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Original Article

Screening of super disintegrants by formulating and evaluating fast dissolving tablets of ondansetron hydrochloride

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ABSTRACT

For a fast dissolving tablet to show fast disintegration, super disintegrants play a vital role. The objective of the present study is to screen three super disintegrants namely Cross carmallose sodium, Sodium starch glycolate and Cross povidone by formulating fast dissolving tablets and evaluating them. First, the tablet blends were subjected to pre compression parameters (bulk density, tapped density, angle of repose, Hausner's ratio and Car's index). Then the tablet blends were formulated in fast dissolving tablets of 200 mg each of Ondansetron Hydrochloride by direct compression method. The tablets of various batches had varied concentrations of the three super disintegrants individually. The tablets were then evaluated for various post compression parameters (weight variation, thickness, hardness, friability, wetting time, water absorption ratio, disintegration time, drug content and *in-vitro* drug release). Out of all the batches the formulation T8 showed best results which implied that Cross Povidone can be considered as a good super disintegrant and that batch was optimised.

Keywords: Fast dissolving tablets, super disintegrants, Ondansetron Hydrochloride

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INTRODUCTION

The drug administration by the oral route has a wide acceptance of about 50-60% of total dosage forms. The dosage forms include tablets, capsules, powders, lozenges, etc. Out of these dosage forms, tablets are the most popular of them because of ease of accurate dosing, good chemical and physical stability, no pain, ease of administration and handling, compact nature, high patient acceptability, etc. But, the most common problem for solid dosage forms is the problem of swallowing (dysphagia) or chewing. This is mainly seen in paediatric or geriatric patients or with individuals with poor muscular or neurological conditions. The difficulty of swallowing can also be seen when there is no water available or in conditions like nausea, vomiting, coughing, common cold, allergic condition and bronchial infection. [1, 2]

To overcome these problems, fast dissolving solid dosage forms are attempted to be formulated. These dosage forms can be dissolved and suspended in water, chewed or rapidly dissolved in mouth. In the last decade fast dissolving tablet (FDT) technology has drawn great attention. FDTs are also called rapid disintegrating tablets, Orodispersible tablets, rapi melts, melt-in mouth dissolving tablets, porous tablets, etc. [2]

The European Pharmacopoeia defines the term Orodisperse as a tablet that can be placed in the mouth where it disperses or disintegrates rapidly before swallowing. United States Food and Drug Administration (USFDA) defines FDTs as 'a solid dosage form containing medicinal substance or active ingredient which disintegrate rapidly usually within a matter of seconds when placed upon the tongue'. FDTs dissolve or disintegrate in the oral cavity without the need of water. Most FDTs contain substances that mask the bitter taste of the drug which increases the palatability of the dosage form. The FDTs when administered turn into a soft paste or liquid form due to rapid disintegration which promotes easy swallowing and reduces risk of chocking. [3]

It can also be said that faster the dissolution, faster will be the absorption and hence faster onset of action. In order to achieve faster dissolution, disintegration of the dosage form should be quick. So, the main factor to be considered in formulation of the FDTs is the disintegration time. Faster disintegration time can be observed with the use of super disintegrants which help the FDTs to disintegrate within a matter of seconds as the time considered for the tablet to disintegrate is less than one minute. [4, 5]

Ondansetron Hydrochloride is a competitive serotonin type 3 (5HT3) receptor antagonist. It is effective in the treatment of nausea and vomiting caused by cytotoxic chemotherapeutic drugs, radiotherapy, anaesthesia or surgery. It is also used for prevention of post-operative nausea and vomiting in adults. Ondansetron hydrochloride is well absorbed from the gastrointestinal tract and undergoes some first-pass metabolism. Mean bioavailability in healthy subjects, following administration of a single tablet, is approximately 56%. [6, 7]

The present aim of the study is to formulate fast dissolving tablets of Ondansetron hydrochloride containing various super disintegrants namely crosscarmallose sodium, sodium starch glycolate and cross povidone. The tablets are formulated by direct compression method. The tablets are evaluated by various tests and the best formulation is optimised.

