FORMULATION AND EVALUATION OF EXTENDED RELEASE TABLETS OF TRAMADOL HYDROCHLORIDE

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ABSTRACT

The objective of this research work was to develop extended release tablets (Twice in a day) of Tramadol Hydrochloride using different Hydrophilic polymers like HPMC K15M, HPMC K4M, Metalose 60SH50, Carbopol 971P, Sodium alginate, Xanthan gum by direct compression method. Various amounts of polymers was used in the twenty four proposed formulations (F1 to F24) for the study of release rate retardant effect at 10 %, 15 %, 20 %, 25 % of total weight of tablet matrix respectively. Then the tablets were evaluated in terms of their physical parameters (weight variation, hardness, friability and thickness), drug content and *in-vitro* release studies. All the formulations showed compliance with pharmacopoeial standards. The *in-vitro* dissolution study were conducted using USP dissolution apparatus type-II (paddle method) in 900 ml 0.1 N HCl for first 2 h and remaining 10 h performed in 6.8 pH phosphate buffer at 100 rpm for a total period of 12 h. Based on the dissolution data comparison with innovator product, formulation F14 was found as the best formulation. The drug release of formulation F14 followed First Order kinetic model and the mechanism was found to be non-Fickian/anomalous according to Korsmeyer-Peppas equation.

Keywords: Tramadol Hydrochloride, Direct Compression, Hydroxy propyl methyl cellulose, Carbopol 971P, Extended Release.

INTRODUCTION

Extended release formulations make the drug available over extended time period after oral administration. The extended release product will optimize therapeutic effect and safety of a drug at the same time improving the patient convenience and compliance.¹ Tramadol is used in the treatment of osteoarthritis when non-steroidal anti-inflammatory drug (NSAIDS), acetaminophen, or cox-2 inhibitors alone produce inadequate pain relief. After oral administration, Tramadol is rapidly and almost completely absorbed. Sustained release tablets reach to peak concentration after 5 h and have a bioavailability of 87 % - 95 %. The mean elimination half-life is approximately 6 to 8 h and requires dosing every 6 h in order to maintain optimal relief of chronic pain. Consequently once or twice daily extended release tablets have been formulated. Long term treatment with extended release Tramadol tablets once or twice daily is generally safe in patients with osteoarthritis or refractory low back pain and is well tolerated. It has the potential to provide patients increased control over the management of their pain, fewer interruptions in sleep and improved compliance. And minimize drug accumulation with chronic dosing.^{2,3}

MATERIALS AND METHODS

Materials

Tramadol Hydrochloride was obtained as a gift sample from Aurabindo Pharma, Hyderabad, India. HPMC K4M, HPMC K15M, Carbopol 971P, Xanthan gum, Metalose 60SH50, Sodium alginate, D Extended release formulations make the drug available over extended time period after oral administration. The extended release product will optimize therapeutic effect and safety of a drug at the same time improving the patient convenience and compliance. By incorporating the dose for 24 h into one tablet/capsule from which the drug is released slowly. This formulation helps to avoid the side effects associated with low and high concentrations. The ideal drug delivery system should show a constant zero-order relei calcium phosphate, Magnesium

stearate, Aerosil, obtained from Richer Pharmaceuticals, Hyderabad, India.

Methods

Drug Excipient Compatibility Studies

Compatibility study was carried for pure Tramadol Hydrochloride and combination of Tramadol Hydrochloride with excipients. Fourier transfer infra red (FTIR) spectroscopic (shimadzu, Japan) studies were carried out by approximately diluting the sample with dried potassium bromide (1:100) and acquiring infrared (IR) spectrum in the range of 400 to 4000 cm^{-1} .

Formulation of Extended release matrix tablets of Tramadol Hydrochloride by direct compression method

Various formulation batches of Tramadol Hydrochloride Extended release tablets were prepared using different polymers at 10 %, 15 %, 20 %, 25 % Concentration of total weight of tablet matrix respectively. All ingredients except magnesium stearate were blended in glass mortar uniformly. Then pass the mixture through sieve $\neq 60$. Add magnesium stearate to the above mixture and pass through sieve $\neq 60$ and mix for 10-15 minutes; finally compressed in concave shaped circular punches 8.5 mm (Cadmach 16 station).

