

DEVELOPMENT AND *IN-VITRO* EVALUATION OF TASTE MASKED ONDANSETRON HCl ORAL DISPERSIBLE TABLETS BY DIRECT COMPRESSION METHOD BY USING DIFFERENT DILUENTS

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ABSTRACT

Ondansetron hydrochloride is a competitive serotonin type 3 receptor (5-HT₃) antagonist. It is effective in the treatment of nausea and vomiting caused by cytotoxic chemotherapy drugs, including cisplatin, and has reported anxiolytic and neuroleptic properties with chemical name of 9-methyl-3-[(2-methylimidazol-1-yl)methyl]-2,3-dihydro-1H-carbazol-4-one. It is an intensely bitter in taste. Bitter taste of the ondansetron is a major problem in ensuring patient compliance. The purpose of this research was to mask the intensely bitter taste of ondansetron HCl and to formulate an Oral dispersible tablet (ODT). In the present study an attempt has been made to mask the bitter taste, by complexation technique using ion-exchange resin, tulsion-335 (polyacrylic hydrogen with carboxylic functionality) and to formulate into an oral dispersible dosage form. Taste masking was done by complexation of ondansetron HCl with different ratios Tulsion 335 resin. The drug loading onto ion-exchange resin was optimized for concentration of resin ratio, swelling time of resin, stirring time and pH of resin solution. Resinate was characterized by DSC. Drug resin complexes were tested for drug content, Taste and *in vitro* release in simulated salivary fluid (SSF) of pH 6.8. Resinate that did not release drug in SSF was considered taste-masked and selected for formulation of oral dispersible tablets. The complex with drug-resin ratio 1:3 showed less amount of drug release in SSF; therefore, it was selected. The tablets were prepared with indion-414 as superdisintegrant. The blend was examined for angle of repose, bulk density, tapped density and hausner's ratio. The tablets were evaluated for hardness, drug content, friability, disintegration time and *in vitro* drug release study. The tablets disintegrated *in vitro* within 16 seconds and complex drug was released from tablet with in 2 min. The results concluded that ondansetron HCl was successfully taste masked and formulated into oral dispersible tablet.

Keywords: Oral dispersible tablets, Ondansetron HCl, Taste masking, Tulsion-335.

INTRODUCTION

The concept of oral dispersible drug delivery system emerged from the desire to provide patient with conventional mean of taking their medication. Difficulty in swallowing (dysphagia) is a common problem of all age groups, especially elderly and pediatrics, because of physiological changes associated with these groups of patients. Solid dosage forms that can be disintegrated dissolved or suspended saliva in the mouth resulting in easy swallowing can provide significant benefits to the paediatric and geriatric population, as well as other patients who prefer the convenience of easily swallowable dosage forms. The tablet disintegrates instantaneously when placed on tongue, releasing the drug that dissolves or disperses in the saliva. In case of taste masking the general aim is minimum free drug release in oral cavity.¹ Ondansetron HCl is a potent antiemetic² drug indicated for the treatment and/or prophylaxis of postoperative or chemotherapy or radiotherapy-induced emesis and also used in the early onset of alcoholism.³ In general, emesis is preceded with nausea and such condition it is difficult to administer drug with glass of water; hence it is incorporated directly into oral dispersible tablets (ODT) the main objective behind formulation of such a dosage form will definitely get futile.^{4, 5} Ion exchange resins are water-insoluble, cross linked polymers containing salt forming groups in repeating position on the polymer chain. These groups have affinity for oppositely charged counter ions, thus absorbing the ions into the polymer matrix. Ion exchange resins are high molecular weight water insoluble polymers and so are not absorbed by the body and therefore inert and safe for oral use. The complex of cationic drug and weak ion exchange resin does not break at the pH of saliva i.e. 6-7 with cationic concentration of 40 meq/l. But at high cationic concentration in stomach and pH 1.2, free drug is immediately released. This implies that while passing through mouth, the drug remains in the complex form, thereby imparting no bitter taste in mouth. This property was exploited to formulate the consumer friendly dosage form.^{6,7}

MATERIALS AND METHODS

Ondansetron HCl was obtained as a gift sample from Aurobindo Pharmaceuticals, Hyderabad, India. Tulsion-335 was obtained as a gift sample from Thermax India, Mumbai, India. Indion-414 was obtained as a gift sample from Ion-Exchange resin of India, Mumbai, India. Mannitol, spray dried lactose and microcrystalline cellulose was purchased from S. D. Fine Chemicals, Mumbai, India. All other materials used were of pharmaceutical grade.

Preparation of Ondansetron HCl -Tulsion 335 Resinate^{8,9}

The resins were first washed with distilled water till neutralization. 100 mg of resin was placed in a beaker containing 25 ml of deionised water and allowed to swell for 60 min. Accurately weighed 100 mg Ondansetron HCl was added to the resin solution and stirred for 6 hr. The obtained mixture was filtered through Whatman filter paper no.41 and residue was washed with 75 ml of deionised water. Unbound drug in filtrate was estimated at 310 nm and drug-loading efficiency was calculated.

Optimization Parameters for highest amount of drug loading

Optimization of Ondansetron HCl -Tulsion 335 Complexation

The drug loading onto resin was optimized by considering various parameters such as concentration of resin, swelling time, stirring time and pH of resin solution. These parameters were studied and optimized for the maximum amount of drug loading.