MATERIALS AND METHODS

Materials: Ondansetron Hydrochloride was obtained as a gift sample from Cadila Pharmaceuticals, Ahmedabad. Crosscarmallose sodium, sodium starch glycolate, cross povidone, mannitol, talc, microcrystalline cellulose and magnesium stearate was obtained from Loba Chemicals, Mumbai.

Methods:

Preparation of Fast Dissolving Tablets of Ondansetron Hydrochloride: Tablets weighing 200 mg containing Ondansetron Hydrochloride (8mg) were formulated by direct compression method using various super disintegrants like crosscarmallose sodium (CCS), sodium starch glycolate (SSG) and crosspovidone (CP) in various concentrations (2%, 4% & 6%). The drug, super disintegrants, mannitol, microcrystalline cellulose (MCC), magnesium stearate and talc were blended together and passed through sieve of 40 mesh. The final blend was then compressed into 200mg tablets using tablet compression machine. Various batches containing different super disintegrants in varied concentrations were prepared. Table 1 shows the composition of various batches of the FDTs.

Pre-compression evaluation parameters

The powder blend were evaluated for the following flow properties: [8]

Bulk density: Bulk density is the mass of the powder divided by the bulk volume and is expressed as g/ml. accurately weighed 10 g of blended powder from each formulation was taken and initial volume of blended powder was poured in the measuring cylinder was noted.

Bulk density = Mass of powder / Bulk volume

Tapped density: It is the ratio of total mass of the powder to the tapped volume of powder. The volume was measured by tapping the powder blend for about 100 times.

Tapped density = Mass of powder / Tapped volume

The mean ± standard deviation values of angle of repose were calculated. The results were determined and mentioned.

Angle of repose: The angle of repose of powder blend was determined using funnel. 10 g of accurately weighed powders was placed into the funnel. The powder was allowed to flow through the funnel freely onto the surface.

The diameter of the powder cone was measured and the angle of repose was calculated using the following equation:
$\Theta = \tan^{-1}(h/r)$
Where, h=height and r = radius.

Hausner's ratio: It is expressed by ratio of tapped density to the bulk density. It is given by formula:
Hausner's ratio = Tapped density / Bulk density

Carr's index: It is the ratio of bulk density and tapped density and is given by formula:
Carr's Index = (Tapped density- Bulk density) / Tapped density X100

Post-compression evaluation parameters of FDTs: [9]

Weight variation:
The United State Pharmacopeia (USP) weight variation test was performed by weighing 20 tablets individually calculating the average weight and comparing the individual tablet weight to the average weight.
Deviation (%) = (Average weight of tablet - Individual weight of tablet) / Average weight of tablet X 100

Hardness: Hardness of the tablet was measured using the Pfizer hardness tester. The indicator remains at the reading where the tablet breaks and returns back to zero by releasing the press button to reset.

Thickness: Thickness and diameter of tablets were measured with the screw gauge micrometre that had a scale of 0–25 mm.

Friability: A total of 20 tablets were weighed and placed in the Roche friabilator test apparatus; the tablets were exposed to the rolling and free falls within the apparatus at 100 revolutions in 25 rpm. The friability test determines the percentage loss % in weight of tablets.
Friability (%) = (Initial weight of tablet - Final weight of tablet) / Initial weight of tablet X 100

Wetting time and water absorption ratio:[10]
Wetting time of dosage form is related to with the contact angle. Lower wetting time implies a quicker disintegration of the tablet. The disintegration time for FDT needs to be modified as disintegration is required without water, thus the test should mimic disintegration in salivary contents. For this purpose, a petridish (10 cm diameter) was filled with 10 ml of water. The tablet was carefully placed in the centre of petridish and the time for the tablet to completely disintegrate into fine particles was noted. The water absorption ratio, R can be the determined according to the following equation:
$R = \frac{(W_a - W_b)}{W_b} X\ 100$
W_b = the weight of the tablet before keeping in the petridish
W_a= the wetted tablet from the petridish is taken and reweighed

Disintegration time (modified): A petridish (10cm diameter) was filled with 10 ml of water. The tablet was carefully put in the centre of petridish and the time for the tablet to completely disintegrate into fine particles was noted.

