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Research Article

FORMULATION AND EVALUATION OF ORAL FAST DISSOLVING TABLET OF ONDANSETRON HYDROCHLORIDE BY COPROCESS EXCIPIENTS

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ABSTRACT

Recent development in fast disintegrating technology mainly works to improve the quality of these delicate dosage forms without affecting their integrity. Current investigations deal with the formulation of fast dissolving tablet of Ondansetron HCl with the effect of different co-processed excipients by using ball mill that disintegrates in oral cavity on contact with saliva & thereby improve therapeutic efficacy because the mannitol was stick to dies and punch therefore ball mill is used to prepare co ground mixtures of crospovidone and mannitol to improve the compatibility and stability of product. The Fast disintegrating tablets of Ondansetron HCl were prepared by direct compression method using different synthetic superdisintegrant such as Crospovidone, and natural superdisintegrant such as Karaya gum and Fenugreek gum in different concentration. The FTIR, DSC analysis revealed that the Betacyclodextrin and superdisintegrants used were compatible with Ondansetron HCl. A complex of Betacyclodextrin and Ondansetron HCl was successfully formed in 1:2 ratios. Disintegration time decrease with increase in the concentration of superdisintegrant. Among all formulation, containing Karaya Gum as superdisintegrants is fulfilling all the parameters satisfactorily. In vitro release studies that almost 98.88% of the drug was released from all the formulation were within 15 minutes. Best Formulation F6 showed faster drug release within 7 minutes in comparison to other formulation. The result shows that Co-processing of excipients is the most suitable approach for formulation of Fast dissolving tablet.

Keywords: Coprocess, Fast disintegrating tablets, Ball mill, Disintegration time, Mannitol etc.

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INTRODUCTION

United States Food and drug administration defined fast disintegrating tablet as “a solid dosage form containing medicinal substance or active ingredient which disintegrate fast usually within a few seconds when placed upon the tongue.” FDTs differ from traditional tablets as they are designed to be dissolved on the tongue rather than swallowed whole. Fast disintegrating tablets are also known as mouth disintegrating tablets, melt-in mouth tablets, Orodispersible tablets, porous tablets, quick dissolving tablets, fast dissolving tablets.¹ According to US Food and Drug Administration 2008 publications of guidance are: FDTs should have an In

vitro disintegrating time of approximately 30 sec or less.² Generally, the FDT tablet weight should not exceed 500 mg, although the combine influence of stable weight, size and component solubility all factor into the acceptability of an ODT for both patients and regulators. Recent advances in novel drug delivery system aim to enhance safety and toxicity of drug molecules by formulating a convenient dosage form for administration and to achieve better patient compliance.⁴ One such approach led to development of fast dissolving tablets. Fast dissolving drug-delivery systems were first developed in the late 1970s as an alternative to conventional dosage forms for paediatric and geriatric patient. Traditional tablets and capsules administered

with an 8-oz. glass of water may be inconvenient or impractical for some patients who experience difficulties in swallowing traditional oral solid-dosage forms. These tablets are designed to dissolve or disintegrate rapidly in the saliva generally less than 60 seconds.⁵

Coprocessed Excipients⁶

Co-processing is based on the novel concept of two or more excipients interacting at the sub particle level, the objective of which is to provide a synergy of functionality improvement as well as masking the undesirable properties of individual. Co-processing excipients leads to the formulation of excipient granules with superior properties compared with physical mixtures of components or individual components. The resulting engineered excipients are commonly known as "coprocessed," "high functionality," "multifunctional," "high functionality," "performance" excipients.⁷

Significance of the co-processed excipients

1. Enhancement in flow properties
2. Absence of chemical change
3. Better dilution potential
4. Fill weight variation
5. Reduced lubricant sensitivity
6. Improved compressibility⁸