Optimization of concentration of resin for drug loading^{2,9}

The resin which showed the highest amount of drug loading was then optimized for various drug and resin concentrations varying from 1:1 to 1:5. Accurately weighed Ondansetron HCl (100 mg) was added to the 100, 200, 300, 400 and 500 mg of Tulsion 335, respectively. Among the entire drug to resin ratio the maximum drug content was then finally optimized for further studies.

Effect of swelling time on drug loading²

Accurately weighed quantity of tulsion 335 (300 mg) of various batches soaked in a beaker contain 25 ml of deionized water for a period of 15-120 min. The complexation was analyzed for drug

loading efficiency at predetermined time intervals i.e. 15, 30, 45, 60, 90 and 120 min.

Optimization of stirring time and stirring speed²

For optimization of stirring time on drug loading, accurately weighed Ondansetron HCl (100 mg) was added to 300 mg of tulsion-335 solution and slurred in 25 ml of deionized water on a magnetic stirrer having magnetic bead. Six batches with stirring time 30, 60, 120, 180, 240, 300, 360 and 420 min were processed. Amount of bound drug was estimated at 310 nm by UV spectroscopy at each time interval and the time required for maximum adsorption of drug was optimized.

For optimization of stirring speed on drug loading accurately weighed Ondansetron HCl (100 mg) was added to 300 mg of tulsion-335 solution and slurred in 25 ml of deionized water on a magnetic stirrer having magnetic bead with different stirring Speeds 50, 100, 150, 200, 250 and 300 rpm were processed. Amount of bound drug was estimated at 310 nm by UV spectroscopy at each speed and the speed required for maximum adsorption of drug was optimized.

Optimization of pH^{8,9}

For optimization of pH on drug loading, accurately weighed, 100 mg of drug was added to 300 mg of resin solution in 25 ml deionized water. The pH of the solution was maintained at 1.2, 2, 3, 4, 5, 6, 7 and 8 using standard solution of hydrochloric acid. The drug loading efficiency at particular pH was estimated.

Compatibility Studies

Differential Scanning Colorimeter (DSC) Study

DSC thermogram of pure drug, pure resin, pure drug + pure resin mixture and Drug resin complex (DRC) was performed by approximately 5 mg of the sample was scanned by using automatic

thermal analyzer. (DSC60 Shimadzu Corporation, Japan). Sealed and perforated aluminium pans were used in the experiments for all the samples. Temperature calibrations were performed using indium as standard. An empty pan sealed in the same way as for the sample was used as a reference. The entire samples were run at a scanning rate of 10°/min from 50-250°C.

Drug content

The drug content in resinate was found to be 96.3%. The percentage of drug dissolved in simulated salivary fluid pH 6.8 was found 0.45± 0.11.

In vitro taste evaluation

0.45 to 1 percentage drug release was observed in SSF from complexes with drug polymer ratio of 1:3, therefore, the ratio 1:3 was considered the optimal drug- resin concentration for taste masking of bitter taste for further studies.

Formulation development

Oral dispersible tablets of Ondansetron HCl and tulsion-335 granules were prepared using direct compression method. All Active pharmaceutical ingredient and excipients were passed through mesh ASTM #40 and lubricants were passed through mesh ASTM #60. All excipients except lubricants are mixed for 10 minutes by using mortar and pestle, than lubricants were added to mortar and mixed for 5 minutes. Above blend was compressed on using 7 mm (diameter) bi concave punches on a 'Rimek mini press 1' a 10 station rotary compression machine. to give a tablet weight of 150 mg. 12 formulations were prepared, F1-F6 contain different concentration of Indion 414 and d-Mannitol mixtures where as F7-F12 contains different concentration of Indion 414 and microcrystalline cellulose mixture. Composition of tablets is mentioned in Table 1.

Table 1: Formulation of Ondansetron HCl oral dispersible tablets

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Ondansetron:	42	42	42	42	42	42	42	42	42	42	42	42
Tulsion(1:3) Complex												
Indion 414	---	2	4	6	8	10	---	2	4	6	8	10
DC-Mannitol	102	100	98	96	94	92	---	---	---	---	---	---
Micro Crystalline cellulose PH 101	---	---	---	---	---	---	102	100	98	96	94	92
Aspartame	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Mint flavour	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Aerosil	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Magnesium Stearate	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Total	150	150	150	150	150	150	150	150	150	150	150	150

Pre compression parameters of tablet blend^{9,10,11,12}

The various characteristics of blends to be tested before compression are:

Angle of repose

Angle of repose is determined by using funnel method. The accurately weighed blend is taken in a funnel. The height of the funnel is adjusted in such a way that the tip of the funnel just touches the apex of the heap of blend. The drug (as solid dispersion)-excipient blend is allow to flow through the funnel freely on to the surface. The diameter of the powder cone is measured and angle of repose is calculated using the following equation.

$$\tan \theta = h/r$$

Where, h and r are the height of cone and radius cone base respectively. Angle of Repose less than 30 ° shows the free flowing of the material.

