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FORMULATION AND EVALUATION OF TRAMADOL HYDROCHLORIDE SUSTAINED RELEASE TABLETS

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ABSTRACT

The objective of the present study was to formulate sustained-release matrix tablets of Tramadol hydrochloride, for treatment of pain. The matrix tablets were prepared by direct compression method using hydroxyl propyl methylcellulose K4M, Carbopol 934 in various concentrations. The powder showed satisfactory flow properties and compressibility. All the formulations showed acceptable pharmacopoeial standards. Successful formulation was found stable after evaluation for physicochemical parameters when kept for 90 days at room temperature, 40^0c and 2-8 ^{0}c. It concluded that sustained release matrix tablets of Tramadol hydrochloride containing of HPMC K4M and Carbopol 934 provide a better option for Sustained release of drug.

Key words:
Tramadol hydrochloride, Sustained release matrix tablets, polymers, direct compression technique, in vitro drug release studies.

INTRODUCTION

One of the least complicated approaches to the manufacture of sustained release dosage forms involves the direct compression of the blends of drug, retardant material and additives to form a tablet in which the drug is embedded in a matrix core of the retardant.[1] Sustained release products are needed for metformin to prolong its duration of action and to improve patient compliances. Matrix systems are widely used in oral controlled drug delivery because of their flexibility, cost effectiveness, low influence of the physiological variables on its release behavior and broad regulatory acceptance.[2] Tramadol Hydrochloride is an opiod analgesic drug which draws attention in the treatment of osteoarthritis. It is a centrally acting drug and blocks the transmission of pain signals sent by nerves to the brain.[3] In the present study, matrix extended-release tablets of Tramadol Hydrochloride were prepared using different polymers like HPMC K15M, Carbopol 934 resulting in less frequent fluctuations in plasma concentrations.[4]

MATERIALS

Tramadol HCL was obtained from Micro labs, HYD. HPMC k 15M and Carbopol 934 were procured from Synpharma Research Labs, Hyderabad, and other chemicals the reagents used were of analytical grade.

METHODOLOGY

Preparation of Tramadol hydrochloride tablets

Table 1: Formulation Table

S. No	INGREDIENTS	F1	F2	F3	F4
1	Tramadol hydrochloride	50	50	50	50
2	HPMC K15M	50	100	--	--
3	Carbopol 934	--	--	50	100
4	Lactose	95	45	95	45
5	Magnesium stearate	3	3	3	3
6	Talc	2	2	2	2
7	Total Wt.	200	200	200	200

Preparation of Sustain release Layer of Tramadol hydrochloride [5]

Direct compression

Sustained release tablets were prepared by direct compression method. All ingredients were weighed and passed through 40# sieve, blended except lubricant. These blends were lubricated with Magnesium stearate, which was previous, passed through 60# Sieve. The lubricated blend was for compressed 200 mg tablet using 8mm die and punches, with hardness between 3 to 5 kg/cm^2. In total, eight formulations containing different combination of polymers were prepared.

Evaluation parameters

Weighinvariation:[6]

Twenty tablets were randomly selected form each batch and individually weighed. The average weight and standard deviation of 20 tablets was calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weight deviates from the average weight by more than the percentage

Thickness:[7]

Twenty tablets were randomly selected from each batch and their thickness was measured by using vernier caliper. The thickness of three tablets from each batch was measured and the mean was calculated.

Hardness:[8]

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm^2. Three tablets were randomly picked and hardness of the tablets were determined.

Friability:[9]

Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche friabilator was used for the purpose. This device subjects a number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at distance of 6 inches with each revolution. Twenty tablets were weighed and placed in the Roche friabilator, which was then operated for 25 rpm for 4 min. After revolution Tablets were dedusted and reweighed. Compressed tablets should not lose more than 1% of their weight.

The percentage friability was measured using the formula,

$$\% F = \{1-(Wo/W)\} \times 100$$

Where,

% F = friability in percentage

Wo = Initial weight of tablet

W = weight of tablets after revolution

Content Uniformity:[10]

Twenty tablets from each batch were powdered and weighed accurately equivalent to 100 mg Tramadol hydrochloride. Dissolve the weighed quantity of powder into 100 ml of 0.1 N NaOH solution by stirring it for 15 min. 01 ml of solution was pipette out into 10 ml volumetric flask and make up the volume with distilled water. Immediately analyse the drug by taking absorbance at nm using reagent blank.

