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Research Article

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Formulation and Evaluation of Sustained Release Tablet of Tapentadol

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ABSTRACT

The objective of the present study was to develop sustained release tablets of Tapentadol (250mg) by wet granulation using various grades of hydrophilic polymer like Hydroxy propyl methyl cellulose K100M and Hydroxy propyl methyl cellulose 5cps or combination of both . The drug excipient mixtures were subjected to preformulation studies. The tablets were subjected to physicochemical studies, *in- vitro* drug release, and kinetic studies.. FTIR studies shown there was no interaction between drug and polymer. The physicochemical properties of tablets were found within the limits. Tapentadol is a centrally acting analgesic that exerts its pharmacological effects primarily by binding to mu-opioid receptors.. It has plasma half-life of 4-6 hrs and 32% bioavailability. The drug release from optimized formulations was extended for a period of 24 hrs. The kinetic treatment of selected formulation (F3) showed that the release of drug follows zero order models.. Results of the present study indicated the suitability of hydrophilic polymers in the preparation of matrix based sustained release formulation of Tapentadol.

Key words: Tapentadol, Sustained release, Wet granulation, Hydroxy Propyl Methyl Cellulose K -100M, zero order models

INTRODUCTION

Matrix tablets composed of drug and polymer as release retarding material offer the simplest approach in designing a sustained release system[1]. To reduce the administered dose and to improve patient convenience, a sustained release matrix tablet formulation of Tapentadol is desirable[2]. In the present study an attempt has been made to develop sustained release matrix tablet of Tapentadol using various grades of hydrophilic polymers, such as hydroxyl propyl methyl cellulose (HPMC) K100M and hydroxyl propyl methyl cellulose (HPMC) 5cps or combination of both along with drug in varying proportions by wet granulation method. For sustained release systems, the oral route of drug administration has received the most attention as it is natural, uncomplicated, convenient and safer route[1]. The drug release for extended duration, particularly for highly water soluble drug using a hydrophilic matrix system is restricted because of the rapid diffusion of the dissolved drug though the hydrophilic network[3]. For such drug with high water solubility hydrophobic polymers are suitable, along with a hydrophilic matrix for developing sustained release dosage forms[4]. Therefore in this study both the hydrophilic polymer was used as matrix material. The main objective of the study is to formulate several hydrophilic matrix systems by polymer material to investigate the effect of both[5].

Many orally administered drugs have poor bioavailability when administered as conventional dosage form. The bioavailability of the drug from a conventional dosage form of Tapentadol is 32% due to the limitation of GI tract i.e. absorption is limited up to upper part of the GI tract and it has plasma half-life of 4-6 hrs. To compensate for this effect, a very large dose is often administered so that absorption of the therapeutically required quantity of the drug can occur. This technique may prove costly with expensive drugs; and the unabsorbed drug may also have undesirable side effect within the gastrointestinal tract. Moreover, poorly absorbed drug often have large inter- and intra subject variability in bioavailability. This problem may be overcome by modified release drug delivery system. So sustained release matrix tablets of Tapentadol can increase the bioavailability of the drug and reduce the frequency of the dosing. Tapentadol produces potent analgesic effects via its dual mechanism of action, ie, mu receptor agonism and norepinephrine reuptake inhibition. Tapentadol has a biological half-life of 4 to 6 hours i.e., it requires 4-6 times a day dosing[6]. The main objective of the study is to formulate several hydrophilic matrix systems by polymer material to investigate the effect of both.

MATERIALS AND METHOD

Materials

HPMC K 100M, HPMC 5cps, PVP K30, mannitol, lactose, ,Isopropyl alcohol(IPA) Magnesium stearate and talc were purchased from Central Drug House (P) Ltd., New Delhi.

Method[7, 8, 9]

Sustained release tablets of Tapentadol were prepared by wet granulation method. Polyvinyl pyrrolidone (PVP K30) was used as binder. Magnesium stearate and Talc was added as lubricant prior to compression. All the powders were passed through 24 mesh. Required quantity of drug, diluents and polymers were mixed thoroughly and a sufficient quantity of binding agent was added slowly. After enough cohesiveness was obtained, the mass was sieved through 16 mesh. The granules were dried at 50ºC for 45minuts and were mixed with talc and magnesium stearate. Finally the tablets were compressed using tablet compression machine.

