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Fast Disintegrating Tablets of Ondansetron Hydrochloride by Direct Compression Technique

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Abstract: In the present work fast disintegrating tablets of taste masked ondansetron hydrochloride were prepared by direct compression method with a view to enhance patient compliance. Taste masking was done by complexing ondansetron hydrochloride with eudragit EPO in ratio 8:2. Two superdisintegrant i.e. crospovidone and croscarmellose sodium were used in different combination ratio. The properties of fast disintegrating tablets such as hardness, *in-vitro* disintegration time, wetting time, percent drug content and for *in-vitro* drug release pattern (in pH 6.8 phosphate buffer) short term stability (at 40ºC / 75% RH for two month) were investigated.
Among the all formulations, the formulation OD-5 (containing 2% wt/wt crospovidone and 1% wt/wt croscarmellose sodium in combination) emerged as the overall best formulation. Short term stability indicates that there were no substantial changes in all parameter.
Keywords: Fast disintegrant tablet, Taste masking, super disintegrant, Eudragit EPO.

Introduction

For the past three decades, there has been an enhanced demand for more patient compliant dosage form. As a result, the demand for such technologies increasing two to three folds annually. Since the development cost of a new chemical entity is very high, so that some of pharmaceutical companies are focusing their research on the development of new drug delivery system for an existing drug, which results in not only improve in efficacy and bioavailability both, but also reduce dosing frequency to minimize side effects. This attempt can lead to extend patient life and convenient dosage forms [1].

Ondansetron hydrochloride is a potent antiemetic drug used for the treatment and/or prophylaxis of postoperative or chemotherapy or radiotherapy induced emesis. In general, emesis is preceded with nausea and in such condition it is difficult to administer drug with a glass of water; hence it is beneficial to administer such drugs as fast disintegrating tablets (FDT). Ondansetron hydrochloride is an intensely bitter drug [2, 3]; hence, and if it is incorporated directly into an FDT then the main objective behind formulation of such a dosage form will definitely get trivial. Thus in the present study an attempt has been made to formulate FDTs with good mouth feel.

Materials and Method

Ondansetron hydrochloride was gifted by Symed Labs Limited, A.P., India. Crospovidone and croscarmellose sodium was gifted by Accutest Research Laboratories, Navi Mumbai. Mannitol, microcrystalline cellulose, talc were from Burgoyne bubidgas company, Mumbai. All other chemicals used were of analytical reagent grade.

Taste masking of drug by precipitation method [4,5]

Ondansetron hydrochloride and eudragit EPO complex were prepared using the precipitation method. Saturated solution of ondansetron hydrochloride and eudragit EPO were prepared in ethanol in ratio 8:2 and injected in to 0.1 N sodium hydroxide solutions with constant stirring at 500 rpm in a mechanical stirrer. The foamy matrix obtained on the top of the solution was separated and dried at room temperature for 24 hr

under vacuum. The dried matrix was subsequently pulverized and finely stored in tightly container for further study.

Preparation of Fast Disintegrating Tablets of Ondansetron Hydrochloride

Fast disintegrating tablet of ondansetron hydrochloride were prepared by direct compression method as per the formulation design given in table no. 1. The drug, super disintegrant, mannitol, microcrystalline cellulose were accurately weighted and passed through sieve no. 30 and added to other ingredient, and then magnesium stearate as a lubricants and talc as a glidant were added and mixed. The blend was directly compressed in to tablet of 150 mg using 9 mm round punch. A batch of 50 tablets was prepared for the designed formulations.

Table No. 1. Formulation design

Formulations / Ingredients*	OD_0 (mg)	OD_1 (mg)	OD_2 (mg)	OD_3 (mg)	OD_4 (mg)	OD_5 (mg)	OD_6 (mg)	OD_7 (mg)
DPC	5	5	5	5	5	5	5	5
Crospovidone	0	1.5	3	0	1.5	3	0	1.5
Croscarmellose sodium	0	0	0	1.5	1.5	1.5	3	3
Talc	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
Mag. Stearate	3	3	3	3	3	3	3	3
Mannitol	60	60	60	60	60	60	60	60
Sod. Saccharin	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
M.C.C.	76	74.5	73	74.5	73	71.5	73	71.5
Total	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

*all quantities are expressed in mg.