Bulk density

Apparent bulk density is determined by pouring a weighed quantity of blend into graduated cylinder and measuring the volume and weight. Bulk density can be calculated by using following formula:

$$\text{Bulk density} = \text{Weight of the powder} / \text{Volume of the packing}$$

Tapped density

It is determined by placing a graduated cylinder, containing a known mass of drug-excipients blend. The cylinder is allowed to fall under its own weight onto a hard surface from the height of 10 cm at 2 second intervals. The tapping is continued until no further change in volume is noted. Tapped density can be calculated by using following formula:

$$\text{Tapped Density} = (\text{Weight of the powder} / \text{volume of the tapped packing})$$

Compressibility index

The Compressibility Index of the blends is determined by compressibility index. Compressibility Index can be calculated by using following formula:

$$\text{Compressibility Index (\%)} = [(TD-BD) \times 100] / TD]$$

Hausner's ratio

A similar index to indicate the flow properties can be defined by Hausner's ratio. Hausner's ratio can be calculated by using following formula:

$$\text{Hausner's ratio} = (\text{Tapped density} \times 100) / (\text{Poured density})$$

Evaluation of tablets

Weight variation

The weight variation test is carried out in order to ensure uniformity in the weight of tablets in a batch. First the total weight of 20 tablets from each formulation is determined and the average is calculated. The individual weight of the each tablet is also determined to find out the weight variation.

Thickness

Ten tablets were selected and average thicknesses were calculated. The thicknesses of the tablets were determined by using vernier calipers.

Hardness test

Hardness indicates the ability of a tablet to with stand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm². Five tablets were ran-domly selected and hardness of the tablets was deter-mined.

Friability test

Friability is the loss of weight of tablet in the container due to removal of fine particles from the surface. Friability test is carried out to access the ability of the tablet to withstand abrasion in packaging, handling and transport. Roche friabilator is employed for finding the friability of the tablets. Weigh the 20 tablets from each batch and place in Roche friabilator that will rotate at 25 rpm for 4 minutes. Dedust the all tablets and weigh again. The percentage of friability can be calculated using the formula

$$\% \text{ Friability} = [(W1-W2)100]/W1$$

Where, W1= Weight of tablet before test, W2 = Weight of tablet after test

Uniformity of dispersion

Keep the tablets in 10ml beaker containing 6 ml of 6.8 pH phosphate buffer and stir gently for 2 min. The dispersion is passed through 22 meshes. The tablets will consider passing the test if no residue remained on the screen.

Wetting time & Water absorption ratio

A piece of tissue paper folded twice was kept in a Petri dish (inter diameter 5.5cm) containing 6ml of purified water. The tablet was placed on the tissue paper and allowed to wet completely. The time required for complete wetting of the tablet was then recorded. For water absorption ratio the wetted tablet was removed and reweighed. Water absorption ratio, R was determined according to the following equation.

$$R = 100 (W_a - W_b) / W_b$$

Where W_a and W_b are the weight before and after water absorption, respectively.

Content Uniformity

Five tablets were powdered and the blend equivalent to 8 mg of Ondansetron hydrochloride was weight and dissolved in suitable quantity of 0.1 N HCl, filtered and drug content analyzed spectrophotometrically at 310 nm.

In vitro Disintegration time

The disintegration test was performed using an USP disintegration apparatus (Electolab, Mumbai, India.), and the tablet rack of the disintegration apparatus was positioned into a 1-liter beaker containing 900 ml of distilled water at 37 ± 2°C and the time of disintegration was recorded.

In- vitro dissolution test

The dissolution study was performed for batch F1 to F12 formulation by using USP type II paddle apparatus (Electolab, Mumbai, India.). At 37°C±0.5°C using 500ml 0.1N HCL as dissolution medium with stirring speed of 50rpm. Aliquot of (1ml) dissolution medium was withdrawn after 10 minutes, it was filtered and absorbance was measured spectrophotometrically at 310 nm by Elico UV/vis double beam spectrophotometer (Model: SL 160). Calculate the release of Ondansetron hydrochloride in percentage with respect to the labelled claim by using the following expression.

$$\frac{A_u \quad W_s \quad 500 \quad MW1}{A_s \quad D \quad L \quad MW2} \times P \times 100$$

Where

A_u = Average area of the peak due to Ondansetron hydrochloride in the sample preparation

A_s = Average area of the peak due to Ondansetron Hcl in the standard preparation

W_s = weight of Ondansetron hydrochloride taken for standard preparation in gm

D = dilution factor of the standard preparation

MW1 and MW2 = Molecular weight of Ondansetron (293.4) and Ondansetron hydrochloride (365.9)

L = Tablet label claim in mg

P = percentage purity of Ondansetron hydrochloride

RESULTS AND DISCUSSION

Preparation of Ondansetron HCl – tulsion-335 resinsates

Ondansetron HCl was loaded on tulsion-335 by batch process. Complexation between drug and resin is essentially a process of diffusion of ions between the resin and the surrounding drug solution. As reaction is an equilibrium phenomenon, maximum efficiency is best achieved in the batch process. Also, higher swelling efficiency in the batch process results in more surface area for ion exchange. Hence, the batch process was selected.

