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RESEARCH ARTICLE

FORMULATION AND OPTIMIZATION OF ONDANSETRON HYDROCHLORIDE ORODISPERSIBLE TABLETS

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ABSTRACT

The demand for mouth dissolving tablets has been growing, during the last decade especially for geriatric and pediatric patients because of swallowing difficulties. Orodispersible tablets of Ondansetron hydrochloride were prepared to achieve quick onset of action and for maximum bioavailability. The objective of the present research was to compare the effect of different superdisintegrants on the mouth dissolving property of Ondansetron hydrochloride tablets. Orodispersible tablets of Ondansetron hydrochloride were prepared using sodium carboxy methyl cellulose, alginic acid, crospovidone, croscarmellose sodium and sodium starch glycollate as superdisintegrants by direct compression technique. Prepared orodispersible tablets were evaluated for weight variation, hardness, friability, content uniformity, wetting time, in vitro dispersion time, in vitro disintegration time and dissolution studies. Disintegration time from all the prepared formulation was found to be in following order: F3<F5<F1<F4<F2. Disintegration time was found to be rapid in F3 formulation. The in vitro dissolution time was found to be 99.77 ± 0.32 in 10 minutes for the formulation F3. Sodium starch glycollate (SSG) showed faster disintegration of tablets among all other superdisintegrants.

KEY WORDS: Ondansetron hydrochloride, orodispersible tablet, Sodium starch glycollate, direct compression, superdisintegrants

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INTRODUCTION:

The tablet is the most widely used dosage form because of its convenience in terms of self- administration, compactness, and ease in manufacturing[1]. Orodispersible tablets are uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed[2].

The various technologies used to prepare orodispersible tablets include freeze drying, tablet moulding, direct compression, spray drying, and sublimation. Direct compression represents a simple and cost effective tablet manufacturing technique. Use of conventional equipment, commonly available excipients and limited number of processing steps are the advantages of this technique[3]. Orodispersible tablets undergo disaggregating in the mouth when in contact with the saliva in less than 60 seconds, preferably in less than 40 seconds, forming a suspension which is easy to swallow. A major claim of some orodispersibles is increased bioavailability compared to traditional tablets[4, 5]. Because of dispersion in saliva while still in the oral cavity, there can be pregastric absorption from some formulation, in cases where the drug dissolves quickly. Buccal, pharyngeal and gastric regions are areas of absorption of the formulation[3, 6]. The dispersible tablets can be swallowed without water in the form of dispersion. They increase the patient compliance as well as provide quicker onset of action. Such a tablet may be swallowed in the form of dispersion, as it is expected to disintegrate quickly when in contact with saliva. When it comes in contact with acidic environment of the stomach, the complex will be broken down quickly and releasing the drug, which may then be absorbed in usual way[7, 8].

Ondansetron hydrochloride is a selective 5-HT3 receptor antagonist. It is used in the management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy[9, 10]. 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%[11-13].

Objective of present study was to develop such as novel drug delivery systems for Ondansetron hydrochloride by simple and cost effective direct compression method. Croscarmellose sodium, sodium carboxy methyl cellulose, crospovidone and sodium starch glycollate were used as superdisintegrant in the formulation for faster disintegration. Micro crystalline cellulose (MCC) is used as diluents and disintigrant.

MATERIALS AND METHODS:

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MATERIALS:

Ondansetron hydrochloride was received as a gift sample from Akums Drug Pharmaceutical Ltd, Utrakhand. Sodium saccharin, Magnesium stearate, talc, sodium carboxy methyl cellulose (sodium CMC), alginic acid, micro crystalline cellulose (MCC), crospovidone, Croscarmellose sodium and sodium starch glycollate (SSG) were purchased from Central Drug House (P) Ltd., New Delhi.

METHOD: [14, 15]

Orodispersible tablets of Ondansetron hydrochloride were prepared by direct compression technique. The composition orodispersible tablet of Ondansetron hydrochloride was shown in Table 1. Weighed quantities of Ondansetron hydrochloride along with appropriate concentrations of superdisintegrants along with excipients were weighed and mixed in geometric progression in a dry and clean mortar. Then the blend was passed through sieve no 60 for direct compression. The powder blend for direct compression was then compressed into tablets using a Rotary Tablet Machine.

Table 1: Composition of orodispersible tablets of Ondansetron hydrochloride

Formulations	Ingredients (mg)										
	Ondansetron hydrochloride	Sodium CMC	Alginic acid	SSG	Croscarmellose sodium	Crospovidone	MCC	Mannitol	Sodium saccharin	Magnesium stearate	Talc
F1	4	20	-	-	-	-	60	110	2	2.5	1.5
F2	4	-	20	-	-	-	60	110	2	2.5	1.5
F3	4	-	-	20	-	-	60	110	2	2.5	1.5
F4	4	-	-	-	20	-	60	110	2	2.5	1.5
F5	4	-	-	-	-	20	60	110	2	2.5	1.5

EVALUATION:

1. WEIGHT VARIATION TEST:[16]

20 tablets were selected at random, individually weighed and the average weight was calculated. None of the tablets deviated from the average weight by more than ±7.5%.

