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Research Article

Formulation and evaluation of taste masked orally disintegrating ondansetron hydrochloride tablet

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ABSTRACT

The present study concerns to mask the bitter taste of ondansetron hydrochloride as an orally disintegrating tablet using Indion 294 (ion exchange resin) as a taste masking agent. FT-IR spectrometries were used to investigate the compatibility of drug: resin complex. Six batches (F1, F2, F3, F4, F5, and F6) of orally disintegrating tablets were prepared by wet granulation method with super disintegrant like Crosscarmellose sodium, Crospovidone, Indion 234. The granules were evaluated for pre-compression parameters like angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. And post-compression parameters like weight variation, thickness, hardness, friability, and in-vitro disintegration and in-vitro dissolution tests. The results indicate that orally disintegrating tablets of ondansetron hydrochloride containing Indion 294 and Indion 234 provides good taste and better option for quick disintegration and fast release and improved bioavailability. The drug release rate was enhanced for formulation F6.

Keywords: Orally disintegrating tablet; Ondansetron hydrochloride; ion-exchange resin; super disintegrant.

INTRODUCTION

Ion exchange resins as a carrier have versatile properties for the oral drug delivery systems, and are one of the most effective methods for systemic delivery of drugs by the method of taste masking (Vimladevi M et al., 2001). Taste masking is one of the most essential parameter for fast dissolving tablets for commercial success. Taste masking technologies prevent the interaction among the drug molecule and the oral mucosal surface. It acts with the mechanism of creating a physical barrier around each particle, by which the drug substance is being prevented from going into solution and interacting directly with taste receptors. Commonly the resinate that is drug: resin is formed when an ionizable drug interacts with a suitable ion exchange resin. Generally the very bitter taste drugs lose their taste when converted into a drug resinate as because drug resinate is insoluble it has virtually no taste. By the suitable - selection of the ion exchange resin, the drug resinate can be made sufficiently stable that it does not break down in the mouth so that the patient unable to taste the drug when it is swallowed. However, when the drug resinate comes into contact with the gastrointestinal fluids, usually the acid of the stomach, the complex is broken down quickly and completely. The drug is released from the resinate, directly into solution and then absorbed in the usual way. The resin passes through the GI tract without being absorbed (Jones, P H et al., 1969). Two approaches are commonly utilized to overcome bad taste of the drug (Brahmankar, D. M. and Jaiswal, S.B, 1995). The first includes reduction of drug solubility in saliva, where a balance between reduced solubility and bioavailability must be achieved. Another approach is to alter the ability of the drug to interact with taste receptor. Most of the bitter drugs have the functional groups like nitrogen atom and amine, which is the main cause of their bitter taste. If the nitrogen atom and functional groups are blocked by complex formation the bitterness of the drug reduces drastically. Ion exchange blocks the functional group responsible for causing the bitter taste by forming complex between ion exchange resin and the drug. Further because of the complex, the drug doesn't release in the saliva. Thus the resin reduces the drug and taste buds interaction (Keating J. W, 1961 & Ashwini R,2007). Ondansetron Hydrochloride is chemically (3RS)-9-Methyl-3-[(2-methyl-1H-imidazol-1-yl) methyl]-1, 2, 3, 9-tetrahydro-4H-carbazol-4-oneHydrochloride, which is a 5-HT $_3$ receptor antagonist. It works by inhibiting serotonin receptors in GI tract or chemoreceptor trigger zone(CTZ) (K D. Tripathi, 2006). The present study concerns to mask the bitter taste of ondansetron hydrochloride as an orally disintegrating tablet using Indion 294 (ion exchange resin) as a taste masking agent.

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EXPERIMENTAL

Materials

Ondansetron hydrochloride was obtained as a gift sample from Cadila pharmaceuticals Ltd., Ahmadabad, India. Indion 294 (Resin), Indion 234(super disintegrant 5%) were obtained as a gift sample from Ion Exchange India Ltd., Mumbai. Croscarmellosesodium, Crospovidone, were obtained from JRS Pharma and ISP sales-UK Limited.

Methods

Preparation of drug-Resin complex

Required amount of drug was mixed with different amount of powdered ion- exchange resin i.e. they were mixed at 1:1, 1:2, 1:3, 1:4, 1:5, 1:6 ratio. The taste masked resinate (equivalent to 4mg of ondansetron USP per tablet) was granulated along with diluents using PVP K 30 as a binder. The wet mass was screened through sieve no. 16 and dried at 60°C for 30min. The dried granules were then screened through sieve no. 40 and collected in an air lock polybag (Gangane PS et al, 2009).