Evaluation Parameters

Evaluation of powder blend

Angle of repose

Static angle of repose was determined according to the fixed funnel method; where by accurately weighed powder (3 g) were carefully poured through the funnel with its tip at 2 cm height (H), until the apex of the conical heap so formed just reached the tip of the funnel⁴. The mean diameter 2R of the base for the powder cone was measured and the angle of repose (θ) was calculated using the following equation.

$$\tan(\theta) = H/R$$

Bulk density and tapped density

Both poured bulk and tapped bulk densities were determined, where by a quantity (3 g) of powder blend from each formula, previously lightly shaken to break any agglomerates formed, was introduced into a 10 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2-second intervals. The tapping was continued until no further change in the volume was noted.

Carr's Compressibility Index and Hausner's ratio

The compressibility of the powder was determined by carr's compressibility index (CI). The Hausner's ratio (HR) is number that is correlated to the flow ability of powder.

$$CI = ((TD-BD)/TD) \times 100$$

where TD = tapped density and BD = bulk density.

Evaluation of Tablets

The prepared extended release tablets were evaluated for hardness, thickness, friability, weight variation test and drug content. Hardness of tablets was tested using Monsanto hardness tester (Serve well, Bangalore, India). Friability of the tablets was determined in a Roche Friabilator (Electrolab, Mumbai, India). The thickness of tablets was measured by vernier calipers. Weight variation test was performed according to official method. Drug content for Tramadol Hydrochloride was carried out by measuring the absorbance of samples at 273 nm using Lab India UV-2400PC spectrophotometer Mumbai, India and comparing the content from a calibration curve of Tramadol Hydrochloride.^{5,6}

Table 1: Composition of the Formulations (per each tablet in mg)

Formulation code	Drug	DCP	HPMC K4M	HPMC K15M	Metolose 60SH50	Carbopo 1 971P	Xanthan gum	Sodium alginate	Aerosil	Mag. stearate	Total (mg/tab)
F1	100	164	30	-	-	-	-	-	3	3	300
F2	100	149	45	-	-	-	-	-	3	3	300
F3	100	134	60	-	-	-	-	-	3	3	300
F4	100	119	75	-	-	-	-	-	3	3	300
F5	100	164	-	30	-	-	-	-	3	3	300
F6	100	149	-	45	-	-	-	-	3	3	300
F7	100	134	-	60	-	-	-	-	3	3	300
F8	100	119	-	75	-	-	-	-	3	3	300
F9	100	164	-	-	30	-	-	-	3	3	300
F10	100	149	-	-	45	-	-	-	3	3	300
F11	100	134	-	-	60	-	-	-	3	3	300
F12	100	119	-	-	75	-	-	-	3	3	300
F13	100	164	-	-	-	30	-	-	3	3	300
F14	100	149	-	-	-	45	-	-	3	3	300
F15	100	134	-	-	-	60	-	-	3	3	300
F16	100	119	-	-	-	75	-	-	3	3	300
F17	100	164	-	-	-	-	30	-	3	3	300
F18	100	149	-	-	-	-	45	-	3	3	300
F19	100	134	-	-	-	-	60	-	3	3	300
F20	100	119	-	-	-	-	75	-	3	3	300
F21	100	164	-	-	-	-	-	30	3	3	300
F22	100	149	-	-	-	-	-	45	3	3	300
F23	100	134	-	-	-	-	-	60	3	3	300
F24	100	119	-	-	-	-	-	75	3	3	300