2. HARDNESS TEST:[3, 17]

Tablets require a certain amount of strength or hardness and resistance to friability to with stand mechanical shocks. The hardness of tablet was measured by Monsanto hardness tester.

3. % FRIABILITY[18]

Twenty tablets were weighed and placed in a Roche friabilator and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, dedusted, and reweighed. The percentage friability of the tablets was calculated by

$$\% \text{ Friability} = \frac{\text{initiat weight} - \text{final weight}}{\text{initial weight}} \times 100$$

4. CONTENT UNIFORMITY:[3, 9, 19]

For estimation of content Ondansetron hydrochloride in prepared tablets, 30 tablets were randomly selected from each batch and 10 tablets were analyzed individually. The amount of Ondansetron hydrochloride in orodispersible tablets was determined spectrophotometrically at 310 nm.

5. WETTING TIME:[20, 21]

A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper and the time required for complete wetting was measured.

6. IN VITRO DISPERSION TIME:[22]

In vitro dispersion time was measured by dropping a tablet in a measuring cylinder containing 6 ml of phosphate buffer pH 6.8 (simulated saliva fluid). The time for the tablet to completely disintegrate into fine particles was noted. Six tablets from each batch were randomly selected and in vitro dispersion time was performed.

7. IN VITRO DISINTEGRATION TIME:[3, 23]

The disintegration time of the tablets was determined as per Indian Pharmacopoeia monograph. The time required for disintegration of six tablets from each batch placed in each tube of disintegration test apparatus were measured at 37 ± 0.5°C using 900 ml of distilled water. The time required to obtain complete disintegration of all the six tablets was noted.

8. DISSOLUTION STUDIES:[9, 11, 24]

In vitro dissolution studies were performed using USP type II dissolution apparatus at 50 rpm, and 900 ml of water was used as a dissolution medium. Temperature of dissolution medium was maintained at 37 ± 0.5°C. Five milliliters aliquot of the dissolution medium was withdrawn at specific time intervals. Absorption of filtered solution was measured by UV–visible spectrophotometer (UV-1800, Shimadzu Corporation, Kyoto, Japan) at 310 nm, and the percent of drug released was determined using standard curve. Dissolution rate was studied for the prepared formulations.

RESULTS:

Orodispersible tablets of Ondansetron hydrochloride were prepared by direct compression techniques using different disintegrating agents are shown in Table 1. Evaluation parameters like weight variation, hardness, friability, drug content, wetting time, in vitro dispersion time and in vitro disintegration are mentioned in Table 2. All formulations evaluated for variation in weight and results indicated that for all formulations exhibit very low weight variation which lies within the pharmacopoeia limits (i.e. ± 7.5%). Orodispersible tablets measured hardness was found to be in the range of 3.1 to 3.5 kg/cm^2. The percentage friability was less than 1% for all formulation ensuring mechanical stability of the formulated orodispersible tablets. Content uniformity in all the formulations were found in the range of 9.54 ± 0.25 to 9.92 ± 0.25 indicating the compliance with the pharmacopoeia limits. Wetting time was found to be in range of 28 to 40 second. In vitro dispersion time was found to be in range of 23 to 37 second. % In Vitro disintegration time was found to be in range of 20 to 33 second. According to the pharmacopoeia standards the dispersible tablet must disintegrate within 3 minute but all formulated batches have shown very low disintegration time indicating suitability of formulation for fast dissolving tablet. Disintegration time from all the prepared formulation was found to be in following order: F3<F5<F1<F4<F2. % Cumulative drug release from F1, F3 and F5 formulations were found to be in 10 minute and from F2 and F5 formulations were found to be in 12 minutes. Cumulative drug release from all the prepared formulation was found to be in following order: F3>F1>F2>F5>F4. Formulation F3 shows fast disintegration and high % Cumulative drug release.

