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DESIGN AND EVALUATION OF RAPID DISINTEGRATING TABLETS OF ONDANSETRON HYDROCHLORIDE

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ABSTRACT
Ondansetron hydrochloride is a selective 5-HT3 receptor antagonist, used in the management of nausea and vomiting induced by cytotoxic chemotherapy and radiograpy it is also used for prevention of postoperative nausea and vomiting in adults. But it is a better drug. In this research work main aim to mask the taste and to formulate rapid disintegrating tablets using superdisintigrating agents, crospovidone (upto3%), Croscarmellose sodium (up to 5%), and Aminoalkyl methacrylate copolymer (Eudragit EPO) as taste masking agent. It is suitable dosage for pediatric and geriatric patients. Estimation of Ondansetron hydrochloride in the prepared tablets was carried out by extracting the drug with methanol and measuring the absorbance at 310nm. The prepared tablets were further evaluated for hardness, friability, drug content, uniformity, *in vitro* dissolution time, wetting time and water absorption ratio. One promising formulation was tested *in vitro* drug release pattern in phosphate buffer pH 6.8
KEY WORDS: rapid disintegrating tablets, crospovididone, croscarmellose sodium, sodium starch glycolate, Eudragit EPO, Ondansetron hydrochloride.

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INTRODUCTION

Tablet is the most widely used solid dosage form because of its convenience in terms of self- administration, compactness and ease in manufacturing. However, geriatric and pediatric patients experience difficulty in swallowing conventional tablets, which leads to poor patient's compliance. To overcome this Problem, scientists have been developed innovative drug delivery systems known as rapid disintegrating tablets. Their characteristic advantages such as administration without water, any where, any time lead to their suitability to geriatric and pediatric patients. They are also suitable for the mentally ill, the bedridden and patients who do not have easy access to water[1].

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. 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%[2].

The objective of the present investigation was to prepare rapid disintegrating tablets of Ondansetron hydrochloride, because in the emesis condition as well as in above mentioned specific conditions, fast onset of action and avoidance of water is highly desirable. Tablets were prepared by direct compression method using Crospovidone and Croscarmellose sodium as superdisintegrants. The combination of these two agents gives better disintegration of the dosage form and also does not adversely affect compressibility and flowability. Mannitol was selected due to its pleasant mouth feel property, good water dispersibility and binding property. It is also an effective tablet disintegrant and provides good hardness on compaction.

MATERIALS AND METHODS

Materials

Ondansetron hydrochloride (OSH) was a gift sample from Medley Pharmaceuticals Ltd., Vapi (Gujarat), Microcrystalline Cellulose (MCC), Aspartame, Eudragit EPO, Mint flavor, Croscarmellose Sodium (CCS), Crospovidone were a gift Sample from Zydus Cadila, Ahmedabad. Mannitol (Hi Media Laboratory Limited, Mumbai), sodium saccharine (Loba Chemicals,

Mumbai), Aerosil (S.D. Fine Chemicals, Mumbai), Magnesium stearate (S.D.Fine Chemicals, Mumbai) were purchased. All other chemicals used were analytical grade.

Preparation of Fast Dissolving Tablets

Taste masking of the drug

Ondansetron HCl and Eudragit EPO complex were prepared using the precipitation method. Saturated solutions of Ondansetron HCl and Eudragit EPO were prepared in absolute ethanol and injected into 0.1 N sodium hydroxide with constant stirring at 500 rpm in a mechanical stirrer. The foamy matrix obtained on the top of the solution were separated and dried at room temperature for 24 hrs under vacuum. The dried matrix was subsequently pulverized[3].

Preparation of Tablet

By Direct compression method

The Drug Copolymer Mixture, pearlitol SD200 (Mannitol), aspartame, crospovidone (superdisintegrants), Aerosil and mixed fruit flavors were admixed for about 15 min to make a uniform blend.

Magnesium stearate was passed through sieve 100 and mixed with the above blend for approximately 5-7 min. Then tablets were prepared by directly compressed using 8 mm punch on a single station tablet machine[4, 5].