All coprocessed and modified excipients are playing very important role in the development of easy dosage form. Compared with existing excipients, the improved physical, mechanical, and chemical properties of such excipients have helped in solving formulation problems such as flow ability, compressibility, hygroscopicity, palatability, dissolution, disintegration, sticking, and dust generation. There is need to develop new specially designed equipment for evaluations of coprocessed excipients & Coprocessed excipients have yet to find their way into official monographs, also we can explore coprocessed excipients in various drug deliveries.^{9,10}

MATERIALS AND METHOD

Ondansetron HCl was obtained as a gift sample Maxheal Pharmaceuticals, MIDC, Nashik Crospovidone, Karaya gum, Fenugreek gum, Sodium bicarbonate, Microcrystalline cellulose, Flavor, Mannitol, Aspartame, Mg. stearate, Talc, Beta cyclodextrin. From Research Lab Fine Chem. Ltd. Mumbai.

Methods:

1. Preformulation study

- a) Identification and characterization of Ondansetron HCl

- b) Determination of Melting point: The melting point of the drug was determined using capillary tube.

- c) Calibration Curve in 6.8 Phosphate Buffer:

- d) Compatibility Study of Drug and Excipients:

- i) FTIR spectrum

- ii) DSC

2. Preparation of drug and BCD complex by kneading method:

A mixture of Ondansetron HCl and Betacyclodextrin was ground in a glass container and a minimum amount of water was added. The mixture was kneading for 5 min and dried at 60°C in the vacuum oven. After drying inclusion complex of Ondansetron HCl and β -cyclodextrin was obtained.

3. Preparation of coprocessed co-ground mixture for FDTs by using ball mill

Coground Mixture and FDTs Coground mixtures prepared by using a ball mill. The Coground mixtures were blended with drug, mannitol, and magnesium stearate in a glass bottle using manual shaking. After blending, the mixtures were compressed using a single tableting machine. The purpose of this study was to prepare oral fast disintegrating tablets (OFDTs) by directly compressing a mixture of mannitol and Crospovidone. When the mixture of mannitol and Crospovidone was co-processed by ball mill. To improve the compatibility and their stability during storage. The (OFDTs) without this co-processing, the powder mixture had poor compatibility, and the stability of the tablet was inferior, probably due to the high Hygroscopicity of Crospovidone. The OFDTs containing co-ground mixture of crospovidone/mannitol showed good stability for six months under humid conditions with rapid disintegration and increase hardness of the tablets Tablet stability could not be achieved using a physical mixture of crospovidone/mannitol without including the co-ground process.^{11,12}

4. Formulation of oral fast disintegrating tablets

The best batch obtained from Kneading method with 1:2 ratio of inclusion complex was prepared by direct compression method containing 12 mg of Ondansetron. Drug + Beta cyclodextrin inclusion complex equivalent to 4mg of Ondansetron was taken and pass through the # 40. Diluents, superdisintegrants, sweetener and flavour were passed through # 40. All above ingredients were mixed and blended properly. Magnesium stearate was passed through # 40 and mixed properly with above blend. Powdered lubricated blend was compressed into tablet by Rimek, minipress-2nd DL 09 station tooling machine using, 7 mm round flat punches.

Table 1: Composition of Oral Fast disintegrating tablets of Ondansetron HCl

Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)
OSH+BCD complex (equivalent to 4mg Drug) (1:2)	12	12	12	12	12	12	12	12	12
Fenugreek Gum	4	8	10	-	-	-	-	-	-
Karaya Gum	-	-	-	4	8	10	-	-	-
Crospovidone	-	-	-	-	-	-	4	8	10
Avicel 101	55.5	55.5	55.5	55.5	55.5	55.5	55.5	55.5	55.5
Magnesium Stearate	3	3	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3	3	3
Orange flavor	1	1	1	1	1	1	1	1	1
Aspartame	2	2	2	2	2	2	2	2	2
Mannitol	QS	QS	QS	QS	QS	QS	QS	QS	QS
Total weight	150	150	150	150	150	150	150	150	150