EVALUATION

1. **Weight variation[10, 11]**
   Twenty tablets were randomly selected from each batch individually weigh, the average weight and standard deviation of 20 tablet calculated.

2. **Hardness[10, 11]**
   Hardness was measured using Pfizer hardness tester, for each batch three tablet were tested.

3. **Friability[6, 11, 12]**
   Roche friabilator was used to measure the friability of the tablets. It was rotated at a rate of 25 rpm. Ten tablets were weighed collectively and placed in the chamber of the friabilator. In the friabilator, the tablets

were exposed to rolling, resulting from free fall of tablets within the chamber of the friabilator. After 100 rotations (4 minutes), the tablets were taken out from the friabilator and intact tablets were again weighed collectively. Permitted friability limit is 1.0%. The percent friability was determined using the following formula.

$$\% \text{ Friability} = \frac{W1 - W2}{W1} \times 100$$

Where,
W1 = weight of the tablets before test
W2 = weight of the tablets after test

4. Content uniformity[11, 12, 13]

Twenty tablets were selected randomly and average weight was calculated. Tablets were crushed in a mortar and accurately average weighed amount of tablets triturate was taken for analysis. Samples were transferred to different volumetric flasks and were diluted up to the mark using 0.1 N HCl. The content was shaken well and kept for 30 minutes for dissolving the drug completely. The mixtures were filtered and appropriate dilutions were made. The drug content in each tablet was estimated at ƛ max 272.20 nm against blank as reference.

5. In vitro drug release study[6, 11, 13]

In vitro drug release study of the samples was carried out using USP – type II dissolution apparatus (Paddle type). The dissolution medium, 900 ml of simulated gastric fluid, was placed into the dissolution flask maintaining the temperature of 37 ± 0.5˚C and rpm of 100. One Tapentadol sustain release tablet was placed in each basket of the dissolution apparatus. The apparatus was allowed to run for 24 hours. Samples measuring 5 ml were withdrawn after every 1 hour interval. First 2 hrs in 0.1 N HCl and then in Phosphate buffer 6.8. During sampling, samples were filtered. The fresh dissolution medium was replaced every time with the same quantity of the sample. Collected samples were analyzed at λmax 272.20 nm using 0.1 N HCl and 6.8 Phosphate buffer as blank. The cumulative percentage drug release was calculated.

Table 1: Composition of Sustained release tablets of Tapentadol

Batch code	**INGREDIANT (mg)**								
	Tapentadol	**Lactose**	**Mannitol**	**HPMC K100**	**HPMC 5 cps**	**PVP K-30**	**Isopropyl alcohol**	**Magnesium stearate**	**Talc**
F1	250	102	-	130	-	10	Q.S.	4	4
F2	250	102	-	-	130	10	Q.S.	4	4
F3	250	51	51	130	-	10	Q.S.	4	4
F4	250	51	51	-	130	10	Q.S.	4	4
F5	250	102	-	65	65	10	Q.S.	4	4
F6	250	-	102	65	65	10	Q.S.	4	4

RESULTS AND DISCUSSION

Formulations were prepared by wet granulation techniques using different polymers (Table 1). All formulations evaluated for weight variation and results indicated that for all formulations exhibit very low weight variation which lies within the pharmacopoeia limits i.e. ± 5%. The hardness of the tablets was found to be in the range of 3.0 ± 0.42 to 4.5 ± 0.66 kg/cm^2. The percentage friability was less than 1% for all formulation ensuring mechanical stability of the formulated tablets. Content uniformity in all the formulations were found in the range of 97.53 to 99.64% indicating the compliance is within the pharmacopoeia limits(85-115%). % Cumulative drug release from all the prepared formulation was found to be in following order: F3 > F4 > F5 > F6 > F1 > F2. % Cumulative drug release from F3 formulation was found to be in 24 hours. Formulation F3 shows higher drug content and high % Cumulative drug release.