Selection of drug-Resin complex ratio

Six batches were prepared containing drug Resin in the ratio of 1:1, 1:2, 1:3, 1:4, 1:5, 1:6, by the wet-granulation method. On the basis of the taste of the granules, ratio 1:4 (Gangane PS et al, 2009) was finalized for further study.

Characterization of solid drug: resin complex

I. Fourier Transform Infra-Red Spectroscopy study (FTIR)

Pure drug, pure resin, and drug- resin complex were analyzed for Fourier Transform Infrared Spectroscopy (FTIR) using KBr disk method. Graphs are shown in Fig no. 1

II. Physical evaluation of drug-Resin granules: Granules were evaluated for angle of repose, bulk density,

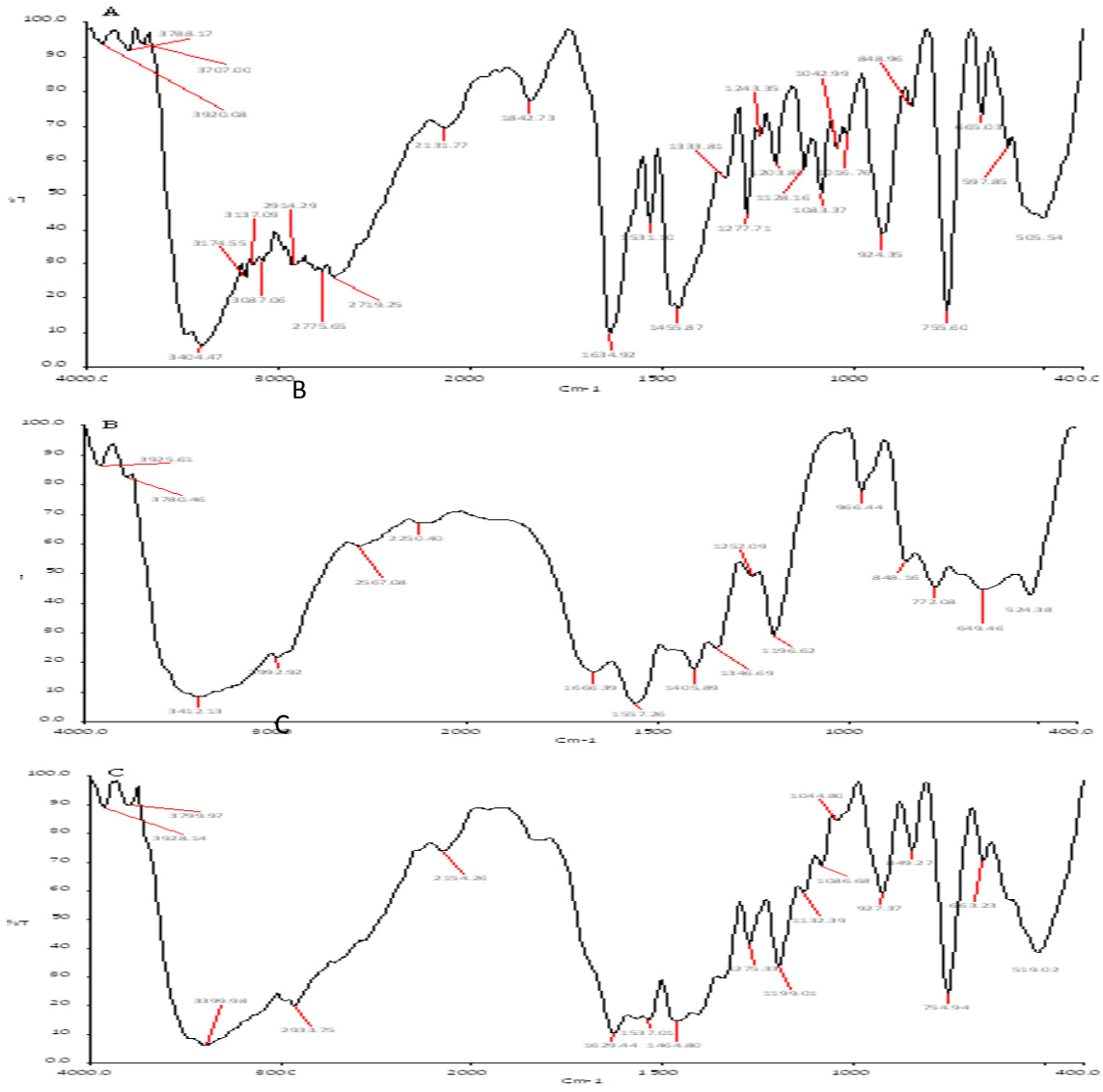

Figure 1: FTIR of drug-resin complex A. FTIR Spectrum of Ondansetron Hcl reference standard, B. FTIR Spectrum of INDION 294, C. FTIR Spectrum of Drug-Resin Complex