Optimization of Ondansetron HCl – tulsion-335 complexation

The drug loading in various drug : Resin concentration was found 73.18 ± 0.22, 84.71 ± 0.24, 85.41 ± 0.22 and 85.41 ± 0.20 respectively for 1:1, 1:2, 1:3, 1:4, 1:5 and 1:6. The drug loading is more while increasing the resin concentration, thus the 1:3 ratio was used as optimized ratio. Because further increasing the resin ratio no increase in the drug loading

Swelling time showed significant effect on drug loading showing that the swelling of resin enhances the drug loading capacity of resin. Percent of drug loading was directly depends with swelling time. Swelling time increases the drug loading of resin also increases. At 90 min the resin shows maximum loading efficiency (89.27 ± 0.15) and used as optimized time. The swelling and hydrated properties of tulsion-335 affect the rate of ion exchange, which in turn affects the percentage loading. The resulted showed in Fig 1.

The effect of percentage drug loading on stirring time was presented in Fig 2. The percentage drug loading was directly proportional to stirring time. The equilibrium ion exchange in solution occurs stoichiometrically and hence it is affected by stirring time. The drug loading was slowly increased and constant stirring up to 6 hr and at end of 6 hr's there is no increase in drug loading was observed. Hence 6 hr (92.39 ± 0.25) contact time between drug-resin at constant stirring was standardized to equilibrium ion exchange resin process to achieve maximum drug loading.

The mode of complexation between drug and resin was effected by pH of the media was presented in Fig 3. The maximum 95.22 ± 0.25 percentage of drug loading was obtained at the pH 3. As pH

increases above pH 5, percentage of drug loading was decreased and also pH of the solution affected the both solubility and degree of ionization of drug and resin. The obtained results can be attributed to the fact that a cationic drug is ionized at lower pH value and high binding capacity. However, while at higher pH protonated fraction of cationic drug decreases. Hence Ondansetron hydrochloride as cationic drug will have maximum solubility and complete ionization at low pH. Decreased complexation at lower pH i.e. below 2 is due to excess hydrogen ions in solution which have more binding affinity to (coo-) group of resin and compete with drug for binding.