Drug content: Five tablets were crushed in mortar and powder equivalent to 8 mg OSH was dissolved in sufficient quantity of distilled water and make up volume in 100 mL volumetric flask. The solution was filtered through Whatmann filter paper (0.45 micron), suitably diluted with distilled water, and analysed at 310 nm, using a UV-Visible double beam spectrophotometer. Each sample was analysed in triplicate.

***In-vitro* dissolution studies:**[11]
USP type II apparatus was used for dissolution of FDTs. Three tablets from each batch were used to determine the dissolution of drug. The dissolution media was 500 mL distilled water, maintained at 37 ± 0.5ºC to permit the sink condition. The rotation speed is 50 rpm. Aliquots were withdrawn at 5, 10, 15, 20, 25 and 30 min time intervals and replenished immediately with same volume of fresh dissolution media. Aliquots were analysed spectrophotometrically at 310 nm, using UV-Visible double beam spectrophotometer.

RESULTS

The aim of the present study was to screen the super disintegrant by formulating fast dissolving tablets containing the three super disintegrants in various ratios. Various batches were formulated by direct compression method with the varying concentrations of super disintegrants (2%, 4% and 6%).

Before commencing the compression process, the tablet blends were subjected for various micromeretic tests namely, bulk density, tapped density, angle of repose, Hausner's ratio and Car's index. In order to get tablets with less weight variation, the powder blend should have good flow properties. The powder blend of the formulation T8 showed excellent flow properties (bulk density 0.32±0.02g/ml, tapped density 0.35±0.01g/ml, angle of repose 23.76±0.01, Hausner's ratio 1.09±0.01and Carr's index 8.57±0.04). The other powder blends also showed good flow properties. The results for all the formulations are given in table 2.

In order to formulate the fast dissolving tablets, direct compression method was used as it is a time saving and cost-effective process. 20 tablets for each batch (200 mg each) were formulated as per the formulation table. The formulated tablets were evaluated for post compression tests namely, weight variation, thickness, hardness, friability, wetting time, water absorption ratio, disintegration time, drug content and *in-vitro* drug release.

The ranges of the various tests were observed as weight variation (0.03-4.71%), hardness (3.10-4.16kg/m^2), thickness (4.15-4.32mm), friability (0.71-1.34%), wetting time (10.86-19.8 seconds), water absorption ratio (71.39-91.36), disintegration time (6.05-15.64 seconds), drug content (92.03-99.97%) and *in-vitro* drug release (95.79-100.04%).

Out of all the formulations T8 batch showed the best results for all the evaluation tests (weight variation 0.03±0.15%, hardness 4.16±0.2 kg/m^2, thickness 4.21±0.00, friability 0.71± 0.00%, wetting time 10.86±0.1 seconds, water absorption ratio 91.36±0.01, disintegration time 6.05±0.02 seconds, drug content 99.97±0.05 and *in-vitro* drug release 100.04±0.02%. The complete results are given in table 3. The graphs of in-vitro drug release studies for all the formulations are given in figure 1 and 2.

DISCUSSION

As per the results obtained, it was observed that the formulation T8 containing 4% Cross Povidone as super disintegrant showed the best flow propertiesand also the best results for all the tests as compared to other formulations. Finally cross povidone as a super disintegrant in the ratio of 4% (T8) was seen to have the fastest disintegration time and immediate release. Hence, it can be considered as an optimised batch as compared to the other batches.

CONLUSION

As aimed, the present study outlines the screening of three super disintegrants namely Cross carmallose sodium, Sodium starch glycolate and Cross Povidone. Fast dissolving tablets of Ondansetron Hydrochloride containing varied concentrations of these three super disintegrants were formulated and evaluated. Out of all the batches T8 showed the best results in disintegration time and immediate and complete release. Thus, this batch was optimised.