Table 2: Result of Pre-compression evaluation parameters

Material	Angle of repose (Degree)	Bulk density (gm/ml)	Tapped density (gm/ml)	Compressibility Index	Hausner ratio
Tapentadol	33.12˚	0.719	0.871	17.5	1.211
F1	28.32˚	0.691	0.781	11.6	1.130
F2	29.77˚	0.642	0.735	12.6	1.144
F3	27.99˚	0.669	0.775	13.7	1.158
F4	27.84˚	0.685	0.789	13.2	1.151
F5	29.52˚	0.695	0.799	13.0	1.149
F6	28.45˚	0.635	0.748	15.1	1.177

Table 3: % Content uniformity of sustained release tablets of Tapentadol

Formulation code	Amount of drug(mg)	Percentage content of drug
F-1	248.19 ± 0.59	99.27
F-2	245.26 ± 0.13	98.10
F-3	249.11 ± 0.24	99.64
F-4	245.91 ± 0.13	98.36
F-5	243.84 ± 0.24	97.53
F-6	246.98 ± 0.79	98.79

Table 4: % Cumulative drug release of sustained release tablets of Tapentadol

Time (hours)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	24.22	25.25	20.41	19.44	23.11	22.32
2	27.98	29.48	24.58	25.89	28.84	27.87
3	31.56	36.36	26.19	28.98	34.78	36.73
4	38.89	44.22	30.46	33.89	39.73	43.74
5	51.93	55.11	36.11	38.33	46.89	51.23
6	58.28	63.25	42.98	44.89	55.42	57.71
9	69.29	74.99	50.34	53.83	57.93	70.22
12	80.68	87.92	62.42	66.98	65.84	78.73
15	87.44	95.59	74.28	75.33	76.56	84.74
18	94.53	95.77	81.39	83.46	85.32	90.28
20	94.69	-	86.34	89.39	94.22	95.31
21	-	-	89.44	93.26	96.54	95.39
22	-	-	94.82	97.02	96.69	-
23	-	-	98.15	97.16	-	-
24	-	-	98.37	-	-	-