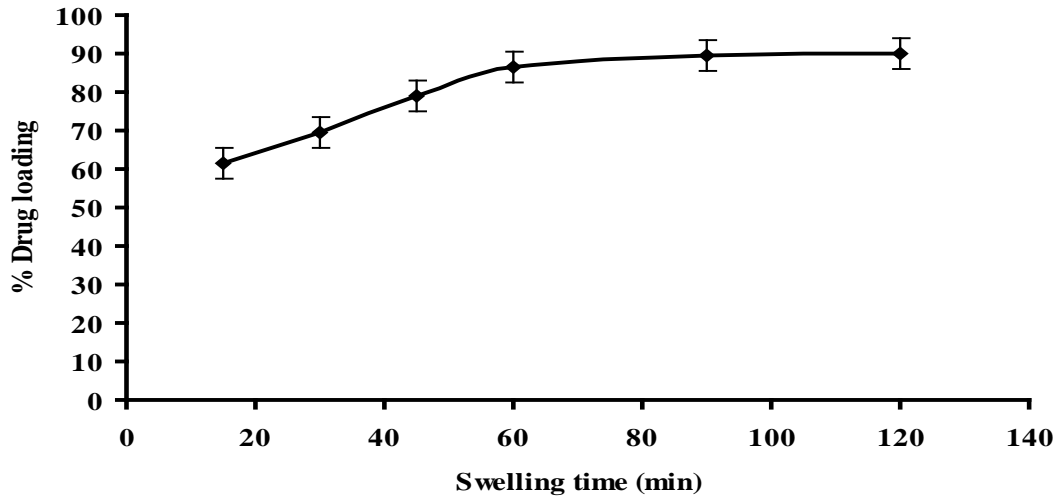


Fig. 1: Effect of swelling time on drug loading of Tulsion 335 complex

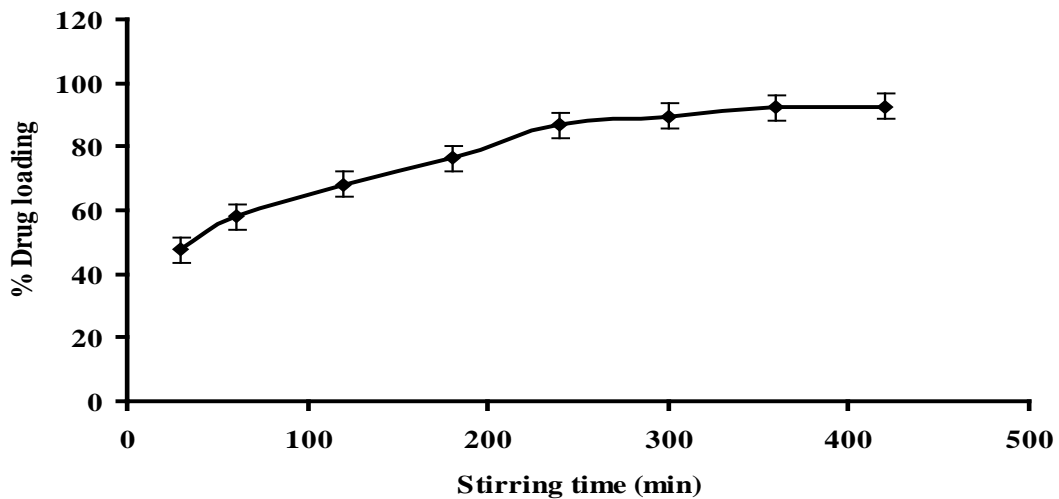


Fig. 2: Effect of stirring time on drug loading of Tulsion 335 complex

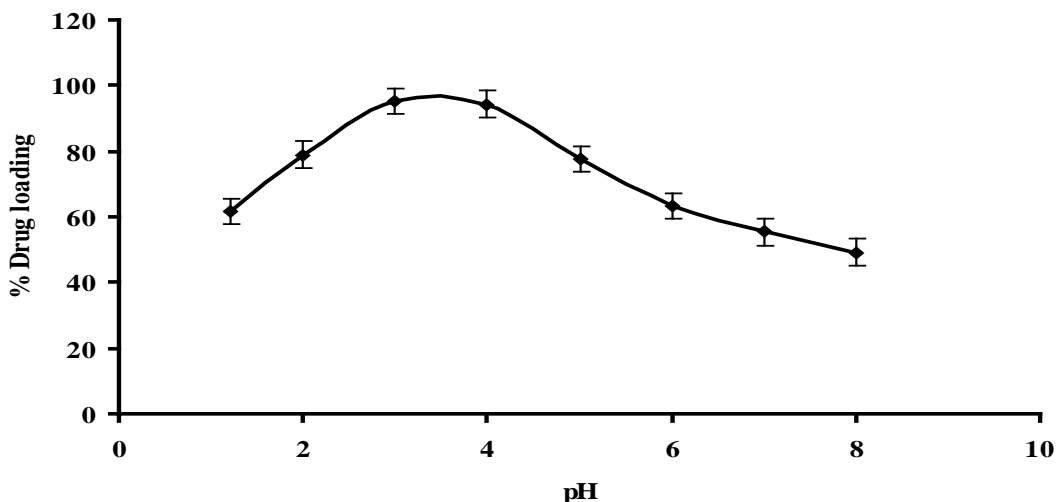


Fig. 3: Effect of pH on drug loading of Tulsion 335 complex

Characterization of Resinate

DSC analysis

DSC analysis of tulsion-335 resinate was carried out to check any changes in a thermal property of drug due to complexation. Pure Ondansetron HCl thermogram was a single, sharp melting

endotherm at 186.43° (Fig 4). There is no endothermic peak appearance in case of tulsion resinate due to its polymeric amorphous state (Fig 5). Thus it was proved that there were no major differences in thermograms, hence the excipients were compatible with the drug chosen and so could be safely used to formulate ODT.

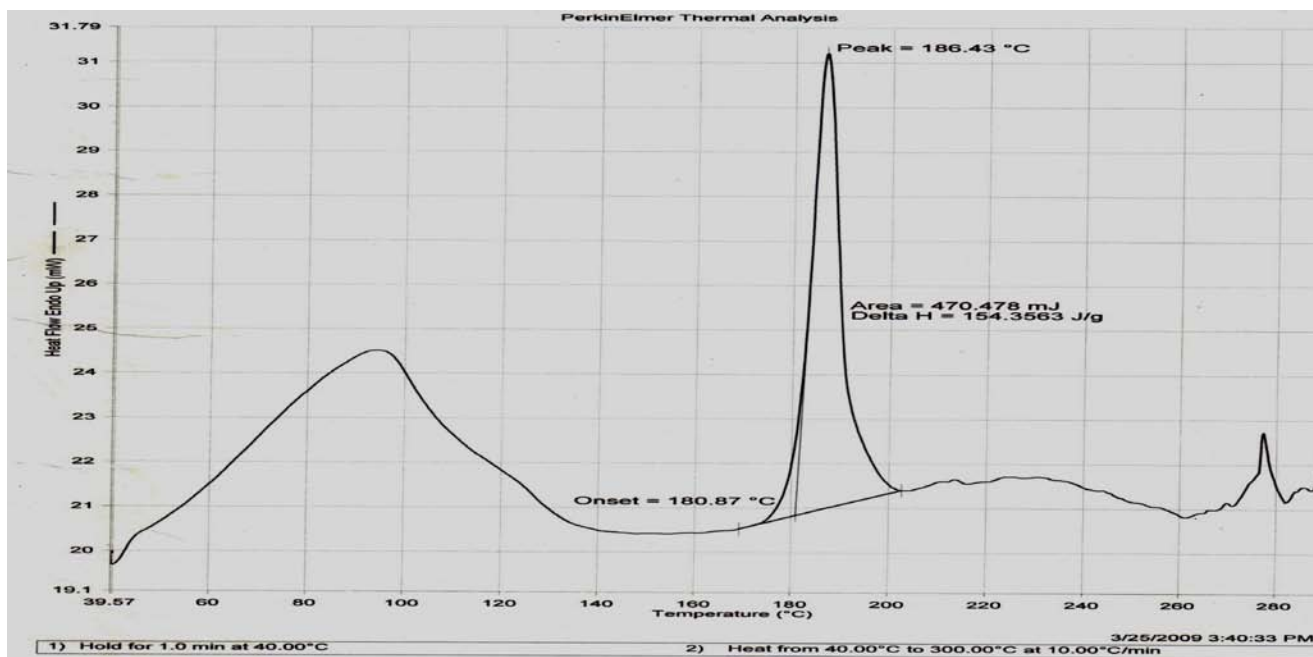


Fig. 4: DSC Thermo gram of pure Ondansetron HCl.