Disintegration time:[11]

The disintegration time of tablets was determined by using Disintegration test apparatus (scientific). Tablets were placed in disintegration test assembly and disc was placed on tablets in each glass tube of assembly. The assembly was dipped in a vessel containing 900 ml distilled water at 37°C. The time for disappearance of tablet residue above mesh was noted as disintegration time.

***In- Vitro* Release study:**[12]

In-Vitro drug release studies were carried out using Tablet dissolution test apparatus USP II at 100 rpm. The dissolution medium consisted of 900 ml of Standard buffer pH 1.2 for the first 2 hrs, followed by pH 6.8 for remaining period of time. Temperature maintained at 37±5.The sample of 5ml was withdrawn at predetermined time intervals and an equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced. From that 5 ml sample, 1 ml sample was withdrawn and placed in a 10 ml volumetric flask and make the volume with distilled water. The diluted samples were assayed at 260 nm against reagent blank.

Stability studies:[13]

The success of an effective formulation can be evaluated only through stability studies. The purpose of stability testing is to obtain a stable product which assures its safety and efficacy up to the end of shelf life at defined storage conditions and peak profile. The prepared Matrix tablets of Tramadol hydrochloride were placed on plastic tubes containing desiccant and stored at ambient conditions, such as at room temperature, 40±2^{o}c and refrigerator 2-8^{o}c for a period of 90 days.

RESULTS AND DISCUSSION

FT-IR Spectrum of Tramadol hydrochloride

The compatibility between the drug and the selected Drug and other excipients was evaluated using FTIR peak

matching method. There was no appearance or disappearance of peaks in the drug-excipients mixture, which confirmed the absence of any chemical interaction between the drug, polymers and other chemicals.

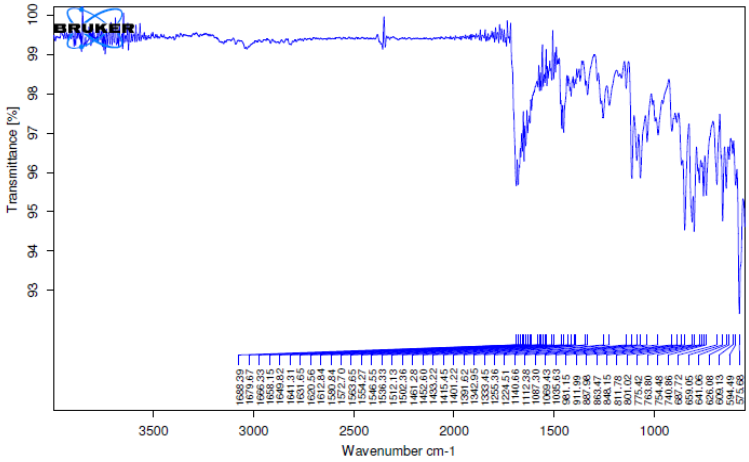

Fig 1: FTIR Studies of Pure Drug

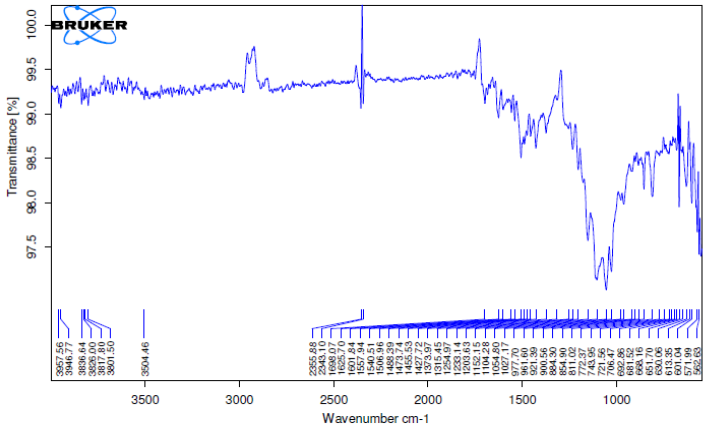

Fig 2: FTIR Studies of physical mixture of drug and excipients

Evaluation studies

Weight variation:

All the formulated (F1 to F4) tablets passed weight variation test as the % weight variation was within the pharmacopoeial limits of ±7.5% of the weight. The weights of all the tablets were found to be uniform with low standard deviation values.

