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Formulation and evaluation of Tramadol Hydrochloride sustained matrix tablets

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ABSTRACT

The present study deals with formulation of Tramadol hydrochloride (TMH) sustained release matrix tablets. Tramadol is a water soluble drug and is prescribed for three to four times a day. Thus it is necessary for the drug to develop a sustained dosage form with reduced risk of drug administration, side effects and patient compliance. The present work describes preparation of matrix tablets using different hydrophilic and hydrophobic polymers. TMH is a centrally acting analgesic and is used to treat moderate to moderately severe pain. Tramadol is rapidly and almost completely absorbed after oral administration, showing good bioavailability. Hence the main objective of the study was to formulate and evaluate tramadol sustained release matrix tablets. Sustained release matrix tablets of TMH of different polymers like hydroxypropyl methyl cellulose (HPMC), polyethylene oxide (PEO), ethyl cellulose (EC), Eudragit were developed and evaluated. All the batches were evaluated for angle of repose, Carr's index, Hausner ratio, hardness, thickness, weight variation, drug content and in-vitro release characteristics. The release kinetics and the mechanism of drug release by regression coefficient analysis and Peppas exponential model equation were investigated. The optimised tablets having HPMC provided more sustained drug release than other polymers.

Keywords : Tramadol Hydrochloride, Sustain Release.

INTRODUCTION

TMH, a centrally acting analgesic, with good oral bioavailability and relatively short elimination half-life, and is used in treating severe acute or chronic pain.

Oral drug delivery is the largest and the oldest segment of the total drug delivery market. It is the fastest growing and most preferred route for drug administration. Sustained release tablets and capsules are commonly taken only once or twice daily, compared with counter part conventional forms that may have to take three or four times daily to achieve the same therapeutic effect (Lachman et al., 1987). Typically, sustained release products provide an immediate release of drug that promptly produces the desired therapeutic effect, followed by gradual release of additional amounts of drug to maintain this effect over a predetermined period. The sustained plasma drug levels provide by sustained release products often times eliminates the need for night dosing, which benefits not only the patients but the care given as well. The basic rationale of a sustained drug delivery system is to optimize the Biopharmaceutic, Pharmacokinetic and Pharmacodynamic properties of a drug in such a way that its utility is maximized through reduction in side effects and cure or control of condition in the shortest possible time by using smallest quantity of drug, administered by the most suitable route. The novel system of drug delivery offer a means of improving the therapeutic effectiveness of incorporated drugs by providing sustained, controlled delivery and / or targeting the drug to desired site (Vyas and Khar 2002).

MATERIALS AND METHODS

Tramadol hydrochloride was obtained as gift sample from Cadila Healthcare (Ahmedabad, India). Ethylcellulose N-20 obtained from Vilin Biomed, New Delhi, Eudragit RLPO and HPMC K15M obtained from Cadila Pharma, Ahmedabad and Polyethylene oxide-18 NF from Glenmark Pharmaceuticals Ltd, Mumbai. MCC (PH 102) and Lactose were obtained from Loba Chemie, Mumbai, India. All other chemicals and reagents used were of high analytical grade.

Preparation of Matrix Tablets

Formulations were prepared by wet granulation and direct compression method using different drug : polymer ratios. The ingredients are blended and the obtained granules were then lubricated and finally punched.

Pre-compression Studies

The flow properties like angle of repose, carr's index, hausner ratio, were measured in order to select optimal formula for compression. Table.1

Evaluation test for tablets

Hardness, thickness, weight variation, friability, drug content were tested for the prepared tablets. Table .2

In-vitro dissolution studies

Dissolution studies were performed according to USP type II apparatus in phosphate buffer. The temperature was maintained at $37\pm 0.5^{\circ}\text{C}$ and was rotated at 50 rpm. The samples were withdrawn at various time intervals and analyzed at 268nm spectrophotometrically.