Evaluation of Tablet [6, 7]

Twenty tablets were selected at randomly and weighted individually. The individual weights were compared with average weight for determination of weight variation. Hardness and friability of the tablets were determined by using monsanto hardness tester and roche friabilator respectively. For content uniformity test ten tablets were weighted and powdered, a quantity of powder equivalent to 4 mg of ondansetron hydrochloride was extracted in to distilled water and filtered. The content of ondansetron hydrochloride was determined by measuring the absorbance at 310 nm with pH 6.8 phosphate buffers. The drug content was calculated using standard calibration curve.

Wetting Time [8, 9]

A piece of tissue paper folds twice was kept in a petri dish having internal diameter 5.5cm, containing 10 ml of distilled water at room temperature, and the time for complete wetting was recorded.

***In-vitro* Drug Release Study** [7, 9, 10]

In-vitro dissolution of ondansetron hydrochloride fast disintegrating tablet was studied in USP type-II dissolution apparatus (Electrolabs, model- EF 1W) employing a paddle in pH 6.8 phosphate buffer at 37ºC ± 1ºC as dissolution medium. One tablet was used in each test. Aliquots of dissolution medium (5 ml) were withdrawn at specified interval of time (5 minute) and analyzed for drug content by measuring the absorbance at 310nm. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium, cumulative percent of ondansetron hydrochloride release was calculated and plotted against time.