Table 2: Pre Compression parameters of Tablets of Batches F1 – F24

Formulation code	Angle of Repose	Bulk Density	Tapped Density	Carr's Index	Hausner's Ratio
F1	33.54 ± 1.07	0.59 ± 0.34	0.69 ± 0.30	14.49 ± 0.43	1.16 ± 0.35
F2	33.35 ± 1.01	0.63 ± 0.25	0.71 ± 0.28	12.50 ± 0.27	1.14 ± 0.54
F3	28.65 ± 0.86	0.64 ± 0.45	0.76 ± 0.19	15.0 ± 0.18	1.18 ± 0.2
F4	27.3 ± 0.89	0.67 ± 0.27	0.74 ± 0.54	9.45 ± 0.12	1.10 ± 0.34
F5	32.13 ± 0.94	0.63 ± 0.51	0.73 ± 0.24	13.15 ± 0.34	1.15 ± 0.28
F6	33.52 ± 0.89	0.64 ± 0.12	0.75 ± 0.17	14.66 ± 0.32	1.17 ± 0.62
F7	31.24 ± 0.99	0.61 ± 0.22	0.68 ± 0.53	10.29 ± 0.43	1.11 ± 0.13
F8	33.49 ± 0.98	0.69 ± 0.46	0.76 ± 0.82	9.20 ± 0.33	1.10 ± 0.42
F9	32.4 ± 0.64	0.60 ± 0.16	0.69 ± 0.24	13.04 ± 0.54	1.15 ± 0.29
F10	33.13 ± 1.05	0.61 ± 0.37	0.70 ± 0.43	12.85 ± 0.39	1.14 ± 0.72
F11	32.23 ± 0.93	0.64 ± 0.25	0.73 ± 0.23	12.32 ± 0.53	1.14 ± 0.22
F12	31.39 ± 1.14	0.64 ± 0.38	0.72 ± 0.65	11.11 ± 0.33	1.12 ± 0.38
F13	30.24 ± 0.69	0.61 ± 0.31	0.68 ± 0.38	10.29 ± 0.21	1.11 ± 0.19
F14	32.49 ± 0.98	0.69 ± 0.28	0.76 ± 0.27	9.2 ± 0.26	1.10 ± 0.21
F15	31.4 ± 0.54	0.67 ± 0.46	0.74 ± 0.46	9.45 ± 0.43	1.10 ± 0.26
F16	32.13 ± 1.25	0.64 ± 0.38	0.73 ± 0.63	12.32 ± 0.56	1.14 ± 0.32
F17	31.23 ± 0.63	0.67 ± 0.48	0.74 ± 0.28	9.45 ± 0.21	1.10 ± 0.18
F18	32.39 ± 1.14	0.63 ± 0.11	0.71 ± 0.18	11.26 ± 0.51	1.12 ± 0.23
F19	31.12 ± 0.29	0.64 ± 0.23	0.73 ± 0.45	12.32 ± 0.32	1.14 ± 0.24
F20	30.42 ± 0.28	0.61 ± 0.41	0.67 ± 0.54	8.95 ± 0.38	1.09 ± 0.32
F21	29.3 ± 0.14	0.67 ± 0.57	0.75 ± 0.73	13.33 ± 0.29	1.11 ± 0.41
F22	31.23 ± 0.45	0.65 ± 0.31	0.75 ± 0.78	13.33 ± 0.83	1.15 ± 0.26
F23	30.13 ± 0.33	0.67 ± 0.24	0.74 ± 0.34	9.45 ± 0.91	1.10 ± 0.39
F24	31.59 ± 1.24	0.58 ± 0.18	0.68 ± 0.26	14.70 ± 0.24	1.17 ± 0.52