Thickness:

Tablets mean thickness were uniform in F1 to F4 formulations and were found to be in the range of 2.56 mm to 2.71 mm.

Hardness:

The measured hardness of tablets of each batch ranged between 2.5 to 2.9 kg/cm^2. This ensures good handling characteristics of all batches.

Friability:

The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable.

Content Uniformity:

The percentage of drug content for F1 to F4 was found to be between 92.35 % to 95.84 % of Tramadol hydrochloride, it complies with official specifications.

Disintegration Time:

In the presented studies, three different types of in vitro methods of tablet disintegration were used: those where the only factor leading to the disintegration was water wicking into the matrix of the tablet, the tests with water agitation or stirring, and the methods where direct destructive forces were put on the tested tablet, such as grinding or pressing with additional weight. Therefore, disintegration tests showed great variability in the data measured with different methods.

Table 2: Evaluation parameters of Tramadol hydrochloride SR tablets

F. No.	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)	Disintegration time
F1	199	2.56	2.4	0.24	92.35	15
F2	200	2.60	2.9	0.26	94.20	13
F3	200	2.71	2.7	0.28	95.84	10
F4	199	2.69	2.5	0.26	93.65	17

Dissolution studies

All the 4 formulation of Tramadol hydrochloride tablets were subjected to *in vitro* release studies these studies were carried out using dissolution apparatus. The dissolution medium consisted of 900 ml of Standard buffer pH 6.8 for period.

Table 3: Drug release studies of all formulations

Time	F1	F2	F3	F4
0	0	0	0	0
1	24.59	20.18	22.25	20.15
2	32.47	30.49	31.90	32.48
3	46.95	42.15	43.58	40.35
4	52.84	50.18	52.49	50.16
5	63.18	62.95	60.98	62.95
6	72.58	70.17	72.40	75.96
7	82.75	80.32	82.45	80.15
8	93.15	94.85	96.92	93.47

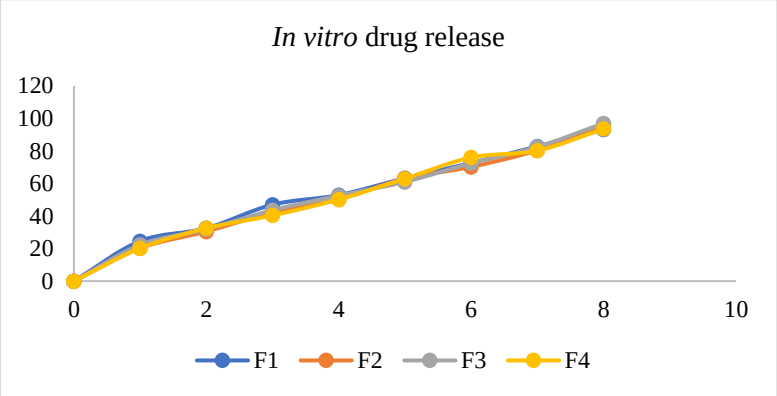

Table 3: Dissolution Profile of F1 to F4 formulations

Stability Study

There was no significant change in physical and chemical properties of the tablets of formulation F-3 after 90 days. Parameters quantified at various time intervals were shown.

Table 4: Stability studies of all formulations

Formulation Code	Parameters	Initial	1st Month	2nd Month	3rd Month	Limits as per Specifications
F-3	25^{0}C/60%RH % Release	96.92	96.80	95.80	94.57	Not less than 85 %
F-3	30^{0}C/75% RH % Release	96.92	96.45	95.74	94.50	Not less than 85 %
F-3	40^{0}C/75% RH % Release	96.92	96.57	95.35	94.45	Not less than 85 %

CONCLUSION

Various formulations of sustained release tablets of Tramadol hydrochloride were prepared by using different polymers viz, HPMC K15M, Carbopol 934 in different proportions and combinations by direct compression technique. The tablets were evaluated for physical parameters, *in vitro* release study and stability studies. All formulations were found to be with in the specifications of official pharmacopoeias and/or standard references. In-vitro release indicated that the formulation F3 had better dissolution profile along with sustained action as compared to other formulations. Stability study was conducted on tablets of Batch F3 stored at room temperature, 40 ^{0}C, and 2-8 ^{0}C for one month. Tablets were evaluated for hardness, friability, in-vitro release profile and drug content. No significant changes were observed in any of the studied parameters during the study period (3 months), thus it could be concluded that formulation was stable.

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