Evaluation of Powder Blend

Bulk density

Apparent bulk density (g/ml) was determined by placing pre-sieved bulk powder blend into a graduated cylinder *via* a large cylinder and measuring the volume and weight[4].

$$Pb = Vb/M$$

Tapped density

Tapped density determined by placing a graduated cylinder, containing a known mass of powder on mechanical tapping apparatus, which was operated for fixed number of taps (around 250) until the powder bed volume reached a minimum. Using the weight of powder in a cylinder and this minimum volume, the tapped density was computed. From the results of bulk density and tapped density, Carr's index was calculated.

$$Pt = Vt/M$$

Angle of repose

For the measurement of angle of repose, a glass funnel was secured with its tip at a given height (H) above a piece of graph paper placed on a horizontal surface. Powder was poured through the funnel until the apex of the conical pile touched the tip of the funnel. The angle of repose was calculated with the formula

$$\tan^{-1} = h/r$$

Where, $\tan^{-1}$ is the angle of repose, **R** is the radius of the conical pile.

Evaluation of Tablets

Uniformity of weight (Weight Variation)

Twenty tablets were selected at a random and average weight was determined. Then individual tablets were weighed and the individual weight was compared with an average weight[6].

Hardness

The tablet crushing load, which is the force required to break a tablet by compression in the radial direction, was determined using a Pfizer hardness tester (Sheetal Scientific Industries, Mumbai, India).

Friability

Friability of tablets was measured by using Roche Friabilator (Electrolab, Mumbai, India). Friability was evaluated from the percentage weight loss of 20 tablets tumbled in a friabilator at 25 rpm for 4 minutes. The tablets were deducted, and the loss in weight caused by fracture or abrasion was recorded as the percentage weight loss. Friability below 0.5 to 1% was considered acceptable.

***In-vitro* disintegration time**

The disintegration time was measured using a paddle method originally proposed by Sunada et al. The assembly utilizes dissolution apparatus USP XXIII paddle apparatus (Electrolab, TDT-06T, Mumbai, India). The vessel was filled with 500 ml of water maintained at 37±2°C and rotated at 100 rpm. The tablet was placed inside the sinker and the time at which it passes completely through the mesh of sinker was taken as the disintegration of the tablet[7].

***In vivo* disintegration time**

Measurements of disintegration time in the mouth were carried out in six volunteers. After the mouth was rinsed with purified water, one tablet was held in the mouth until the tablet disintegrated without chewing and then spat out and the mouth was rinsed again. The disintegration time was recorded[7].

Wetting time

The wetting time of the tablets was measured using a simple procedure. Five circular tissue papers of 10-cm diameter were placed in a Petri dish with a 10-cm diameter.10 ml of water containing eosin (water-soluble dye) was added to the Petri dish. A tablet was carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablets was noted as the wetting time.

Dissolution study

The dissolution study was performed for pure drug OSH, prepared batches and marketed conventional tablet formulation by using USP XXIII paddle apparatus (Electrolab, TDT- 06T, Mumbai). The dissolution medium was distilled water (900 ml, 37 ± 0.5^{0}C). The

rate of agitation of the paddle was 50 rpm. Sample was withdrawn at specific time interval of 5 minute, it was filtered and absorbance was measured at 310 nm by UV spectrophotometer (UV-1700, Shimadzu Corporation, Kyoto, Japan) [8].

RESULTS AND DISCUSSION

The present investigation was undertaken to formulate and evaluate fast melting tablets of Ondansetron hydrochloride by direct compression method using sodium starch glycolate and croscarmellose sodium as superdisintegrants. Superdisintegrants are generally used by formulation scientists for developing Rapid Disintegrating Tablets and fast melting tablets or for improvement of solubility for active pharmaceutical ingredients. The primary requirement for both dosage forms is quicker disintegration. The values obtained for bulk density and tapped density does not affect the compression of tablets. The angle of repose gives important information about the flow characteristics of the powder mixture. The powder flow depends on three general areas: the physical properties of the particle (e.g., shape, size, compressibility), the bulk powder properties (e.g., size distribution, compaction); and the processing environment (e.g., storage, humidity) the angle of repose <30° indicates free flowing material and >40° with poor flow properties. Values for angle of repose were found in the range of 26 to 31° showing that the blend of powder was free flowing[9].

