. In TI-2 having 5% Ispagula husk powder had no great variation and but however showed 75.6% drug release. In TI-3 and TI-4 the Ispagula husk

powder succeeded in disrupting the gel barrier to a satisfactory level and by the end of 12 hrs released 82.22 and 95.88%. Whereas formulations TI-5 and TI-6 had greater disintegrating effect of husk powder and drug release was rapid and hence could not sustain till 12 hrs and they released 100% of drug by 10 hrs and 6 hrs respectively. In the prepared formulations TI-4 showed an optimum release with more than 95% in 12 hrs and hence it is considered as optimum formulation and subsequent concentrations were not tested. Thus higher concentrations of Ispagula husk powder can increase the drug release from gel barriers by disrupting the matrix either by diffusion or by erosion. The optimized formulation was further compared with commercially available immediate release formulation of Tramadol HCL as there was no twice daily formulation of Tramadol HCL in the market. Commercial formulation having trade name ULTRAM was purchased from ortho-McNeil-Janssen Pharmaceuticals and formulation released 98.27% within 3 hrs. The data of optimized formulation and commercial formulations were fitted to zero order, first order, higuchi and erosion equations. TI-4 exhibited zero order release with diffusion mechanism were as commercial formulation exhibited first order with diffusion. Drug polymer interaction studies were planned to known the interaction.

4. CONCLUSION

The Ispagula husk powder effectively disrupted the thick gel barrier formed due to the quick hydration of polymer. The increase in concentration of husk increased the percent drug released and formulation TI-4 with 15% Ispagula husk to that of the drug has extended the drug release up to 12 hrs making twice daily formulation.

5. ACKNOWLEDGEMENTS

Authors are grateful to TINI pharmaceuticals for their generous help in contributing Tramadol HCL as gift sample for the above work.

6. REFERENCES:

1. Meredith AF, Catherine LJ, Dennis LM, *Int J Neuropsychopharmacol.*, 2009, 12(8), 1055-1065.
2. Hakki U, Sibel T, Geylan I, *J Opioid Manag*, 2009, 5(5), 247-255.

3. Berrin I, Mustafa A, Mehmet A, *Ann Pharmacother*, 2009, 43(3), 430-435.

4. Mohta M, Kumari N, Singh M, *Anaesthesia*, 2009, 64(2), 141-146.

5. Harati Y, Gooch C, Swenson M, Edelman SV, Greene D, Raskin P, Donofrio P, Cornblath D, Olson WH, Kamin M., *J. Diabetes Complications*, 2000 14(2), 65-70.

6. Harati Y, Gooch C, Swenson M, Edelman S, Greene D, Raskin P, Donofrio P, Cornblath D, Sachdeo R, Siu CO, Kamin M., *Neurology*, 1998, 50(6), 1842-1846.

7. Hara K, Minami K, Sata T, *Anesthesia and Analgesia*, 2005, 100 (5), 1400–1405.

8. Bareja SK, Gupta BM, *Indian. J.Pharm.*,1968, 30, 187.

9. United States Pharmacopoeia, Vo. XXII, USP Convention, Rockville, 1990, 1578.

Corresponding Author:

Dr. K.V. Ramana Murthy*,
Professor, Pharmaceutical Technology Division,
A.U.College of Pharmaceutical Sciences,
Andhra University,
Visakhapatnam-530 003.
Andhra Pradesh, INDIA.
Email: *drkvrmurthy@rediffmail.com,*
shaik_pharmacy@yahoo.com