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Research Article

Effect of Super Disintegrants on Formulation of Ondansetron HCL Immediate Release Tablets by Direct Compression method

*Anirudh Srivatsa.P, Harish.G, Pragath kumar.B, Debjit Bhowmik, Duraivel.S

Department of Pharmaceutics, Nimra College of Pharmacy, Vijayawada-521456

ABSTRACT

The objective of the present investigation was to formulate Oro-dispersible tablets of Ondansetron hydrochloride, due to its application in emesis conditions where fast on set of action is required. Tablets which were prepared by direct compression using sodium starch glycolate and crosprovidone as a combination of these two agents a better disintegration was observed. The tablets were evaluated for weight variation, mechanical strength, and In-vitro disintegration time, wetting time, drug release, hardness, friability and dissolution studies. Finally all the formulation parameters were within the pharmacopoeial limits and the drug disintegration time was less and the drug release was fast. Formulation F3 was found to effective hence the disintegration time was found to be 24sec which is rapid compared to that of the marketed formulation. It was concluded that super disintegration addition technique is a useful method for preparing Oro dispersible tablets by direct compression.

Keywords: Ondansetron Hcl, Immediate release, Direct compression, Super-disintegrants

INTRODUCTION

Most of An ideal dosage regimen in the drug therapy of any disease is the one, which immediately attains the desired therapeutic concentration of the drug in plasma (or at the site of action) and maintains it as constant for the entire duration of treatment. This is possible through administration of conventional dosage forms in a particular dose at a particular frequency. Thus drug may be administered by various dosage forms and by various routes of administration. Drugs are more frequently taken by oral administration. Although some drugs taken orally are dissolved within the mouth, rest of the vast variety of drugs is swallowed. Compared with other routes oral route of administration is most popular and is been successfully used for conventional drug delivery which are easy for production and are of low cost. Tablets and Capsules constitute a major portion of drug delivery system that is currently available. However many patient groups like Elders, children and mentally retarded patients have difficulty during the swallowing these type of dosage Forms [1-3]. Many elderly people face difficulty in administrating the conventional dosage forms because of hand tumors etc. Swallowing problems are common in children as their muscular and nervous system is underdeveloped. In some cases of motion sickness and unavailability of water, administration of conventional dosage form is difficult. To fulfill these medical needs formulators have developed a novel type of dosage forms for oral administration Known as mouth dissolving tablets(MDT).Various categories of drugs like ibuprofen, lansoprazole, hydrochlorothiazide, nimesulide, furosemide, and atenolol which were prepared to achieve desired pharmacological response. Various tech used to prepare ODTs include Freeze drying, tablet molding, direct compression, spray drying, and sublimation. Direct compression is simple and cost effective tablet manufacturing technique. Use of conventional equipment's, commonly available excipients and limited number of processing steps are the advantages of this technique. The commonly used Superdisintegrants are Croscarmellose, sodium, Sodium Starch glycolate. Several orally disintegrating tablet (ODT) technologies based on Direct compression, the addition of super disintegrates effect the rate of disintegration and hence dissolution. Ondansetron HCL is a selective 5-HT3 receptor antagonist. It is used in the treatment of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy. It is used in prevention of post-operative

Table 1Formulation table of Ondansetron HCL Immediate Release Tablets

INGREDIENTS	F1	F2	F3	F4	F5	F6
Ondansetron	4	4	4	4	4	4
Anhydrous lactose	56	56	56	56	56	56
Preglelatinise starch	-	-	-	8	8	8
Magnesium stearate	2	2	2	2	2	2
CCS	10	-	-	10	-	-
SSG	-	10	8	-	10	-
Crosprovidone	-	-	10	-	-	10
MCC	8	8	-	-	-	-