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Table 1: Formulation table for various batches.

CONTENTS	T1	T2	T3	T4	T5	T6	T7	T8	T9
Drug	8	8	8	8	8	8	8	8	8
CCS	4	8	12	-	-	-	-	-	-
SSG	-	-	-	4	8	12	-	-	-
CP	-	-	-	-	-	-	4	8	12
MCC	92	46	138	92	46	138	92	46	138
Mannitol	92	138	46	92	138	46	92	138	46
Talc	2	2	2	2	2	2	2	2	2
Magnesium stearate	2	2	2	2	2	2	2	2	2

All the contents are in mg. Each tablet is of 200 mg

Table 2: Pre-compression parameters of tablet blends

FORMULATION	BULK DENSITY (g/ml)	TAPPED DENSITY (g/ml)	ANGLE OF REPOSE	HAUSNER'S RATIO	CARR'S INDEX
T1	0.45±0.01	0.51±0.01	25.36±0.02	1.13±0.01	11.76±0.02
T2	0.43±0.02	0.48±0.01	25.22±0.01	1.11±0.02	10.41±0.01
T3	0.31±0.01	0.37±0.01	27.32±0.01	1.19±0.01	16.21±0.02
T4	0.35±0.01	0.41±0.01	26.15±0.02	1.17±0.02	14.63±0.01
T5	0.42±0.01	0.48±0.03	24.96±0.02	1.14±0.02	12.50±0.01
T6	0.44±0.02	0.51±0.02	24.27±0.01	1.15±0.01	13.72±0.01
T7	0.34±0.02	0.39±0.03	25.28±0.02	1.11±0.01	12.82±0.02
T8	0.32±0.02	0.35±0.01	23.76±0.01	1.09±0.01	8.57±0.04
T9	0.34±0.02	0.38±0.02	26.12±0.01	1.11±0.01	10.52±0.02

(Mean±SD), n=3

Table 3: Post compression parameters of tablets

TESTS	T1	T2	T3	T4	T5	T6	T7	T8	T9
Weight variation (%)	4.18± 0.01	4.69± 0.01	4.71± 0.02	1.05± 0.02	1.55± 0.02	4.55± 0.06	3.16± 0.01	0.03± 0.05	3.19± 0.15
Hardness (kg/m^2)	3.57± 0.5	3.10± 0.2	3.85± 0.2	3.34± 0.2	3.89± 0.5	3.87± 0.2	3.83± 0.2	4.16± 0.2	3.26± 0.2
Thickness (mm)	4.26± 0.01	4.32± 0.01	4.18± 0.01	4.24± 0.01	4.22± 0.00	4.16± 0.01	4.25± 0.00	4.21± 0.00	4.15± 0.00
% Friability	0.98± 0.02	1.34± 0.1	0.97± 0.01	1.21± 0.00	0.98± 0.01	0.96± 0.02	1.22± 0.01	0.71± 0.00	1.18± 0.02
Wetting time (seconds)	12.26± 0.02	12.85± 0.02	18.92± 0.3	12.55± 0.2	19.8± 0.3	19.39± 0.2	12.34± 0.2	10.86± 0.1	12.52± 0.3
Water absorption ratio	77.61± 0.01	81.82± 0.02	90.05± 0.02	82.61± 0.01	71.39± 0.00	85.92± 0.03	72.05± 0.01	91.36± 0.00	89.04± 0.01
Disintegration time (seconds)	14.25± 0.02	13.57± 0.02	8.75± 0.03	12.28± 0.03	15.64± 0.04	12.07± 0.03	15.16± 0.02	6.05± 0.02	10.18± 0.03
Drug content	96.68± 0.01	93.87± 0.02	97.55± 0.02	95.78± 0.02	92.03± 0.02	99.41± 0.01	94.75± 0.02	99.97± 0.05	98.57± 0.04
% Drug release (after 30 minutes)	97.15± 0.02	97.75± 0.02	99.55± 0.01	99.22± 0.02	95.79± 0.03	98.85± 0.02	99.07± 0.03	100.04± 0.02	99.58± 0.03