*All the quantities mentioned above in mg

5. Evaluation of oral fast disintegrating tablets

a) Weight variation: Average weight of 20 tablets were selected randomly from the lot and weighed individually to check for weight variation.

b) Tablet Thickness: Ten tablets were taken and their thickness was recorded using Vanier calliper. It is measured in mm

c) Tablet Hardness: Hardness of the tablet of each formulation was determined using Monsanto hardness tester.

d) Friability (F): Friability of the tablet is determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at a height of 6 inches in each revolution. Pre weighed sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

$$\% \text{Friability} = \frac{\text{loss in weight}}{\text{Initial weight}} \times 100$$

e) Wetting Time: The wetting time of the tablets can be measured using a simple procedure. Twice folded circular tissue papers of 10 cm diameter were placed in a Petridis with a 10 cm diameter. 10 ml of pH 6.8 phosphate buffer. A tablet is carefully placed on the surface of the tissue paper. The time required for phosphate buffer to reach upper surface of the tablet is noted as a wetting time.

f) Water Absorption Ratio: A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of pH 6.8 phosphate buffer. A tablet was put on the tissue paper and allowed to completely wet. The wetted tablet was then weighed. Water absorption ratio, R was determined using following equation.

$$R = 100 \times \frac{(W_a - W_b)}{W_a}$$

Where, W_a = Weight of tablet after water absorption

W_b = Weight of tablet before water absorption.

FTIR Analysis:

g) In vitro dispersion time: In vitro dispersion time was measured by dropping a tablet in a 10 ml measuring cylinder containing 6 ml of buffer solution simulating saliva fluid (pH 6.8) at $37 \pm 0.5^\circ\text{C}$ and the time required for complete dispersion was determined.

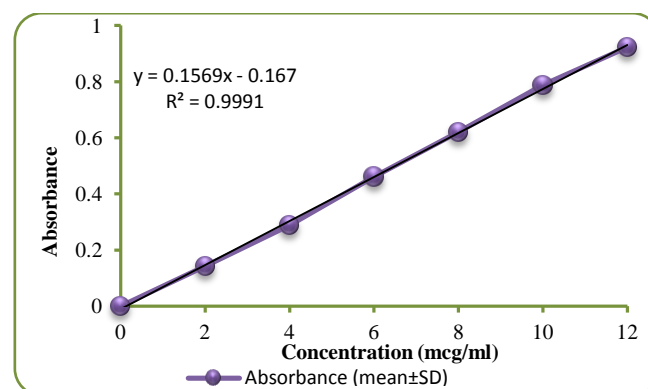
h) Content Uniformity: The content uniformity of the prepared formulas orodispersible tablets was performed by taking ten tablets and assayed individually. The requirement for this test is met if the amount of ingredient in each of the ten tablets lies within the range of 95%-102%. Taken five tablets were powdered and the blend equivalent to 20 mg of Ondansetron was weight and dissolved in 100 ml of phosphate buffer (pH 6.8). Stock solutions are sonicated for 14 minute. Filter the sample and withdraw 1ml filtrate was taken in 25 ml phosphate buffer (pH 6.8) and analyzed spectrophotometrically at 310 nm. The amount of Ondansetron was estimated by using standard calibration curve of drug

RESULT AND DISCUSSION

Identification and Characterisation of Ondansetron HCl

Melting Point

The melting point of the Ondansetron HCl was found to be 231°C , which complies with BP.