Table 3: Post Compression parameters of Tablets of Batches F1 – F24

Formulation code	Weight variation (mg)	Thickness (mm)	Hardness (kp)	Friability (%)	Drug content (%)
F1	300 ± 1.09	4.42 ± 0.3	5-7	0.16 ± 0.03	99.22 ± 0.49
F2	299 ± 0.94	4.41 ± 0.5	5-7	0.13 ± 0.02	97.40 ± 0.62
F3	301 ± 0.59	4.38 ± 0.6	5-7	0.16 ± 0.01	98.98 ± 1.06
F4	300 ± 1.01	4.43 ± 0.4	5-7	0.31 ± 0.02	99.8 ± 0.54
F5	300 ± 1.36	4.44 ± 0.4	5-7	0.11 ± 0.01	100.18 ± 0.54
F6	301 ± 1.57	4.41 ± 0.5	5-7	0.22 ± 0.02	97.68 ± 0.16
F7	300 ± 0.49	4.42 ± 0.8	5-7	0.14 ± 0.05	98.77 ± 0.95
F8	300 ± 1.46	4.40 ± 0.9	5-7	0.12 ± 0.03	99.56 ± 1.49
F9	300 ± 0.95	4.39 ± 0.9	5-7	0.19 ± 0.08	100.37 ± 1.21
F10	299 ± 1.65	4.42 ± 0.3	5-7	0.25 ± 0.02	99.86 ± 0.39
F11	300 ± 0.43	4.44 ± 0.2	5-7	0.12 ± 0.02	99.53 ± 1.09
F12	300 ± 1.03	4.45 ± 0.8	5-7	0.28 ± 0.01	98.73 ± 0.98
F13	300 ± 0.76	4.46 ± 0.6	5-7	0.25 ± 0.03	99.69 ± 1.07
F14	300 ± 0.52	4.43 ± 0.6	5-7	0.17 ± 0.01	97.98 ± 1.65
F15	300 ± 0.40	4.44 ± 0.3	5-7	0.2 ± 0.01	100.2 ± 1.2
F16	300 ± 0.7	4.42 ± 0.5	5-7	0.19 ± 0.005	98.27 ± 1.22
F17	300 ± 0.23	4.43 ± 0.8	5-7	0.18 ± 0.015	99.29 ± 0.56
F18	301 ± 0.65	4.48 ± 0.7	5-7	0.18 ± 0.04	99.43 ± 0.54
F19	300 ± 0.37	4.46 ± 0.5	5-7	0.22 ± 0.01	99.21 ± 1.23
F20	298 ± 1.45	4.42 ± 0.2	5-7	0.43 ± 0.02	98.34 ± 1.32
F21	299 ± 0.43	4.48 ± 0.4	5-7	0.20 ± 0.02	100.28 ± 0.76
F22	300 ± 0.61	4.39 ± 0.4	5-7	0.38 ± 0.03	99.67 ± 0.48
F23	299 ± 0.34	4.45 ± 0.7	5-7	0.12 ± 0.01	99.87 ± 1.27
F24	300 ± 0.57	4.43 ± 0.4	5-7	0.24 ± 0.03	99.34 ± 0.43

*All values are expressed as mean ± SD, n = 3

Table 4: % Cumulative drug release of formulations F1-F24

Formulation Code	% Drug release in hours						
	1	2	4	6	8	10	12
F1	29.12 ± 0.6	43.36 ± 0.4	60.21 ± 0.5	79.86 ± 0.8	98.14 ± 0.4		
F2	28.24 ± 0.8	40.54 ± 0.5	59.32 ± 0.5	75.23 ± 0.5	89.65 ± 0.6	100.35 ± 0.2	
F3	26.39 ± 0.2	34.71 ± 0.4	52.64 ± 0.9	66.22 ± 0.5	83.12 ± 0.5	98.26 ± 0.2	
F4	22.21 ± 0.5	32.89 ± 0.6	46.44 ± 0.5	59.56 ± 0.4	69.36 ± 0.2	83.65 ± 0.6	100.23 ± 0.2
F5	29.32 ± 0.6	43.26 ± 0.4	59.49 ± 0.5	78.85 ± 0.8	97.24 ± 0.4		
F6	25.24 ± 0.8	39.54 ± 0.5	57.32 ± 0.5	74.23 ± 0.5	88.65 ± 0.6	99.35 ± 0.2	
F7	24.49 ± 0.2	33.62 ± 0.4	48.56 ± 0.9	66.34 ± 0.5	78.16 ± 0.5	90.28 ± 0.2	100.85 ± 0.4
F8	20.32 ± 0.5	27.24 ± 0.6	42.3 ± 0.5	57.23 ± 0.4	66.67 ± 0.2	79.35 ± 0.6	97.76 ± 0.2
F9	35.12 ± 0.6	60.36 ± 0.4	89.21 ± 0.5	101.86 ± 0.8			
F10	34.25 ± 0.24	58.64 ± 0.46	86.26 ± 0.61	98.56 ± 0.17			
F11	32.44 ± 0.48	54.87 ± 0.56	74.74 ± 1.20	85.22 ± 0.51	91.31 ± 0.65	98.42 ± 0.23	
F12	30.21 ± 0.32	49.34 ± 0.12	60.86 ± 1.1	75.53 ± 0.7	87.22 ± 0.4	95.61 ± 0.2	100.01 ± 0.9
F13	26.12 ± 0.6	40.36 ± 0.4	55.21 ± 0.5	69.86 ± 0.8	83.14 ± 0.4	96.32 ± 0.6	101.21 ± 1.3
F14	19.24 ± 0.8	28.2 ± 0.5	43.2 ± 0.5	54.32 ± 0.5	67.8 ± 0.6	78.98 ± 0.2	99.2 ± 0.4
F15	17.39 ± 0.2	25.71 ± 0.4	34.64 ± 0.9	39.22 ± 0.5	46.12 ± 0.5	58.26 ± 0.2	70.56 ± 0.6
F16	15.24 ± 0.5	22.37 ± 0.6	29.21 ± 0.5	33.43 ± 0.4	39.23 ± 0.2	44.98 ± 0.6	48.21 ± 0.2
F17	27.11 ± 0.6	41.36 ± 0.4	55.32 ± 0.5	69.75 ± 0.8	82.15 ± 0.4	97.28 ± 0.6	
F18	25.25 ± 0.24	38.64 ± 0.46	49.26 ± 0.61	60.56 ± 0.17	78.85 ± 0.43	88.34 ± 0.39	100.66 ± 1.12
F19	22.44 ± 0.48	30.87 ± 0.56	41.74 ± 1.20	50.22 ± 0.51	59.31 ± 0.65	67.42 ± 0.23	76.29 ± 0.64
F20	14.21 ± 0.32	21.34 ± 0.12	30.86 ± 1.1	39.53 ± 0.7	46.22 ± 0.4	57.61 ± 0.2	65.01 ± 0.9
F21	45.12 ± 0.6	70.36 ± 0.4	92.21 ± 0.5	101.16 ± 1.8			
F22	34.24 ± 0.24	48.52 ± 0.46	69.29 ± 0.61	80.44 ± 0.17	100.72 ± 0.43		
F23	31.32 ± 0.48	48.84 ± 0.56	64.72 ± 1.20	78.53 ± 0.51	94.31 ± 0.65	100.42 ± 0.2	
F24	22.32 ± 0.32	34.56 ± 0.12	52.83 ± 1.1	66.24 ± 0.7	83.31 ± 0.4	97.56 ± 0.2	
MP	18.65 ± 0.36	26.28 ± 0.43	39.26 ± 0.28	49.17 ± 0.65	62.21 ± 0.37	74.54 ± 0.81	96.43 ± 0.31