Table 2: Evaluation of Ondansetron hydrochloride orodispersible tablets

TESTS	Formulations				
	F1	F2	F3	F4	F5
Weight variation (mg)	Pass	Pass	Pass	Pass	Pass
Hardness kg/cm^2	3.2	3.1	3.5	3.3	3.1
% Friability	0.52	0.63	0.35	0.44	0.67
Content uniformity (mg)	9.62 ± 0.43	9.54 ± 0.25	9.92 ± 0.25	9.78 ± 0.46	9.69 ± 0.33
Wetting time (second)	33	40	28	38	31
In Vitro dispersion time (second)	29	37	23	35	27
In Vitro disintegration time (second)	26	33	20	29	23

Table 3: In vitro dissolution studies of orodispersible tablets of Ondansetron hydrochloride

Time (minutes)	% Cumulative drug release				
	F1	F2	F3	F4	F5
2	55.43 ± 0.41	49.34 ± 0.59	60.43 ± 0.45	54.64 ± 0.65	52.35 ± 0.44
4	62.48 ± 0.65	63.57 ± 0.34	68.93 ± 0.98	66.58 ± 0.77	64.54 ± 0.22
6	76.57 ± 0.54	74.49 ± 0.89	86.19 ± 0.12	73.97 ± 0.34	79.98 ± 0.34
8	96.83 ± 0.69	87.76 ± 0.33	97.65 ± 0.33	83.63 ± 0.33	96.55 ± 0.99
10	98.45 ± 0.44	95.60 ± 0.62	99.77 ± 0.32	93.56 ± 0.66	97.69 ± 0.75
12	-	98.05 ± 0.49	-	97.09 ± 0.89	-

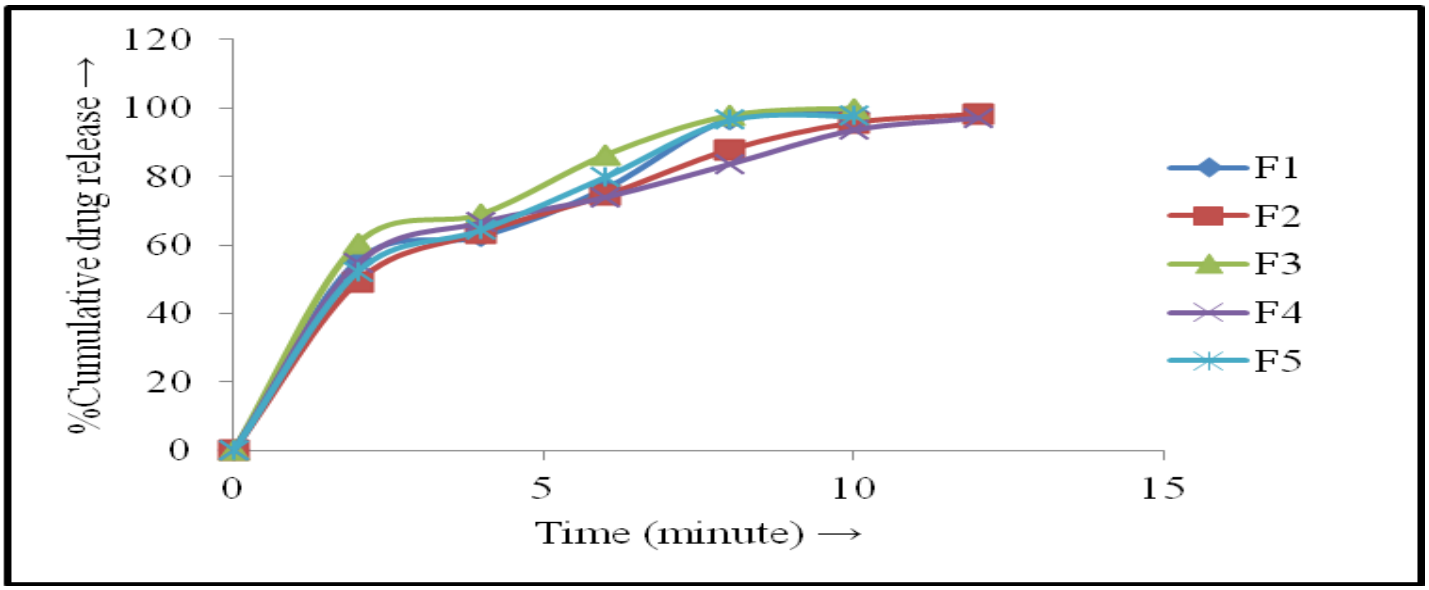

Figure 1: In vitro release profile for formulation F1 to F5.

DISCUSSION:

The present study demonstrate that objective of preparing fast disintegrating tablets of ondansetron hydrochloride by direct compression technique is achieved. Different formulations were prepared using 10% superdisintegrant like sodium carboxy methyl cellulose, alginic acid, crospovidone, Croscarmellose sodium and sodium starch glycollate. The tablets prepared by direct compression technique were found to have adequate hardness, friability, content uniformity, wetting time and in vitro dispersion time. Prepared tablets disintegrate within few seconds without need of water; thereby enhance absorption resulting in increased bioavailability and increased patient compliance. Among all the superdisintegrant sodium starch glycollate showed maximum effect of disintigrantion. Effect of superdisintegrant from all the prepared formulation was found to be in following order: SSG> Crospovidone >Sodium CMC> Croscarmellose sodium >Alginic acid. The formulated tablet F3 showed fast disintegration and in vitro dissolution.

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