Table 1: Formulation table of batch F1-F6

Ingredients (mg/tablet)	F1	F2	F3	F4	F5	F6
DRC (equivalent to Ondansetron Hcl 4mg)	20.0	20.0	20.0	20.0	20.0	20.0
Polyvinyl pyrolidine k-30	0.8	0.8	0.8	0.8	0.8	0.8
Aspartame	8.0	8.0	8.0	8.0	8.0	8.0
Crosscarmellose sodium	10.0	15.0	-	-	-	-
Crospovidone	-	-	10.0	15.0	-	-
Indion 234	-	-	-	-	10.0	15.0
Lactose	100.0	100.0	100.0	100.0	100.0	100.0
Mannitol (spray dried)	147.7	142.7	147.7	142.7	147.7	142.7
Aerosil	1.5	1.5	1.5	1.5	1.5	1.5
Orange flavor	5.0	5.0	5.0	5.0	5.0	5.0
Pepper mint flavor	1.0	1.0	1.0	1.0	1.0	1.0
Magnesium stearate	6.0	6.0	6.0	6.0	6.0	6.0

tapped density, Compressibility Index and Hausner's ratio.

Formulation of taste masked ODT tablet of Ondansetron Hcl 4mg USP

Orally disintegrating tablets of ondansetron hydrochloride: Indion 294 granules were prepared using direct compression method after incorporating different super-disintegrants such as, crosscarmellose sodium, crospovidone and indion 234. Six formulations of ondansetron hydrochloride: Indion 294 granules were prepared and each formulation contained one of the three disintegrants. Finally these granules were compressed on multiple tablet compression machine using 9.5 mm standard concave punches to give tablet weight of 300 mg. Ingredients are shown in table no .1

Evaluation of formulated tablet (Avari, N.G 2004, United State Pharmacopoeia 24/NF 19, 2000)

Weight Variation Test

Twenty tablets were selected randomly form each batch and weighed individually to check for weight variation using Sartorius electronic balance and the test was performed according to the official method.

Thickness

Five 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 randomly selected and hardness of the tablets was determined.

Friability test

The friability of the tablets was determined using electro-lab USP tester. It is expressed in percentage (%). Ten tablets were initially weighed ($W_{Initial}$) and transferred into friabilator. The friabilator was operated at 25rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (W_{Final}). The % friability was then calculated by –

$$\%F = W_{initial} - W_{final} / W_{intial} \times 100$$

Acceptable Limit: Not more than 1%

Content Uniformity

Five tablets were powdered and the blend equivalent to 300 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 test

The disintegration time was measured using a paddle method. The dissolution apparatus USP type III was filled with 500 ml of water maintained at 37°C. The paddle was rotated at 100 revolutions per minute. The tablet was placed inside the sinker, stop watch were started and the time at which it passes completely through the mesh of sinker was taken as the disintegration of the tablet.

Table 2: Evaluation of tablets

Parameters	F1	F2	F3	F4	F5	F6
Hardness (kg/cm^2)	3.52	3.64	3.40	3.42	3.31	3.14
Friability (%)	0.29	0.42	0.61	0.36	0.14	0.17
Content Uniformity (%)	97.2	99.5	98.0	102.0	98.50	99.25
Thickness (mm)	4.72	4.76	4.70	4.38	4.30	4.28
Disintegration time (seconds)	37 econds	34 seconds	32 seconds	35seconds	26 seconds	22 seconds

Table 3: Dissolution of different formulation after 10 minutes

Formulation	Percentage drug release after 10 minutes	Specification as per USP
F1	83.58 ± 2%	Not less than 80% after 10 minutes
F2	85.72 ± 2%	
F3	87.09 ± 2%	
F4	90.29 ± 2%	
F5	94.82 ± 2%	
F6	99.64 ± 2%	