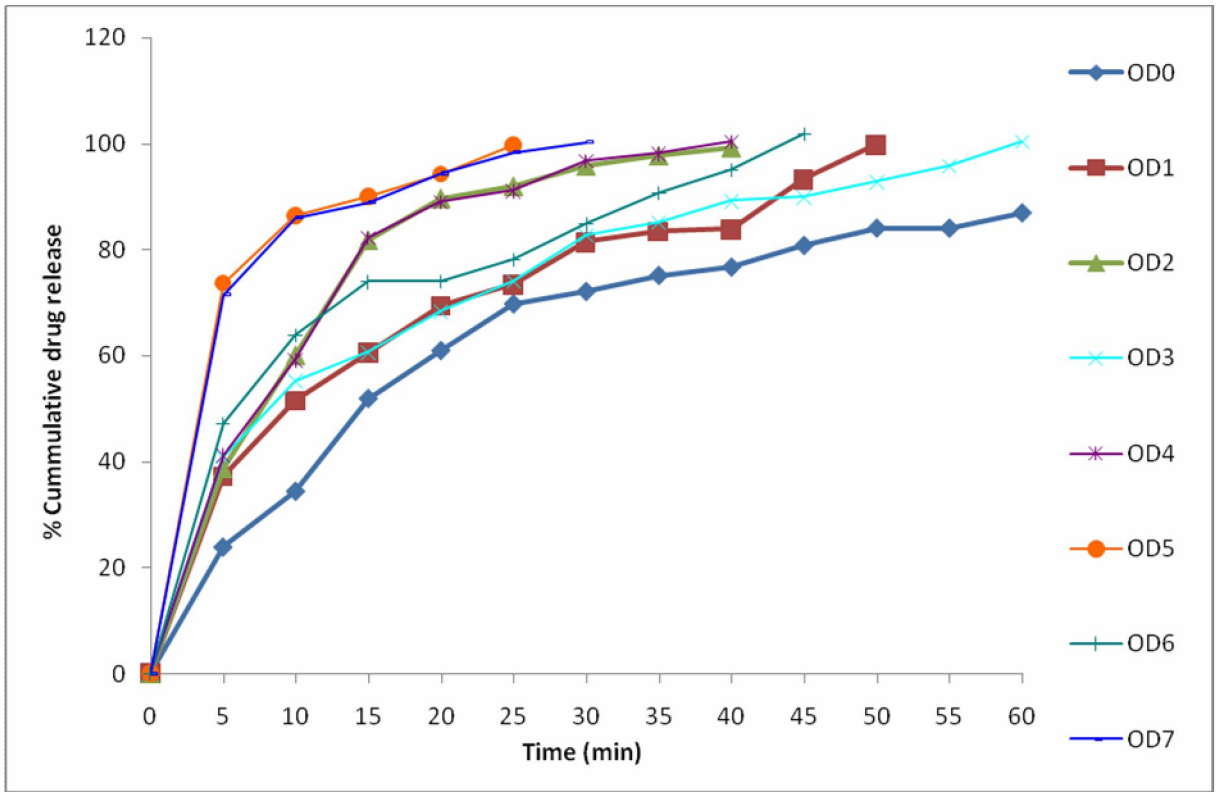

Figure No. 1. *In-vitro* drug release study of formulations OD0 to OD7

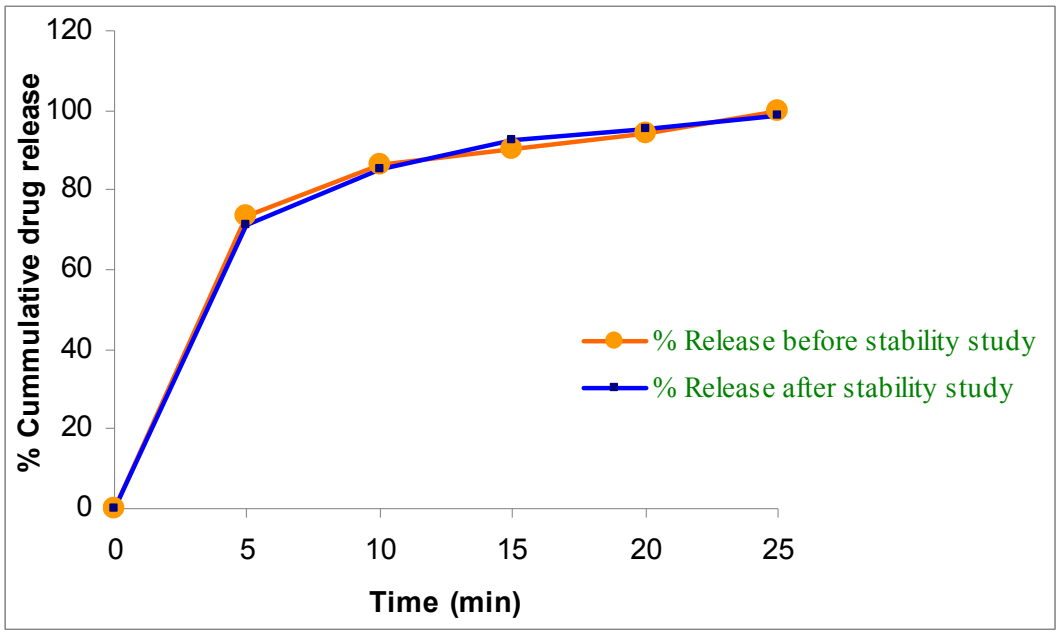

Figure No. 2. *In vitro* drug release study of OD5 batch before and after stability study

Stability Testing [10, 11]

Short term stability studies of the promising formulation (OD-5) was carried out by storing the tablets at 40ºC / 75 RH over a period two month. After 60 days samples were withdrawn and tested with regards to the parameters i.e. thickness, hardness, friability, weight variation, drug content and drug release study. After analysis it was found that there were no substantial changes in all parameter. The results revealed that product is sufficiently stable for the period of 60 days at 40ºC ± 2ºC / 75 ± 5% RH.

Result and Discussion

Fast disintegrating tablets of ondansetron hydrochloride were prepared by direct compression method using two superdisintegrats crospovodone and croscarmellose sodium along with mannitol and sodium saccharin which serve as a sweetening agent and help in masking bitter taste of the drug. A total seven formulations were designed. As the materials was free flowing (angle of repose value <30 and carr's index <17) tablets obtained were of uniform weight (due to uniform die fill), with acceptable variation as per IP specification. Drug content was found to be in the range of 97-100%. This is within the acceptable limits. Hardness of tablet was found to be 3 to 4 Kg/cm^2 and friability below 1% was indication of good mechanical resistance of the tablets (table no.2)

Among all the formulations, the formulation OD-5 (contain 2% wt/wt crospovidone and 1% croscarmellose sodium) was found to be good. *In-vitro* drug release studies of all formulation were carried out in pH 6.8 phosphate buffer, sample were withdrawn at a interval of time 5 min. Formulation OD-5 has shown complete drug release with 25 minute and emerged as the overall best formulation.

Conclusion

The present study demonstrate that objective of preparing fast disintegrating tablets of ondansetron hydrochloride by direct compression technique is achieved. Formulation OD5 containing 2% crospovidone and 1% croscarmellose sodium gives the maximum drug release in minimum time this may be due to the combination effect of superdisintegrant. These patient compliant tablets that had a good taste and fast disintegration in mouth may be alternative to conventional method.

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