*All values are expressed as mean ± SD, n = 3

Figure 1: *In-vitro* Dissolution Profile For Batches F1 – F12 Figure 2: *In-vitro* Dissolution Profile For Batches F13 – F24 Figure 3: Comparison of *In-vitro* drug release of Reference and optimized F14

***In-vitro* drug release study**

Release of the prepared tablets was determined up to 12 h using USP XXIV (type-II) dissolution rate test apparatus (Electro lab Mumbai, India). 900 ml of 0.1N HCl was used as dissolution medium for first two hours then using 6.8phosphate buffer for up to 12 h. The rotation of paddle was fixed at 100 rpm and the temperature of $37 \pm 0.5^\circ\text{C}$ was maintained throughout the experiment. Samples of 10 ml were withdrawn at 1, 2, 4, 6, 8, 10, 12 h time intervals and were placed with same volume of fresh dissolution media after each with drawn. The samples were analyzed spectrophotometrically for drug content on UV/Visible spectrophotometer-2400PC Lab India Mumbai at 273 nm^{7-9} .

RESULTS AND DISCUSSION

Drug Excipient Compatibility Studies reveals that the pure drug and the solid admixture of drug and various ingredients used in the preparation of extended release tablets were characterized by FTIR spectroscopy to know the compatibility. There was no significant difference or the characteristic peak of pure drug was unchanged in spectrum of optimized formulation (F14). Micromeritic properties like angle of repose value of $27.3-33.54^\circ$, Carr's index value of $8.95-14.7$ and Hausner's ratio $1.09-1.18$ indicating flow property excellent to good. Hence powder mixture was found suitable for direct compression method. Post compression parameters like hardness of the tablet were acceptable and uniform from batch to batch variation, which was found to be $5 - 7 \text{ kg/cm}^2$. All the formulations passed the weight variation test as the % weight variation was within the pharmacopoeial limits of $\pm 7.5 \%$ of the tablet weight. Friability values were found to be less than 1% in all the formulations F1 – F24 and considered to be satisfactory ensuring that all the formulations