Author for correspondence: Email: anipeddibhotla@gmail.com

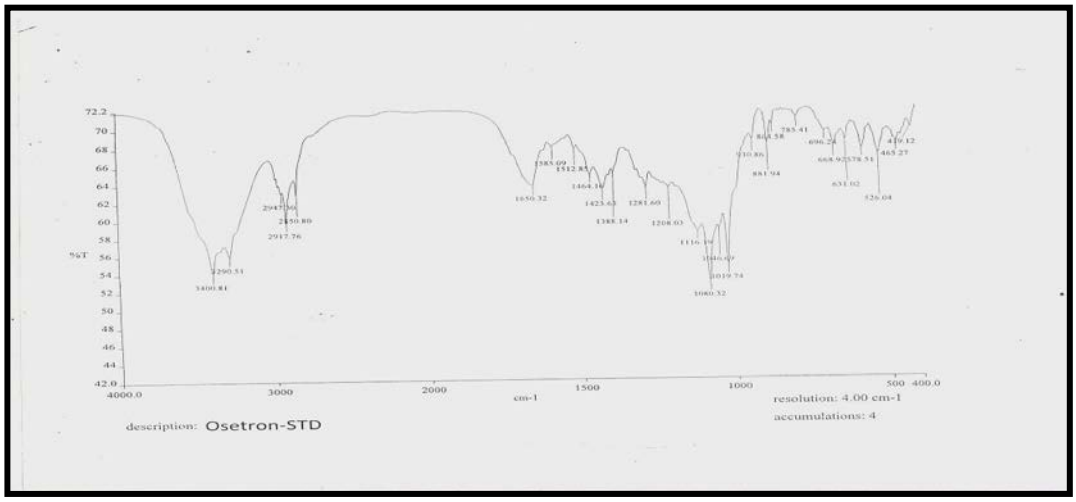

Figure 1 FT-IR of the drug (Ondansetron HCL) STD drug

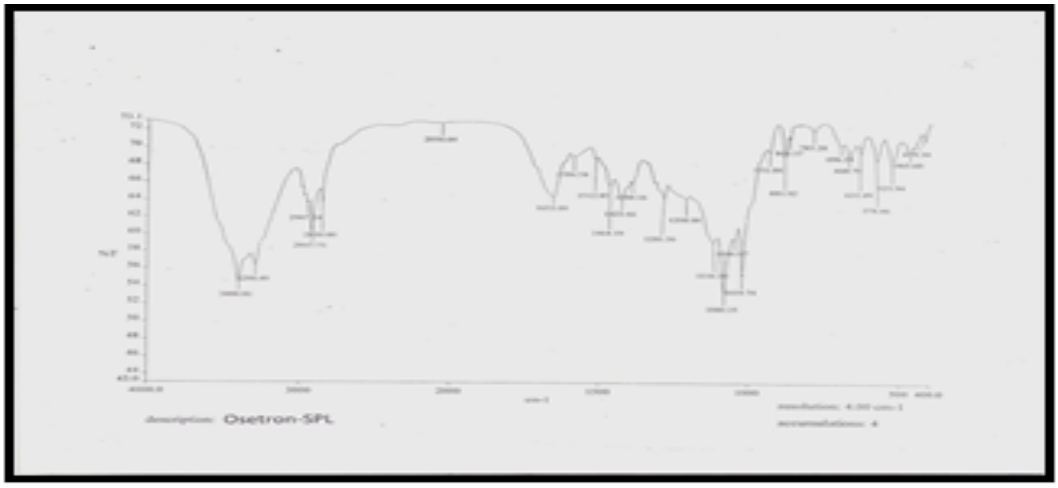

Figure 2 FT-IR of both the Drug and excipients

Table 2 Pre-formulation studies of Ondansetron HCL

S. No	Parameters	Observations	As Per Monographs
1	Solubility	Sparingly soluble in water and acidic solutions	Sparingly soluble in water and acids
2	Bulk density	0.42 gm/ml	0.42 gm/ml
3	Tapped density	0.6251 gm/ml	0.622 gm/ml
4	Melting point	231-232^{0}c	231-232$^0{}_c$