In- vitro dissolution test

The dissolution study was performed for batch F1, F2, F3, F4, F5 and F6 formulation by using USP type III paddle apparatus 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 UV spectrophotometer (UV-I6O1, shimadzu corporation, Kyoto, Japan). Calculate the release of Ondansetron hydrochloride in percentage with respect to the labeled claim by using the following expression.

$$\frac{Au}{As} \times \frac{Ws}{D} \times \frac{500}{L} \times \frac{MW_1}{MW_2} \times P \times 100$$

Where

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

As = Average area of the peak due to Ondansetron hydrochloride in the standard preparation

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

D = dilution factor of the standard preparation

MW_1 and MW_2 = Molecular weight of Ondansetron (293.4) and Ondansetron hydrochloride (365.9)

L = Tablet label claim in mg

P = percentage purity of Ondansetron hydrochloride

Optimization of Formula

From the above formulations the optimized formula from Drug: Resin tablets (F6) was selected, depending upon the several factors such as less disintegrant concentration, less disintegration time and fast dissolution rate**.** Dissolution profile is given in figure No. 2.

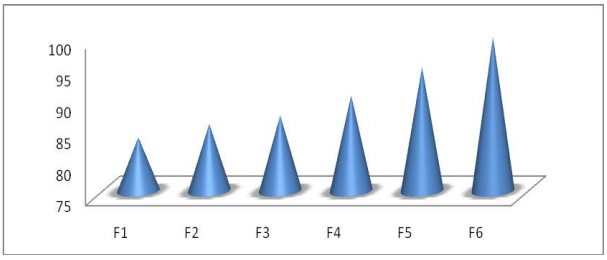

Figure 2: Dissolution release profile for the formulation F1 to F6

RESULTS AND DISCUSSION

Indion 294 was selected for the taste masking of Ondansetron hydrochloride. The taste-masked granules of drug and Indion 294 were prepared by wet granulation method. Drug to resin ratio 1:4 and above shows better results as compared to other ratio. IR studies revealed that there was no interaction between Ondansetron Hcl and excipients used in the preparation of tablet. The granules of all the batches were evaluated for different derived properties viz. angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio, in order to determining the flow characteristics. All the batches show satisfactory flowability, six formulations of drug Indion294 granules (F1-F6) were prepared by varying the concentration of superdisintegrant. Tablets were prepared using wet granulation method. Tablets were obtained of uniform weight due to uniform die fill, with acceptable weight variation as per pharmacopoeial specification. The drug content found in the range of 97.20-102.0 % (acceptable limit) and the tensile strength of the tablet was found 3.14 – 3.52 kg/cm^2. Friability of tablet was found below 1% indicating good mechanical resistance. The disintegration time of all batches was found in the range of 22 - 37 sec. Batch F-6 was selected as optimized batch containing Indion 234 as superdisintegrant in 5 % concentration. It has less disintegration time of 22sec. The dissolution study was carried out and 99.64% of drug release was occurring within 10 min.. The formulation F6 was found to be best as this formulation showed less disintegration time, good hardness, and good content of active ingredient. Out of three superdisintegrant formulation containing Indion 234 (F6) shows best result. It was concluded that fast dissolving tablet of Ondansetron hydrochloride can be successfully prepared by superdisintegrant addition. Taste masking with Indion 294 was also found to be effective.

CONCLUSION

In the present study orally disintegrating tablet of Ondansetron Hcl was prepared by wet granulation technique. Different formulations were made by using three super disintegrants such as Crosscarmellose sodium, Crosspovidone, Indion 234. All the formulations were evaluated for physical characteristics, disintegration, in-vitro dissolution studies. Following conclusion have been made from the present study. On the basis of the taste of the granules, ratio 1:4 was finalized.IR

studies revealed that there was no interaction between Ondansetron Hcl and excipients used in the preparation of tablet. The physical characteristics of the blend of all the formulation were satisfactory. The tablets prepared were found to be within the official limits with respect of weight variation, hardness and friability. The disintegration studies shows that the formulation F6 prepared by using indion-234 disintegrated in 22 seconds. The in-vitro dissolution studies were performed for the F1, F2, F3, F4, F5 and F6 formulations. But dissolution results of F5 and F6 were only came within the limit. Among these two formulations F6 showed the maximum cumulative percentage drug release. Form the above study the formula used for F6 formulation was concluded as an optimized formula due to its least disintegration time and good in-vitro release characteristics. All the physical and chemical characteristics of the Ondansetron Hcl prepared by using optimized formula (F6) were found to be satisfactory.

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