(Mean±SD), n=3

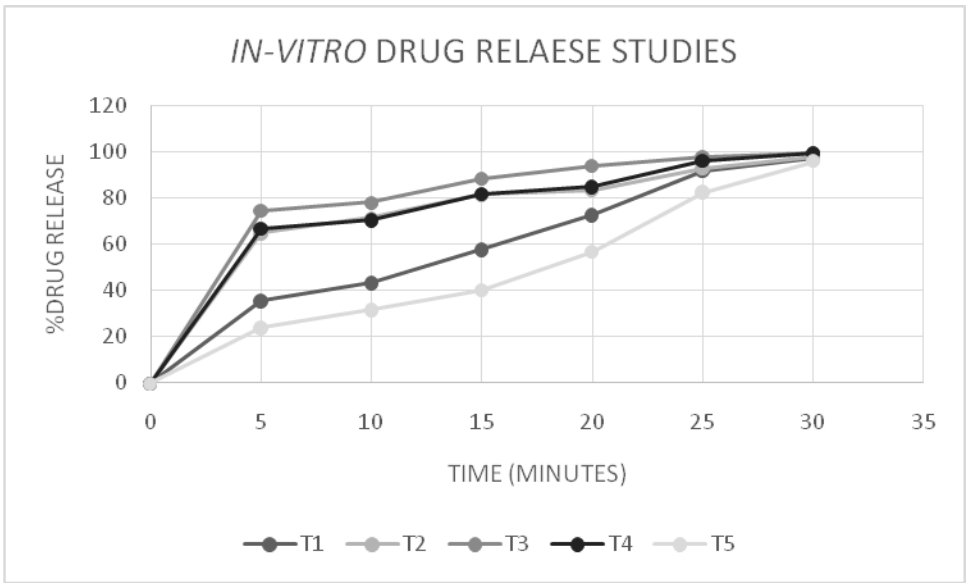

Figure 1: *In-vitro* drug release studies of T1, T2, T3, T4 and T5

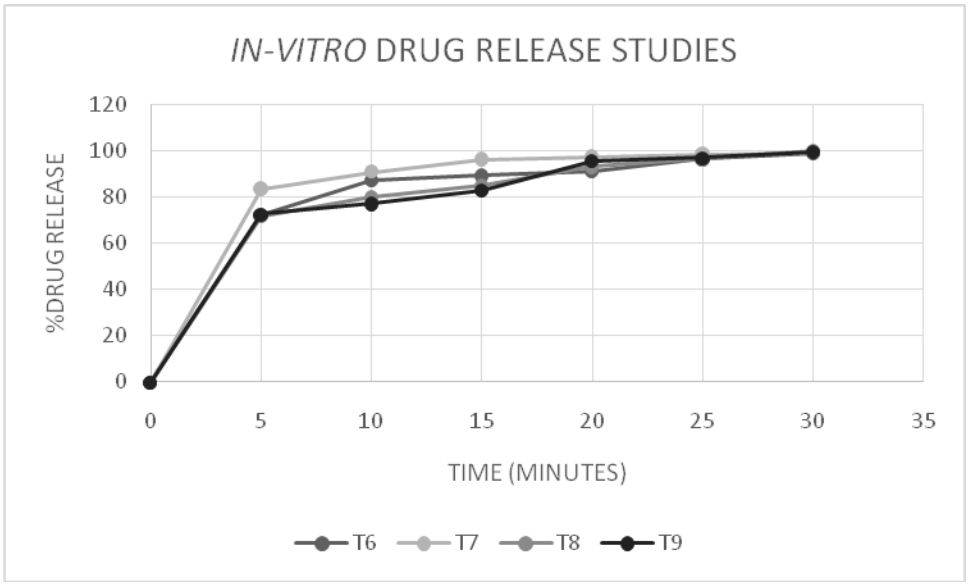

Figure 2: *In-vitro* drug release studies of T6, T7, T8 and T9

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