Table 3 Evaluation of the Blend

Formulation Code	Bulk Density	Tapped Density	Powder Flow properties	Hausner ratio
F-1	0.46	0.55	16.36	1.01
F-2	0.45	0.54	16.66	1.2
F-3	0.46	0.55	16.52	1.19
F-4	0.32	0.38	14.73	1.18
F-5	0.45	0.52	18.75	1.15
F-6	0.48	0.57	15.32	1.18

nausea and vomiting in adults. Ondansetron HCL 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%. The Objective of the present investigation was to prepare ODTs of Ondansetron HCL .The tablet was prepared by direct compression method using sodium starch glycolate and Crosprovidone. The combination of these two agents as super disintegrating agents gives better results. Micro crystalline cellulose, pre-gelatinized starch, anhydrous

Tablet 4 Evaluation of the physical parameters of MDTs of Ondansetron Hcl

Formulation Code	Weight Variation	Hardness Kg/cm^2	Friability %	Disintegration Time (sec)	Wetting Time (sec)
F-1	passes	3.7	0.41	35	45
F-2	passes	3.6	0.46	30	40
F-3	passes	3.6	0.46	24	35
F-4	passes	3.5	0.3	48	55
F-5	passes	3.8	0.3	40	50
F-6	passes	3.6	0.42	38	47

Table 5 *In-vitro* Disintegration test of MDTS of Ondansetron HCL

S. No	Formulation Code	Disintegration Time (sec)
1	F-1	35
2	F-2	30
3	F-3	24
4	F-4	48
5	F-5	40
6	F-6	38
7	Marketed product	39

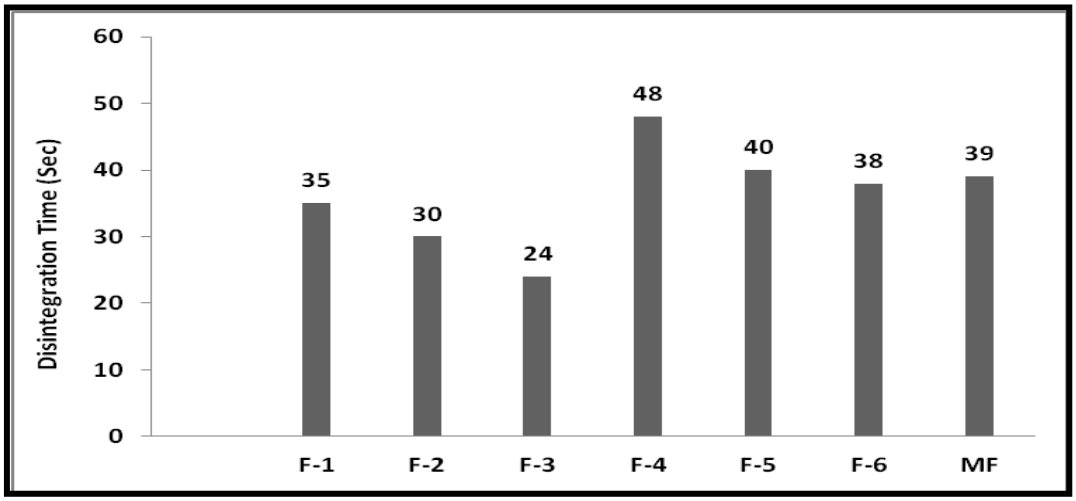

Figure 3 *In-vitro* Disintegration time of MDTS of Ondansetron HCL

Table 6 *In-Vitro* Dissolution studies

Time in Min	Formulation Code						
	F-1	F-2	F-3	F-4	F-5	F-6	MF
0	0	0	0	0	0	0	0
5	65.7	98.2	48.6	53.5	69.00	80.67	25.09
10	70.1	96.8	57.5	52.5	67.88	81.50	41.4
15	77.2	101.4	65.97	55.2	71.71	82.53	50.29
20	74.7	97.4	78.92	60.7	68.34	83.10	68.32
30	74.6	97.5	91.42	57.8	70.9	84.81	89.32
45	67.1	97.3	102.2	60.34	71.19	85.31	97.12

Lactose, magnesium stearate was used as excipients in the formulation.

MATERIALS AND METHODS

Materials: Ondansetron Hydrochloride was obtained as a gift sample from Lee Pharma, Hyderabad. Sodium Starch Glycolate, Crosprovidone, Magnesium Stearate; Anhydrous Lactose was obtained from Syndicate pharma, Vizag. All other excipients and chemical used were of Analytical grade.