The various results for the evaluation of different batches of Ondansetron hydrochloride rapid disintegrating tablets prepared by direct compression method are shown in **Table 2**. Percent weight variation was observed between 5.0±0.54 and 6.0± 0.22 which were well within the acceptable limit for uncoated tablets as per United States Pharmacopoeia. One of the primary requirements of immediate release preparation is faster disintegration. It is well known to formulation scientists that the tablets with higher crushing strength show longer disintegration time. Since mechanical integrity is of paramount importance in successful formulation of RDTs, hence the hardness of tablets was determined and was found to be in the range of 2.8 to 4.3 Kg/cm^2. Friability was observed between 0.12 to 0.22%, which were below 0.5 to 1% indicating sufficient mechanical integrity and strength of the prepared tablets. Thus, hardness and friability data indicates good mechanical resistance of tablets. *In- vitro* disintegration time for different batches of RDTs was 32 to 73 seconds respectively. The tablet formulations containing Crospovidone and Croscarmellose sodium alone at low concentration (8mg/tablet) showed higher values of 47 to 73 seconds for *in- vitro* disintegration time. Hence the batch F_2 was used for further studies like wetting time, wetting volume, dissolution profile study.

Wetting time was determined to get idea of wetting lag time before disintegration. The wetting time for batch F_2 was 52 seconds, which shows that very small amount of water is required for wetting of tablet. It has been reported that wetting is closely related to the inner structure of the tablets and the hydrophilicity of the excipients, crospovidone and Croscarmellose sodium show its disintegrant effect by the mechanism of swelling. Thus these results indicate that these tablets would disintegrate almost instantaneously when they will come in contact with even slight quantity of saliva in the mouth.

The cumulative percentage drug release from pure drug, prepared RDT batch F_2 and marketed conventional tablet formulation is shown in **Table 4**. It was observed that in first 10 minutes, only 2.0 % drug was released from pure drug and marketed conventional tablet formulation while it was 89.0 % in case of RDT. At the end of 30 minutes, 98.0 % of drug was released from the batch F2. Thus the release rate of Ondansetron hydrochloride was significantly enhanced by formulating RDTs by using superdisintegrants.

CONCLUSION

Rapid disintegrating tablets of Ondansetron hydrochloride were prepared by direct compression method using crospovidone and croscarmellose sodium as superdisintegrants. The tablets disintegrated rapidly in oral cavity and had acceptable hardness and friability. *In vitro* drug release from the tablets shows significantly improved drug dissolution. Hence it could be concluded that the superdisintegrants based rapid disintegrating tablets of Ondansetron hydrochloride would be quite effective in emesis, providing quick onset of action without need for water for swallowing or administration.

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REFERENCES

1. Chang R Guox, Burnside B, Couch R., A review of fast dissolving tablets, pharma tech north Am. 2008; 24-25.
2. Keny RV. Desouza Chrisma and Lourenco C.F., formulation and evaluation of Rizatriptan benzoate mouth disintegrating tablets, Indian journal of pharmaceutical sciences. January - February 2010; 21; 331-347.
3. Gosai Avani R, B Patil, Sanjay B and Sawant Krutika K. Formulation and evaluation of oro dispersible tablets of Ondansetron hydrochloride, international journals of

pharmaceutical science and nanotechnology. April – June 2008 ;(1)8; 706-712'

4. Khan Shagufta, Kataria Prashant, Nakhat Premchand, and Yeole Pramod, Taste masking of Ondansetron hydrochloride polymer carrier system and formulation of rapid disintegration tablets. AAPS pharma. Sci Tech 2007: 8(2). 296-302.
5. Ishikawa T, Watanabe Y, Utoguchi N, Matsumoto M. Preparation and evaluation of tablets rapidly disintegrating in m saliva containing bitter taste masked granules by compression method. Chem Pharm Bull (Tokyo). 1999; 43: 284-288.
6. Sheetal Malke, Supriya Shidhaye and Vilasrao kadam, Novel melt granulation using sugars from metochlopramide hydrochloride oral disintegrating tablets. Asian journals of pharmaceutical and clinical research January – march 2009; (1); 235-241.
7. Narmada GY, Mohini K, Prakash Rao B, Gowrinath DXP, kumar KS, Formulation, Evaluation and Optimization of Fast Dissolving Tablets Containing Amlodipine Besylate by Sublimation Method. ARS pharm 2009: 185-189.
8. Sreenivas SA, Gadad AP. Formulation and evaluation of Ondansetron Hcl directly compressed mouth disintegrating tablets."Indian Drugs, 2006, 43: 35-38.