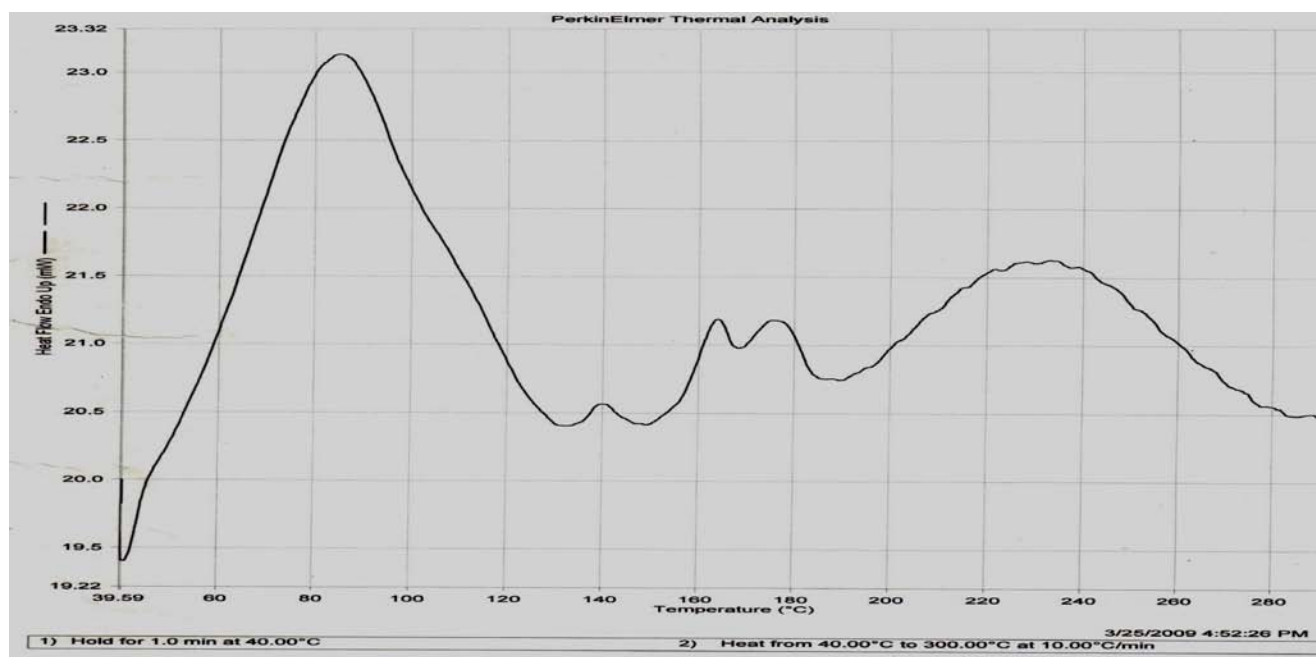


Fig. 5: DSC Thermo gram of Ondansetron HCl and Tulsion 335 Resinate

Pre compression parameters of tablet blend

The powder blend was evaluated the physical properties such as The Angle of repose between prepared tablet blend $20.30 \pm 0.13 - 28.14 \pm 0.21$ this indicates good flow, Bulk density was found to be 0.41 to 0.54 gm/cm^3 and tapped density between 0.45 to 0.56 gm/cm^3 . The % compressibility was found to be between 7.40 to 14.54% and the results are shown in the Table 2.

Evaluation of tablets

Weight variation test results indicated that all the tablets of different formulations were within the U.S.P. specifications i.e. ± 7.5 . All the formulations show thickness in between 3.13 ± 0.03 to $3.70 \pm 0.03 \text{ mm}$ respectively (Table 3). Hardness was found to be in between 3.8 ± 0.37 to $4.2 \pm 0.3 \text{ kg/cm}^2$ respectively (Table 3). Friability of the tablets was found to be 0.5% indicating good mechanical resistance;

in vitro dispersion test was done for all the formulations. Tablet disintegration was effected by wicking and swelling of the different concentration of superdisintegrant (Indian 414). Water absorption ratio for F6 is 85.26% . The wetting time decreased with increase concentration of indion-414 (Table 3). The wetting time of formulation F6 was 16 s . So it shows good water absorption capacity, the wetting time decreased with increase concentration of indion-414 (Table 3). The wetting time of formulation F6 was 16 s . The most important parameter that is needed to be optimized during the development of oral dispersible tablets is disintegrating time of the tablets (Table 3). The drug content was found in the range of $95-105\%$ (Acceptable limit). The formulation F6 shows 14 s disintegration time containing the DC-mannitol as diluent. Disintegrating study showed that the disintegrating times of the tablets decreased with increase in the concentration of indion-414.