Methods: Sodium starch glycolate (SSG) and crosprovidone were used as super disintegrating agents for preparation of ODT by direct compression method. Various Batches of tablet formulation was worked out

Table 7 Drug content estimation by UV spectroscopy

Batch no	Area/abs	%assay	Assay in mg
F1	0.3272	94.81	3.79
F2	0.304	88.09	3.52
F3	0.3504	101.54	4.06
F4	0.2039	59.26	2.11
F5	0.2513	73.01	2.65
F6	0.2977	86.52	3.15

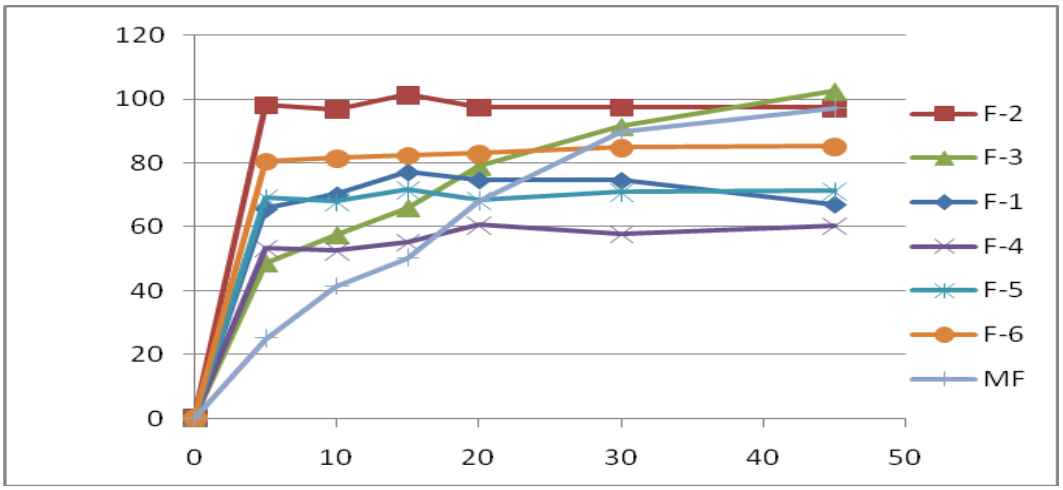

Figure 4 *In-vitro* Drug release studies of Ondansetron immediate release tablets

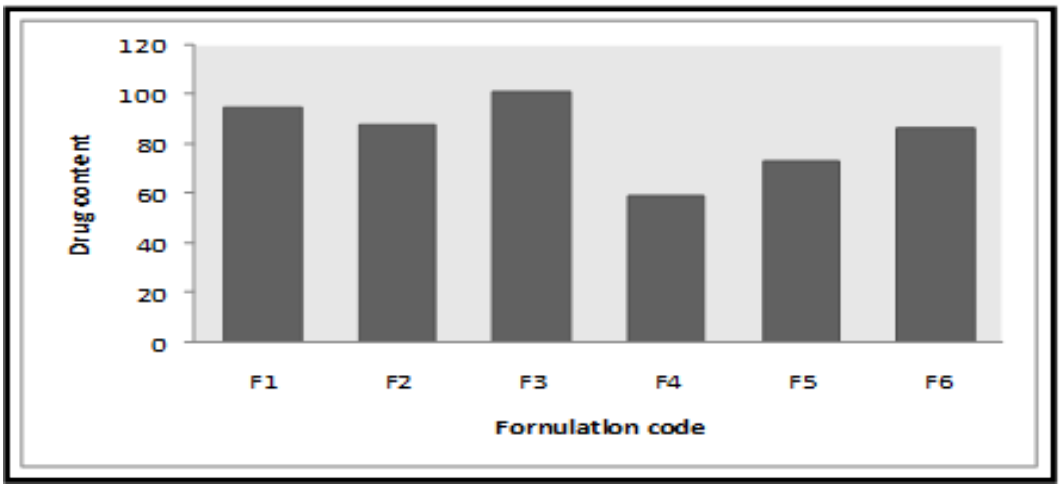

Figure 5 Drug content estimation of Ondansetron immediate release tablets

Table 8 Percentage drug release profile of Marketed Tablet

Time (min)	Optimized Formulation (F3)	Cumulative % drug release of marketed sample
0	0	0
5	48.6	25.09
10	57.5	41.40
15	65.97	50.29
20	78.92	68.32
30	91.42	89.93
45	102.2	97.12