Standard calibration curve of Ondansetron HCl

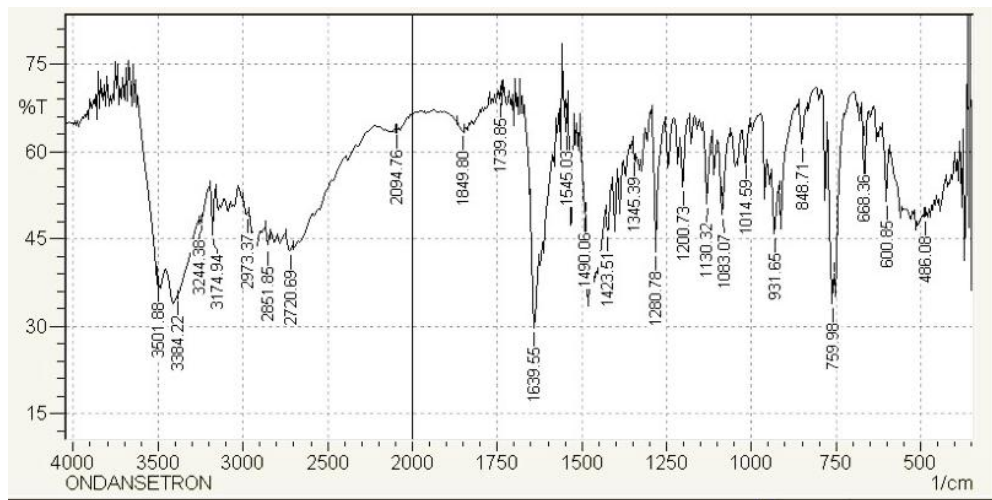


Figure 1: FTIR spectrum of Ondansetron HCL

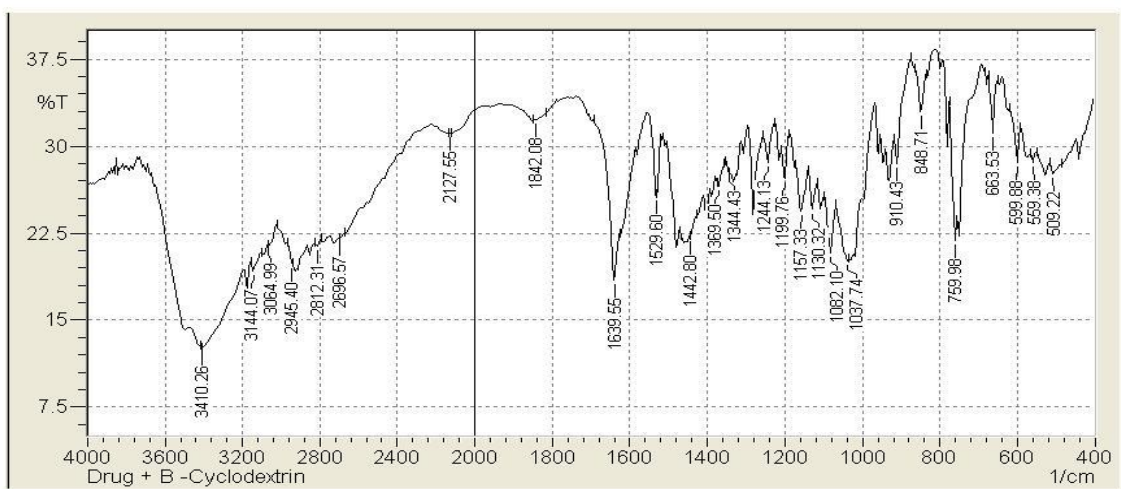


Figure 2: FTIR spectrum of Ondansetron HCL with cyclodextrin complex

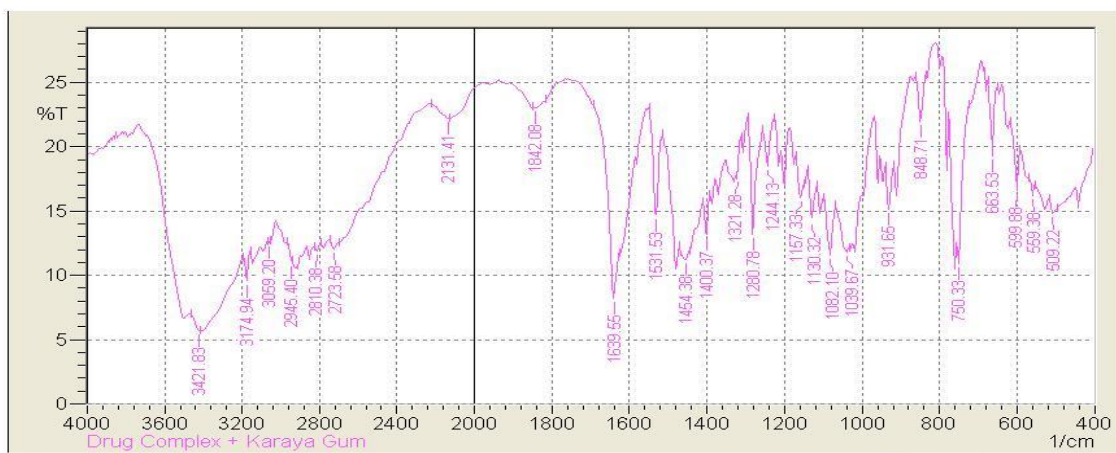


Figure 3: FTIR spectrum of Ondansetron HCL in powder blend

From FTIR study it can be concluded that the drug Ondansetron HCL has maintained its identity without losing its characteristic properties.