Table: 1 Formulation of rapid disintegrating Ondansetron hydrochloride Tablets

Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)
Ondansetron Eudragit EPO mixture	13	13	13	13	13	13
Microcrystalline cellulose	25	27	20	25	27	20
Mannitol	96	65.25	76	102	80	95
Croscarmellose Sodium	6	8	10	-	-	-
Crospovidone	-		-	6	8	10
Aspartame	4	-	4	4	3	3
Flavour	3	3	2.5	2	3	2
Colloidal Silicon dioxide	5	3.75	5	5	3.75	3.75
Magnesium stearate	10	10	10	10	10	10

Table 2: Evaluation of RDT of Ondansetron HCL

Batch code	Weight variation	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	*In-vitro* Disin. Time (sec)	Assay (%)	Wetting time (sec)
F-1	5.7± 0.51	4.11	3.1	0.18	73	98.98	70
F-2	6.0± 0.22	4.18	2.85	0.12	32	100.84	52
F-3	5.5± 0.34	4.15	3.5	0.22	43	99.25	46
F-4	5.0± 0.10	4.14	4.3	0.16	47	99.45	53
F-5	5.4± 0.30	4.16	4.1	0.17	38	99.58	64
F-6	5.0± 0.54	4.18	3.8	0.18	34	100.65	37

The data are expressed as mean±S.D. (n=3)

Table 3: Percent drug release from RDT of Ondansetron Formulations

Time (min).	Cumulative percent drug release					
	F1	F2	F3	F4	F5	F6
0	0.000	**0.000**	0.000	0.000	0.000	0.000
1	3.947	**4.605**	2.212	3.467	4.820	4.102
2	23.206	**49.350**	19.219	15.796	20.215	23.789
3	39.180	**89.262**	35.014	23.206	37.018	45.180
4	41.451	**91.230**	46.738	29.871	48.731	55.120
5	49.000	**95.080**	51.467	33.110	50.551	64.142
6	59.045	**98.380**	59.149	35.180	60.189	78.086

Table 4: Percent Drug Release from prepared tablet and marketed product

Time (min.)	Cumulative % Drug Release	
	prepared tablet	marketed tablet
0	0	0
5	4.60	3.032
10	49.35	42.48
15	89.26	71.88
20	91.23	82.56
25	95.08	90.28
30	98.38	96.89

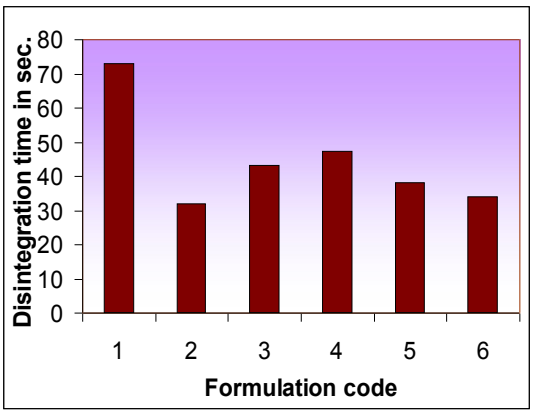

Figure 1: Comparatives Study of Percent Disintegration in Different Formulations

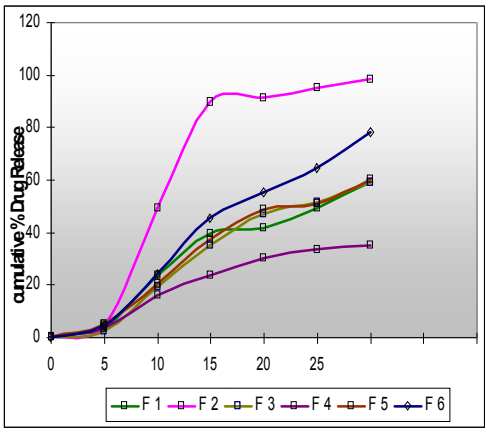

Fig. 2: Comparative % drug release from all formulation

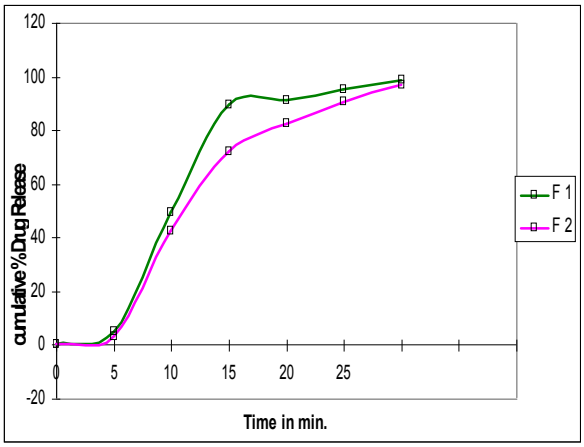

Fig. 3: Comparative % drug release from prepared batch F2 and Marketed product

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