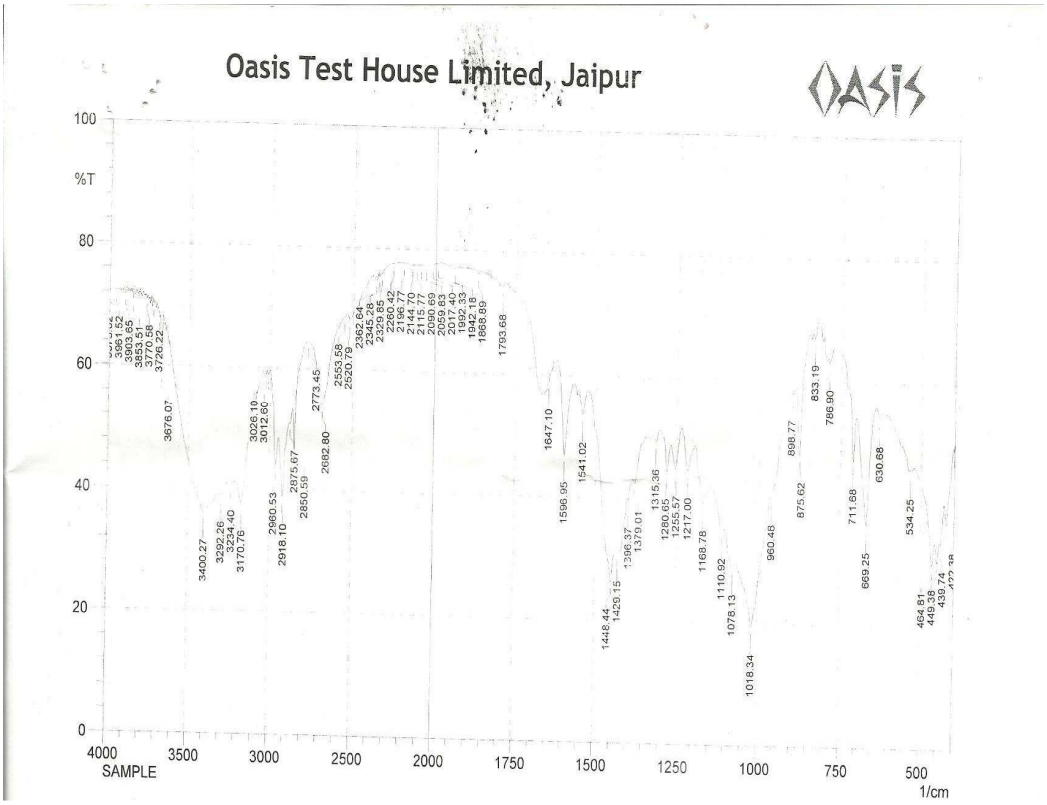

Figure 1 : FTIR of Drug, polymer and excipient granules

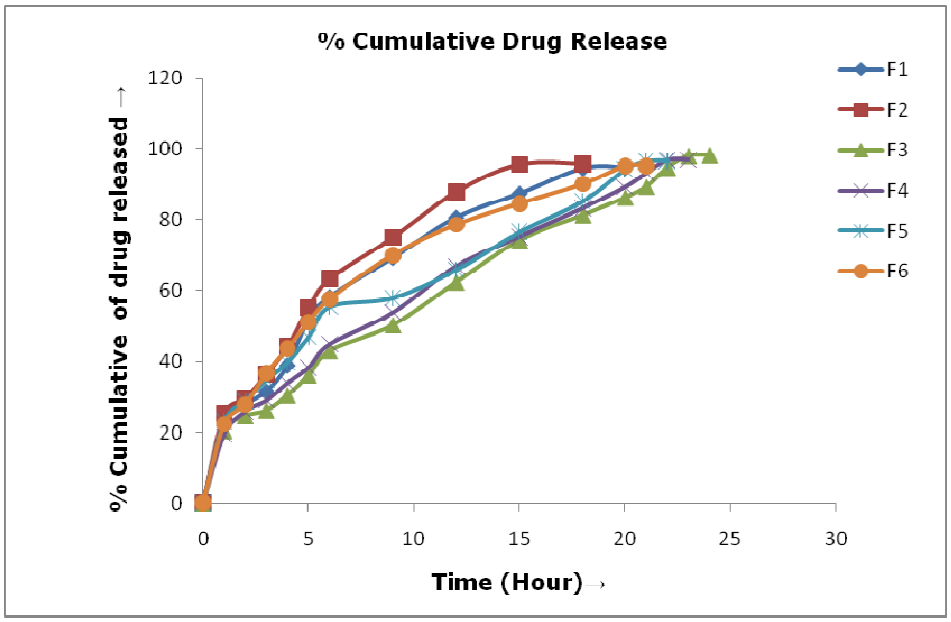

Figure 2: *In vitro* release profile for F1 to F6.