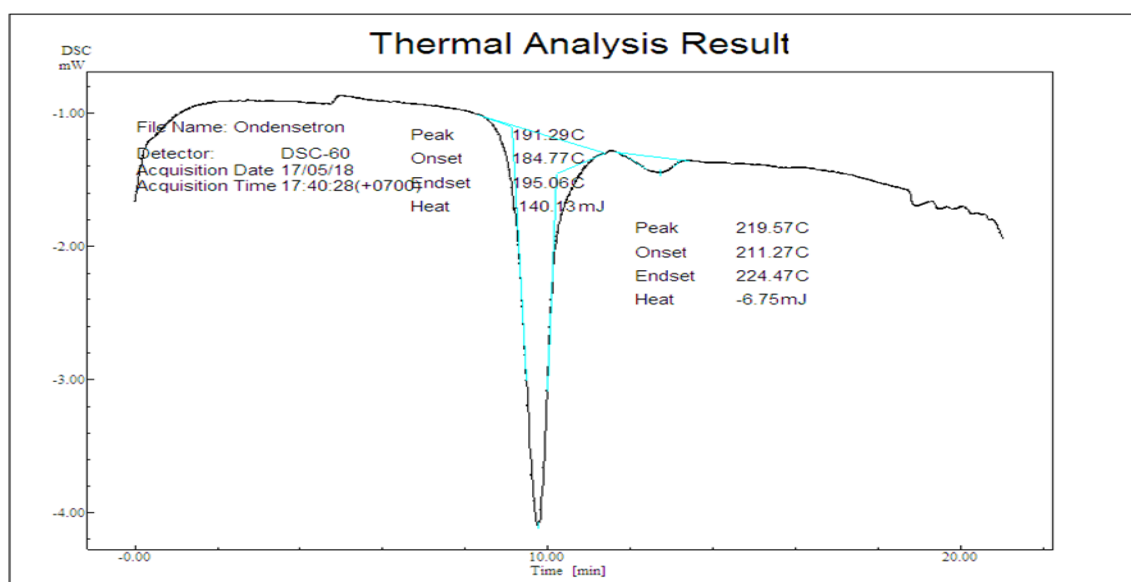


Figure 4: Differential Scanning Calorimetry of Ondansetron HCl

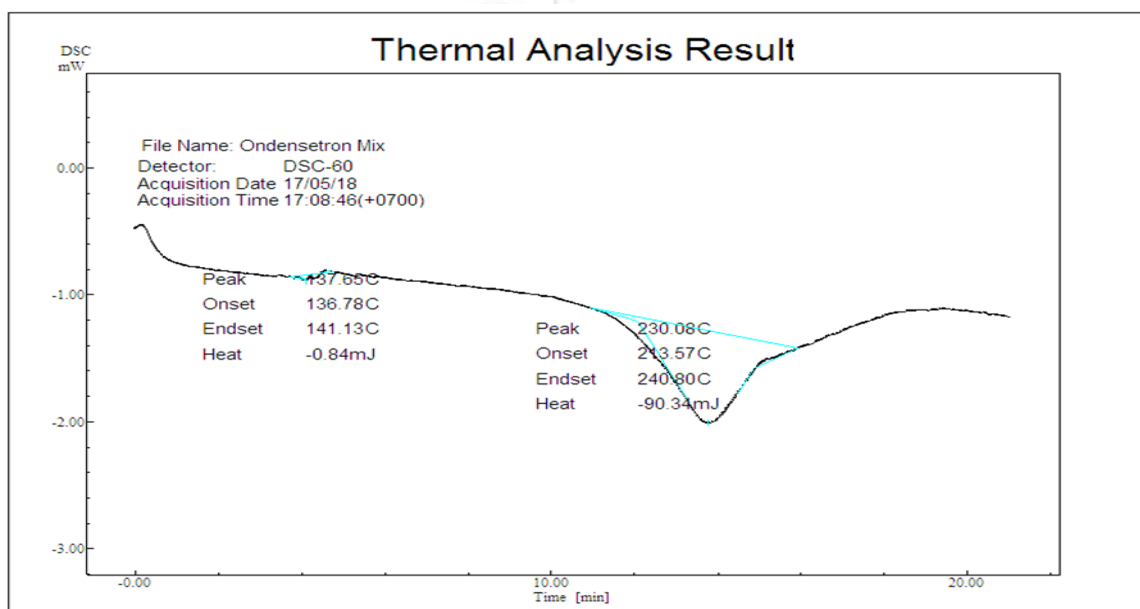


Figure 5: Differential Scanning Calorimetry of Ondansetron HCl with Excipients

The DSC thermogram of Ondansetron Fig.4 and Losartan Potassium Fig.5 exhibited a single sharp endothermic peak at 230°C respectively, related to its melting transition temperature.

Table 2: Post-compression parameter of batches F1-F9

Formulation	Thickness (n=3) (mm)(SD)	Hardness (kg/cm ²) (n=3) (SD)	Friability (%)	Weight Variation (n=20)(mg) (SD)
F1	2.49± 0.2	3.13 ± 0.04	0.81	Passable
F2	2.95± 0.1	2.99 ± 0.04	0.45	Passable
F3	2.43± 0.3	3.02 ± 0.06	0.71	Passable
F4	2.58± 0.2	3.04 ± 0.31	0.64	Passable
F5	2.56± 0.2	2.84 ± 0.04	0.56	Passable
F6	3.03± 0.3	3.45 ± 0.09	0.80	Passable
F7	3.02±0.3	2.90± 0.02	0.33	Passable
F8	3.06± 0.2	3.00 ± 0.02	0.66	Passable
F9	2.67± 0.1	2.89 ± 0.05	0.75	Passable

Table 3: Other Post-Compression parameters of batches F1-F9

Formulation	Wetting time (Sec)	Water absorption Ratio (SD)	Dispersion Time (sec) (SD)
F1	44	53± 0.2	33 ± 0.2
F2	36	55± 0.1	34± 0.3
F3	39	64± 0.5	34 ± 0.2
F4	42	62± 0.2	43 ± 0.5
F5	49	54± 0.2	50 ± 0.4
F6	43	63± 0.6	46 ± 0.2
F7	38	53± 0.1	33 ± 0.4
F8	35	62± 0.4	32± 0.4
F9	43	58± 0.4	66 ± 0.6