Table1

Formulations	Angle of repose (°) ‡	Bulk Density (g/mL) ‡	Tapped Density (g/mL) ‡	Carr's Index (%)	Hausner's ratio
F1	25.18±0.26	0.53 ± 0.04	0.61±0.25	12.69	1.14
F2	23.73±1.04	0.46±0.07	0.53±0.08	13.24	1.15
F3	26.68±0.79	0.50±0.02	0.59±0.32	15.77	1.18
F4	29.80±0.27	0.52±0.05	0.60±0.18	16.60	1.19
F5	25.74±0.71	0.49±0.17	0.57±0.33	16.55	1.17
F6	29.44±0.17	0.44±0.12	0.52±0.19	14.04	1.16
F7	31.55±1.08	0.49±0.06	0.59±0.65	16.47	1.19
F8	32.69±0.68	0.41±0.22	0.50±0.23	16.89	1.20
F9	32.27±0.74	0.43±0.08	0.54±0.31	18.12	1.22
F10	25.99±0.55	0.51±0.21	0.60±0.51	14.38	1.16
F11	28.75±0.99	0.47±0.25	0.54±0.36	12.94	1.14
F12	27.15±0.59	0.51±0.79	0.56±0.41	9.53	1.10
F13	25.43±1.06	0.45±0.12	0.51±0.16	13.28	1.15
F14	24.46±0.98	0.42±0.15	0.47±0.36	10.32	1.11
F15	29.53±0.22	0.50±0.18	0.56±0.48	10.32	1.15
F16	25.74±0.71	0.51±0.23	0.57±0.63	11.91	1.13
F17	28.73±0.32	0.48±0.41	0.58±0.48	17.59	1.21
F18	19.29±0.91	0.49±0.45	0.59±0.54	16.65	1.19

‡All values represent mean ± Standard Deviation (SD), n=3

Table2

Formulation Code	Hardness (kg/cm ²) †	Thickness (mm) ‡	Weight (mg) ‡	Friability (%)	Drug content * (%)
F1	5.31±0.11	3.80±0.16	248.65±0.99	0.37	97.35±0.96
F2	5.38±0.17	3.94±0.21	250.19±1.82	0.31	95.61±1.04
F3	5.33±0.35	4.20±0.39	249.65±1.91	0.46	99.29±0.55
F4	4.6±0.25	3.98±0.23	251.70±0.89	0.17	101.24±0.37
F5	4.81±0.41	4.17±0.51	250.14±0.98	0.51	100.21±0.42
F6	4.51±0.18	3.78±0.41	248.97±1.54	0.55	99.32±1.18
F7	4.53±0.24	4.15±0.32	251.51±0.96	0.62	94.70±1.53
F8	5.11±0.23	3.85±0.20	248.90±1.29	0.37	93.49±1.23
F9	5.08±0.19	3.83±0.15	250.02±1.87	0.75	96.35±2.20
F10	5.48±0.14	4.62±0.74	250.03±1.03	0.46	96.87±0.38
F11	5.36±0.26	3.90±0.22	249.89±0.92	0.42	98.10±0.58
F12	4.46±0.26	4.25±0.61	249.65±1.68	0.17	92.93±1.48
F13	4.55±0.27	4.02±0.36	252.16±1.30	0.22	94.88±2.38
F14	4.73±0.33	4.28±0.57	252.01±0.87	0.28	91.33±1.72
F15	4.83±0.29	3.97±0.12	249.86±0.97	0.53	99.62±2.12
F16	5.23±0.12	4.40±0.83	250.29±1.07	0.64	100.06±1.83
F17	5.46±0.28	3.88±0.34	250.39±0.86	0.71	94.90±1.18
F18	5.48±0.14	3.95±0.25	250.15±0.91	0.48	97.68±1.19

* All values represent mean ± Standard Deviation (SD), n=3

† All values represent mean ± Standard Deviation (SD), n=6

‡ All values represent mean ± Standard Deviation (SD), n=20

RESULTS AND DISCUSSION

Various physical parameters were evaluated the angle of repose, carr’s index, hausner ratio, thickness, weight variation, hardness, friability and drug content values of all the prepared tablets in reference to average values for each parameter were found within official limits. In-vitro release study of different polymers were studied. In figure1, formulations with 40% of polymer concentration i.e., PEO, HPMC, EC and EUDRAGIT RLPO respectively showed sustained drug release, of which the HPMC (40%) is been optimized. Drug relase kinetics were fitted in peppas equation and first order.