Table 2: Precompressional parameters of Blend

Formulations	Bulk density g/cm^3	Tapped density gm/cm^3	Angle of repose, (θ) (\pm SD), n=3	%Compressibility (\pm SD), n=3	Hausner's ratio (\pm SD), n=3
F-1	0.43 ± 0.21	0.48 ± 0.14	25.17 ± 0.13	10.41 ± 0.21	1.13 ± 0.02
F-2	0.44 ± 0.22	0.49 ± 0.14	22.05 ± 0.17	10.20 ± 0.42	1.09 ± 0.02
F-3	0.47 ± 0.15	0.52 ± 0.12	21.19 ± 0.21	9.60 ± 0.14	1.11 ± 0.02
F-4	0.50 ± 0.21	0.54 ± 0.14	20.80 ± 0.23	7.40 ± 0.26	1.08 ± 0.02
F-5	0.48 ± 0.14	0.52 ± 0.11	20.38 ± 0.23	7.69 ± 0.21	1.08 ± 0.02
F-6	0.52 ± 0.15	0.56 ± 0.14	20.30 ± 0.13	7.47 ± 0.16	1.10 ± 0.02
F-7	0.47 ± 0.24	0.55 ± 0.12	28.14 ± 0.21	14.54 ± 0.26	1.14 ± 0.02
F-8	0.54 ± 0.25	0.62 ± 0.11	26.92 ± 0.12	12.90 ± 0.26	1.13 ± 0.02
F-9	0.49 ± 0.21	0.55 ± 0.11	25.55 ± 0.12	11.32 ± 0.21	1.12 ± 0.02
F-10	0.53 ± 0.21	0.45 ± 0.14	25.54 ± 0.12	10.90 ± 0.13	1.13 ± 0.02
F-11	0.41 ± 0.24	0.46 ± 0.11	24.04 ± 0.23	10.86 ± 0.39	1.12 ± 0.02
F-12	0.45 ± 0.23	0.50 ± 0.14	22.69 ± 0.21	10.00 ± 0.12	1.15 ± 0.02

Table 3: Postcompressional parameters of all formulations

Formulations	Average weight (mg)	Hardness (kg/cm^2) \pm SD, n=3	Friability (%), \pm SD, n=10	Thickness (mm), SD, n=5	Drug content (%) \pm SD,	Wetting Time(s) \pm SD, n=4	Disintegration Time(sec)	Water absorption ratio
F-1	150.8 ± 0.74	4.1 ± 0.35	0.33 ± 0.01	3.23 ± 0.03	98.33 ± 0.25	32.14 ± 1.6	38.43 ± 1.2	84.1 ± 0.32

F-2	151.4±0.31	3.9 ± 0.55	0.34 ± 0.01	3.42 ± 0.03	99.08 ± 0.35	23.07 ± 1.4	26.90 ± 0.9	78.3±0.24
F-3	152.3±0.14	4.0 ± 0.64	0.34 ± 0.01	3.49 ± 0.03	98.59 ± 0.65	21.04 ± 1.1	23.45 ± 0.5	77.3±0.32
F-4	149.5±0.16	4.0 ± 0.35	0.39 ± 0.01	3.14 ± 0.03	99.78 ± 0.75	25.11 ± 1.8	17.63 ± 2.2	72.0±0.45
F-5	152.6±0.52	3.8 ± 0.35	0.37 ± 0.01	3.32 ± 0.03	99.58 ± 0.75	19.16 ± 1.4	17.34 ± 0.8	83.5±0.87
F-6	151.2±0.34	4.0 ± 0.35	0.38 ± 0.01	3.13 ± 0.03	99.85 ± 0.35	16.21 ± 1.2	14.07 ± 0.6	85.6±0.63
F-7	149.6±0.48	4.2 ± 0.35	0.31 ± 0.01	3.34 ± 0.03	98.73 ± 0.25	41.23 ± 1.6	42.80 ± 0.9	79.6±0.53
F-8	152.1±0.76	4.0 ± 0.35	0.34 ± 0.01	3.47 ± 0.03	99.98 ± 0.72	38.31 ± 1.2	36.14 ± 0.8	75.9±0.45
F-9	153.3±0.35	4.1 ± 0.35	0.39 ± 0.01	3.22 ± 0.03	99.63 ± 0.65	28.11 ± 1.1	30.09 ± 0.9	63.6±0.71
F-10	148.5±0.42	4.1 ± 0.34	0.34 ± 0.01	3.22 ± 0.03	99.33 ± 0.45	25.10 ± 1.8	25.02 ± 0.7	71.5±0.46
F-11	150.5±0.23	4.0 ± 0.35	0.33 ± 0.01	3.15 ± 0.03	99.88 ± 0.45	24.10 ± 1.3	20.08 ± 0.5	73.5±0.57
F-12	152.4±0.31	3.9 ± 0.35	0.38 ± 0.01	3.56 ± 0.03	99.52 ± 0.39	19.18 ± 1.4	17.33 ± 0.6	72.8±0.64