Table 9 Evaluation of the mouth dissolving tablets (selected formulation) at various time interval for the studies at 30^0C/ 65 % RH

Batch details	Parameters	0days	30days	60days	90days
Optimized formula (F3)	% Drug release	99.85	97.11	97.83	98.00
	Disintegration time (sec)	24	25	23	24

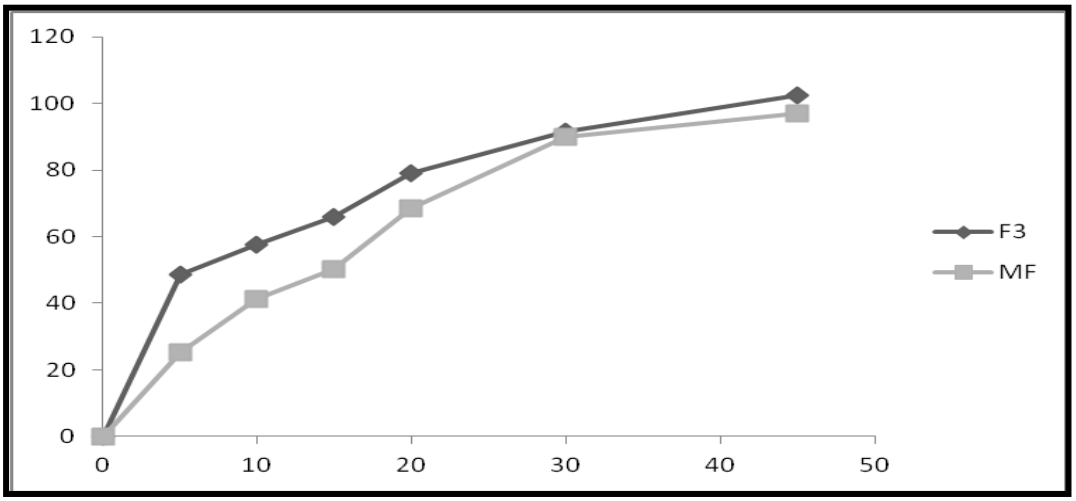

Figure 6 Drug dissolution comparison of marketed sample and Optimized Batch

based on powder blend properties and disintegration time of tablets. Initially SSG and crosprovidone were passed through a screen 60# and mixed well for half an hour in polybag, followed by adding the lubricating agents and mixed for 15minutes and compressed in Single punch Cadmach Compression machine.

Evaluation of powder blend: The powder blend was evaluated for the following parameters such as Bulk Density (D_b), Tapped Density (D_t), Angle of Repose (θ) [4-5].

Evaluation of tablet: The post compressional evaluation parameters such as weight variation, hardness, thickness, diameter, friability, disintegration and dissolution as per USP has been evaluated and the results has been tabulated in table 4 [6].

RESULTS AND DISCUSSION

Drug excipients compatibility studies: The compatibility studies of the drug Ondansetron HCl and the combination of drug and excipients were subjected to FT-IR spectral analysis. Based on the spectral data it has been observed that there are no shift of any major peaks is appearance or disappearance of the peak when compared with FTIR graph of the Pure drug and combination of the drug in figure 1 and 2

Pre-formulation studies: Per-formulation studies of Ondansetron hydrochloride drug has been carried out and the all the results were found to be within the pharmacopoeial specification and hence the granules impacts good flow characteristics and the results were tabulated in table 2.

Evaluation of the Blend: The Pre-formulation blend characteristic had been evaluated for Ondansetron hydrochloride immediate release granule for the following parameter such as Tapped Density, Bulk Density, % Compressibility and Hausner's ratio. The results are shown in the Table 3.