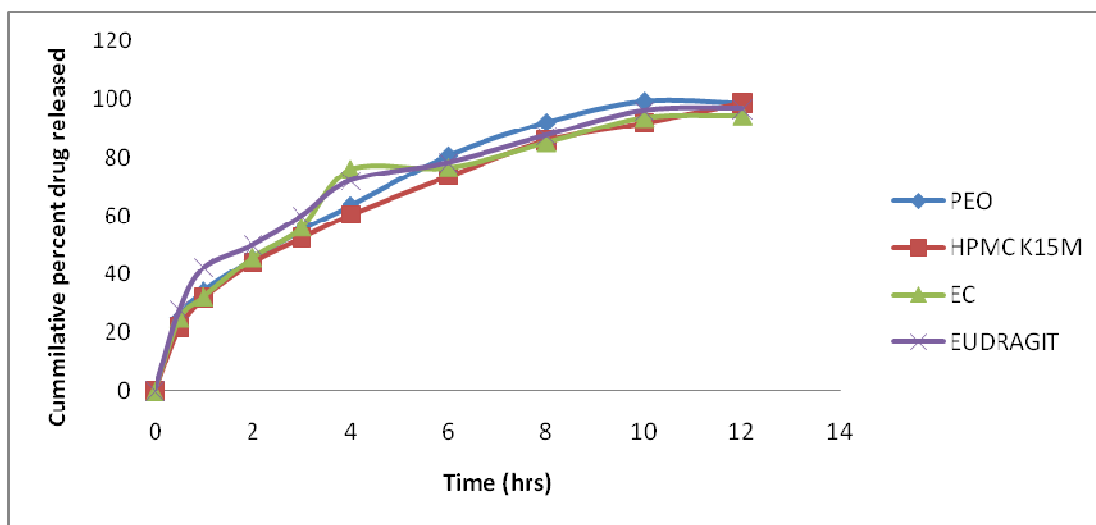


Figure 1: Effect of different polymers on the release rate of tramadol hydrochloride matrix tablets.

Table 3. Drug Release Kinetics of Batch (F9) Matrix Tablets

Zero order		First order		Higuchi		Korsmeyer-Peppas			MDT (h)	f2 factor
r ²	K ₀ (h ⁻¹)	r ²	K ₁ (h ⁻¹)	r ²	K _H (h ^{-1/2})	r ²	n	K _{KP} (h ⁻ⁿ)		
0.818	7.001	0.934	0.3247	0.935	25.89	0.948	0.43	0.4421	1.03	86

r² = Correlation coefficient; K = Kinetic constant; n= Diffusional exponent.

Table 4. Drug Release Kinetics of Optimized (F12) Matrix Tablets

Zero order		First order		Higuchi		Korsmeyer-Peppas			MDT (h)	f2 factor
r ²	K ₀ (h ⁻¹)	r ²	K ₁ (h ⁻¹)	r ²	K _H (h ^{-1/2})	r ²	n	K _{KP} (h ⁻ⁿ)		
0.916	6.991	0.991	0.2924	0.971	30.99	0.978	0.57	0.3429	1.83	95

r² = Correlation coefficient; K = Kinetic constant; n= Diffusional exponent.

CONCLUSION

Results indicated that viscosity and amount of polymer in formulation significantly affect the Tramadol hydrochloride release from Matrix tablet. Thus, it was concluded that the potential

sustained release matrix tablets of Tramadol could be prepared using optimized amount of polymer (HPMC).

Optimized formulation F12 (drug to polymer ratio 1:1) which includes HPMC K15M has successfully sustained the drug release for 12 hours and the drug release pattern was similar to theoretical release profile. The release process involves anomalous diffusion mechanism, as indicated by the n value of 0.57 in Korsmeyer's plot. FTIR studies indicated that there was no interaction between the drug and excipients and stability studies had proved the integrity of the developed matrix tablets.

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