are mechanically stable. The % drug content for all the formulations were close to 100 and varied between 98.27 to 100.37% indicating consistency in the manufacturing process. *In-vitro* drug release study of formulations F4 and F8 prepared with HPMC K4M and HPMC K15M polymers has successfully extended the model drug release up to 12 h and they were formulated at 25% concentration. But Formulation F-14 formulated with Carbopol 971P NF as the polymer has extended the model drug release up to 12 h at 15% concentration only. All formulations compared with the marketed product for drug release pattern and were matched using similarity factor $70.11 (f_2)$; which showed that formulation F14 performed similar to the marketed product therapeutically. Based on the evaluation results the formulation F-14 containing Carbopol 971P was selected as best formulation. Different kinetic models were applied to the optimized formulation and observed that F-14 followed first order kinetic model and it was complied with Reference sample. The best linearity was found in Korsmeyer-peppas model (where $n = 0.583$ is the release exponent); Applicability of data indicating Non-Fickian diffusion (or) Anomalous Transport as mechanism of drug release. The stability study for the selected formulation of F-14 was performed as per ICH guidelines. Stability study is carried out for 3 months at 40°C ; 75% RH, according to ICH guidelines. The tablets were tested for release during the stability period and confirmed that results were found within the limits.

CONCLUSION

Drug release of Optimized Formulation F-14 formulated with Carbopol 971P NF as the polymer has extended the Tramadol Hydrochloride release up to 12 h at 15% concentration only.

Excipients used in the formulation reduce the cost, which are available at lower price in market. As the excipients used are mostly available and cheaper at cost. The study includes development of the robust and stable product, which complies with the marketed product.

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REFERENCES

1. Robinson Lee. Controlled drug delivery; fundamentals and applications. 2nded. Marcel Dekkar; New York; 1978. p. 24-26.
2. Robinson R, Lee VH. Influence Of Drug Properties And Route Of Drug Administration On The Design Of Sustained And Controlled Release Drug Delivery System, In Controlled Drug Delivery System, In Controlled Drug Delivery Fundamentals And Applications. 3rded; 1995.
3. Chien YW. Oral Drug Delivery And Delivery Systems, In Novel Drug Delivery Systems. 2nded., Marcel Dekker, Inc, New York; 1990. p. 139-141.
4. Herbert Lieberman, Leon Lachman, Joseph B Schwartz. Pharmaceutical dosage forms: Tablets, Vol.1, 2 and 3, second edition.
5. Qiu Y, Zhang G. Research and development aspects of oral controlled release dosage forms. Handbook of Pharmaceutical Controlled Release Technology. Ed. DL Wise, Marcel Dekker Inc., New York, NY, USA; 2000. p. 465- 503
6. Kincil M, Veber M. Characterization of factors affecting the release of low solubility drug from prolonged release tablets. *Chem Acta* 2004; 502: 107-113. <http://dx.doi.org/10.1016/j.aca.2003.09.050>
7. Higuchi T. Mechanism of sustained-action medication: theoretical analysis of rate of release solid drugs dispersed in solid matrices. *J Pharm. Sci* 1963; 52: 1145 -1149. <http://dx.doi.org/10.1002/jps.2600521210> PMID:14088963
8. Peppas NA, Sahlin JJ. A simple equation for the description of solute release: Coupling of diffusion and relaxation. *Int. J. Pharm* 1989; 57:169–172. [http://dx.doi.org/10.1016/0378-5173\(89\)90306-2](http://dx.doi.org/10.1016/0378-5173(89)90306-2)
9. Alfonso R Gennaro. Extended Release and Targeted Drug Delivery Systems, In the Science and Practice of Pharmacy. 21sted. Lippincott Williams and Wilkins Vol -1; 2005. p. 939-94
10. Mr Chaudhary Amol. Formulation Development And Evaluation Of Extended Release Tablets Of Lamotrigine IJPBS 2011; 3(4).
11. Afsar C Shakh. Formulation and evaluation of sustained release tablets of Aceclofenac using Hydrophillic matrix system. *Int J pharm sci* 2011; 3: 145-148.
12. Subramania Nainar Meyyanathan. Formulation and evaluation of sustained release tablets of Aceclofenac using Hydrophillic matrix system. *Int J pharm sci* 2012; 3: 135-142.

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