Evaluation of Mouth Dissolving Tablets

Physical Characterization: The compressed tablets were observer for its physical appearance visually and finally all the All the formulations are Round and Spherical shape

Weight Variation: All the formulations were complying with weight variation test as per U.S.P. The results are shown in table 4. Tablets were selected at a random and average weight was compared with individual weight [9]

Hardness: Hardness of the tablets was in the range of 3 to 4Kg/cm^2.The results are shown in table 4 by use of Monsanto hardness tester [11]

Friability: Friability of the tablets was in the range of 0.3 to 0.49 %. The results are shown in table 4 . Friability was evaluated from the percentage weight loss of 20 tablets tumbled in a friabilator at 25rpm for 4 minutes the tablets were then discarded and the tablets were weighed and percentage was calculated [12-13]

Disintegration test: The tablet disintegration test is carried out using single basket disintegration apparatus and the disintegration time of the tablet was found to be in the range of 30-40 seconds, due to the rapid disintegration of the tablets will cause immediate therapeutic effect[11-13]. The results were tabulated in tablet 5.

Various super-disintegrants were utilized for formulation of mouth dissolving tablets. The effect of super disintegrates on disintegration time is shown in table no 5. It shows that the use of CP and use of MCC found in batch F6 exhibits the lowest disintegration due to the solubility of the agents in aqueous medium is rapid. The quicker disintegration time may be attributed to faster water uptake by the tablets followed by disintegration and de-aggregation.

In-vitro Dissolution Studies: The formulated batch and

Table no 10 Evaluation of the mouth dissolving tablets (selected formulation) at various time interval for the studies at 40^0C/ 75 % RH

Batch details	Parameters	0days	30days	60days	90days
Optimized formula (F3)	% Drug release	99.85	97.23	98.91	98.42
	Disintegration time (sec)	24	23	24	24

pure drug were subjected to *in-vitro* dissolution studies by using USP pharmacopoeial method [14-15]. Distilled water used as dissolution medium, Paddle rotates at 50 RPM, the bath maintained at 37^0C and the samples were withdrawn for every 5min once up to 45min and measured at 310nm by UV spectroscopy and the results obtained were shown in Table 6. The following are the results of the dissolution studies (% of drug release) of the formulated tablets and pure drug [8].

Comparisons of best formulated tablet with marketed tablet: The best formulated tablet was then compared with marketed tablet Zofran ODT. Formulation F3 was compared with marketed tablet for *in vitro* dissolution study. The results were revealed in Table 8.

Stability studies: The stability studies were carried out for one month and the result has been tabulated in table 9 and 10. The stability study has been carried out in both accelerated and real time condition for a period three months during the period which there was no significant change has been observed for the optimized batch F3.

CONCLUSION

In the present work, mouth dissolving tablets were prepared by super-disintegrants addition, and evaluated for disintegration time, hardness and friability. From all these techniques, Super-disintegrants addition technique was selected based on less disintegration time. The mouth dissolving tablets of Ondansetron were prepared by super-disintegrants addition method using crosprovidone, Croscarmellose sodium and Microcrystalline cellulose There are total six formulations were prepared and evaluated for Weight variation, thickness, friability, hardness, disintegration time, Wetting time, assay and in-vitro dissolution study. The results of all formulations for weight variation, friability, hardness and assay were found to be within the IP limit and no significant variation. The Disintegration time for all formulations was found to be 25 to 60 seconds and wetting time was between 20 to 60 seconds. Based on the In-vitro dissolution studies, it was found that the drug release for all the formulations were less than 10 minutes. Formulation B3 containing crosprovidone and MCC in concentration of 10% and 12.5 % showed minimum disintegration time, wetting time as compared to other formulations. Dissolution studies conclude that the total drug was released within 6 minutes. Disintegration time was increased in the following manner Crosprovidone < Croscarmellose sodium. It is showed and concluded that F3 is the best formulation which is done by use of super disintegration addition technique which is known to be cost effective

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