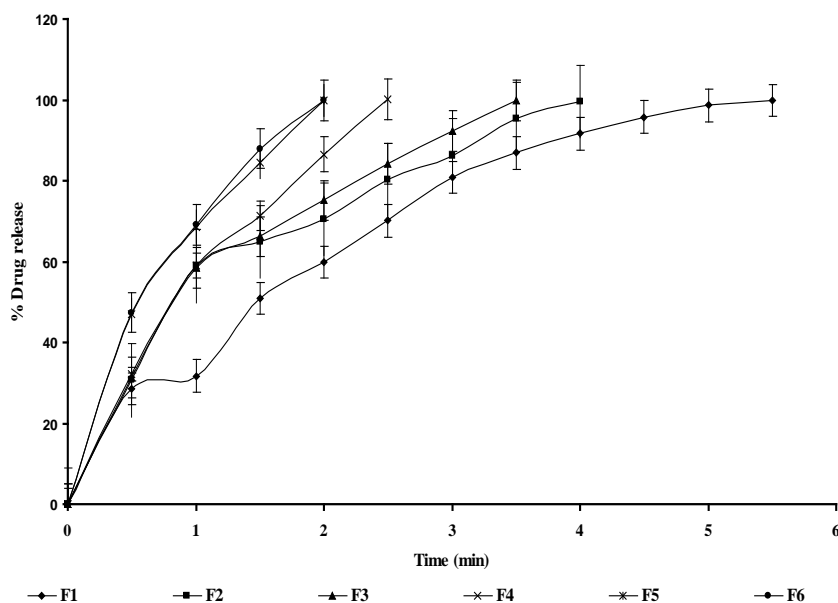


Fig. 6: Dissolution profiles of Ond HCl-Tulsion 335 based complex formulations mannitol as diluent

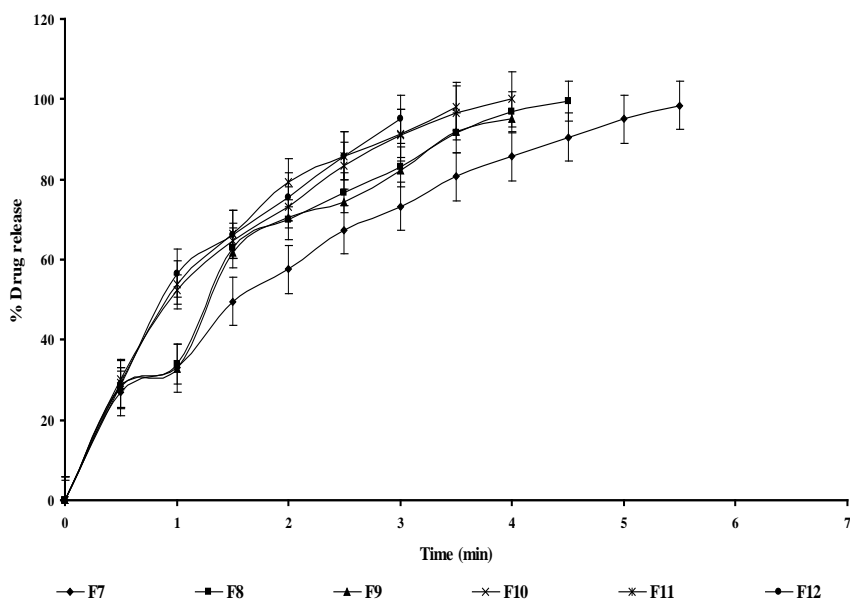


Fig. 7: Dissolution profiles of Ond HCl-Tulsion 335 based complex formulations MCC PH101 as diluent

In vitro release study

The *in vitro* dissolution of Ondansetron HCl was studied in 0.1 N HCl. The percentage drug release from formulations is shown (Fig 6 and 7). These values changed with change of carriers and method of preparation of tablets, $t_{50\%}$ and $t_{90\%}$ values decreased with increase in the concentration of indion-414. An Indion-414 containing tablet

rapidly exhibits high capillary activity and pronounced hydration with a little tendency to gel formation and disintegrates the tablets rapidly but into larger masses of aggregated particles. Thus difference in the size distribution generated with different superdisintegrants might have contributed to difference in the $t_{50\%}$ and $t_{90\%}$ values with the same amount of superdisintegrants in the

tablets. The indion-414 concentration was effected the release of drug from tablet.

The diluent also affects the release of drug from tablets. In tablets consisting of MCC as filler binder shows significant effect on water absorption ratio and disintegration time. This may be attributed to the fact that MCC is a swell able material and its disintegration characteristics in water have been attributed to capillary action or swelling. In tablets consisting directly compressed mannitol as diluent shows significant effect on drug release because when compression, the structure crumbles into finer particles, which fill in the interstitial spaces between larger porous particles. The tablets containing directly compressed mannitol as diluent shows better release compares the tablets containing MCC as diluent. The formulation F6 shows $t_{50\%}$ and $t_{90\%}$ value 0.85 ± 0.8 and 2.46 ± 1.2 respectively. The drug release from F6 formulations is too fast compared to marketed formulations in the optimized formulation F6 shows the presence of all the characteristic peaks of ondansetron indicates lack of any strong interaction between the drug and the excipients.

CONCLUSION

The micrometric properties of powder blend were determined and observed good flow characteristics the tablet containing 6.67% of indion 414 and with DC-mannitol as diluent (F6 Formulation) is the optimized formulation due to its fast *in-vitro* dispersion when compared to other formulations, the wetting time is 16 sec. The DSC studies are done for optimized formulation there is no interaction between the drug and excipients. All physical and chemical characteristics of Ondansetron Hydrochloride ODT tablets prepared by using optimized formula (F6) were found to be satisfactory.

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