In vitro Dissolution study of formulation batches F1-F9

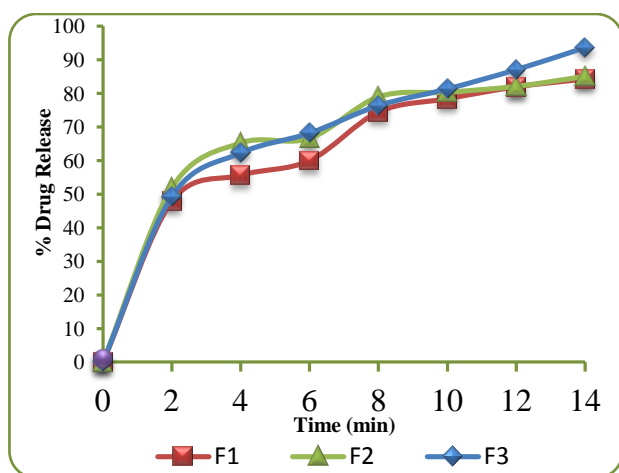


Figure 6: Comparative in vitro release profile of Ondansetron HCl Fast disintegrating tablets for formulation F1 to F3

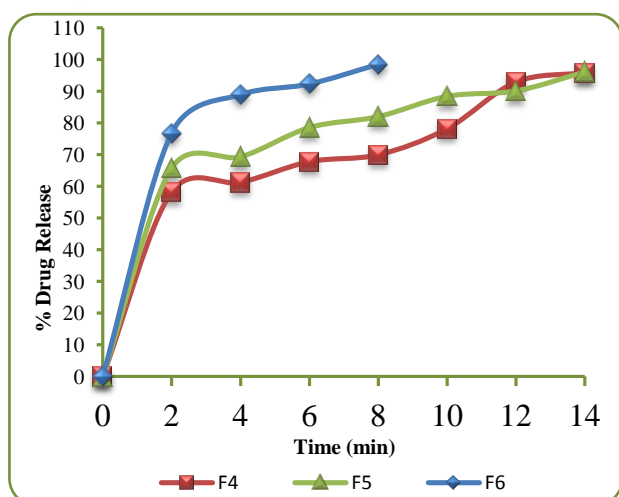


Figure 7: Comparative in vitro release profile of Ondansetron HCl Fast disintegrating tablets for formulation F4 to F6.

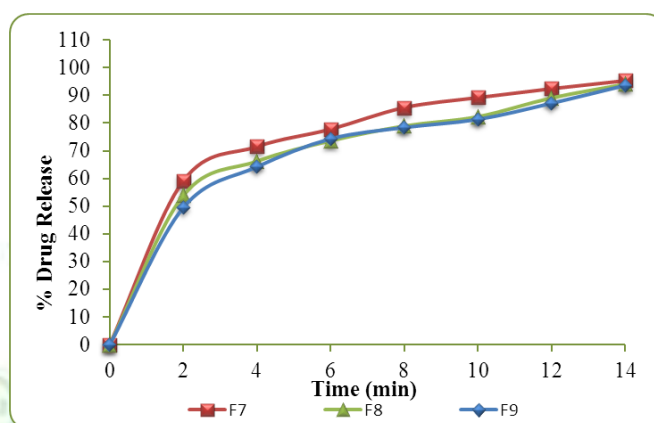


Figure 8: Comparative in vitro release profile of Ondansetron HCl Fast disintegrating tablets for formulation F7 to F9

CONCLUSION

The Fast disintegrating tablets of Ondansetron HCl were prepared by direct compression method using different superdisintegrant such as Crospovidone, Karaya gum and Fenugreek gum in different concentration with help of ball mill for coprocessing. The mannitol was stick to dies and punch therefore ball mill is use to prepare coground mixtures of crospovidone and mannitol to improve the compatibility and stability of product. The FTIR, DSC analysis revealed that the Betacyclodextrin and polymer used were compatible with Ondansetron HCl. Disintegration time decrease with increase in the concentration of superdisintegrant. Among all formulation, containing Karaya Gum as superdisintegrants is fulfilling all the parameters satisfactorily. In vitro release studies that almost 98.88% of drug was release from all the formulation were within 15 minutes. Formulation F6 showed faster drug release within 7 minutes in comparison to other formulation. Thus result shows that Co-processing of excipients is most suitable approach for formulation of Fast dissolving tablet.

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