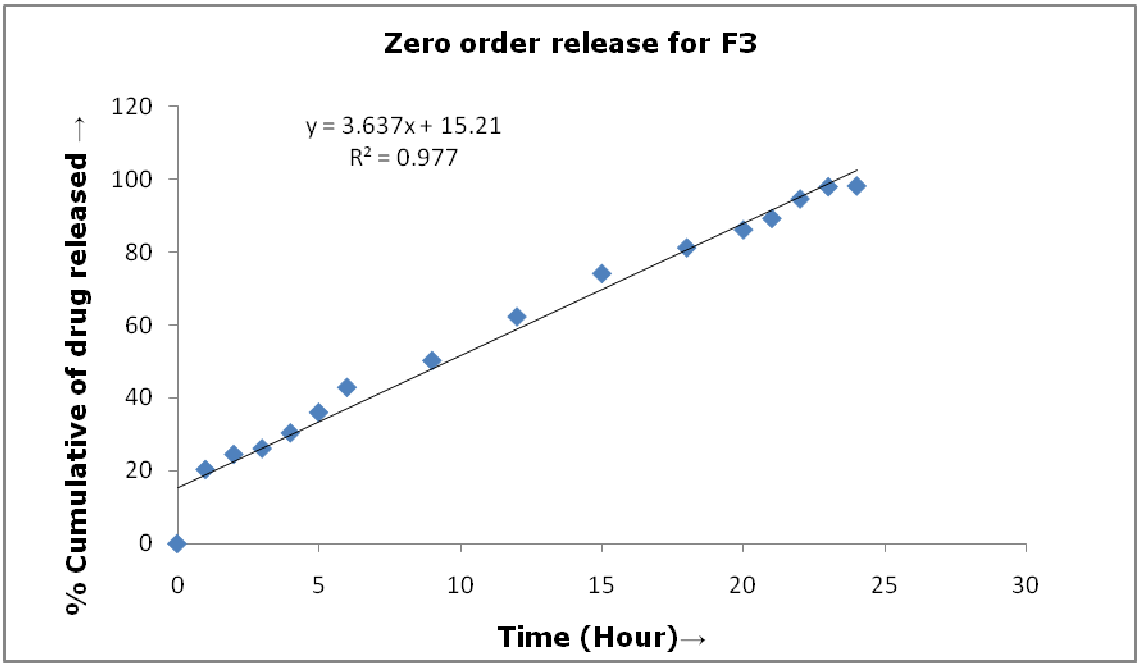

Figure 3: zero order release for F-3 sustained release tablets of Tapentadol

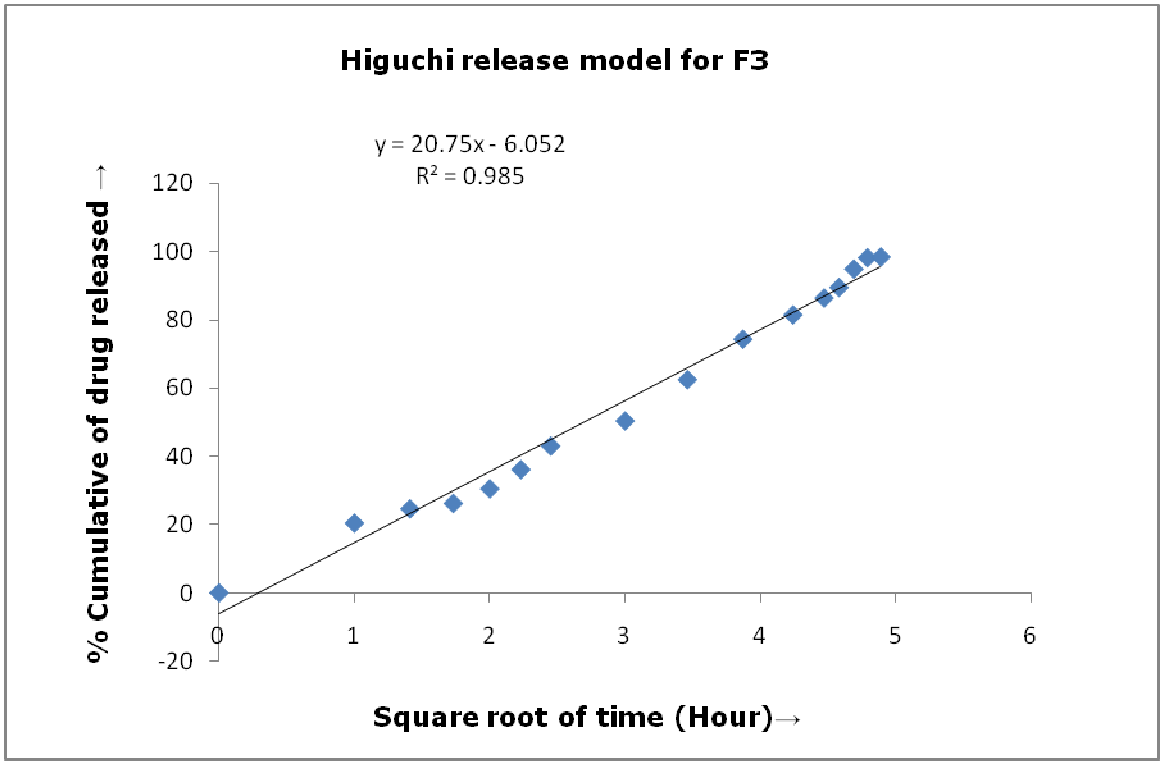

Figure 4: Higuchi release for F-3 sustained release tablets of Tapentadol

CONCLUSION

On the basis of present study it was concluded that sustained release tablets of Tapentadol prolong the time for drug release and thus better patient compliance can be achieved. Results show that it is better to use polymer HPMC K 100M alone than combination of both polymers that used.

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