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FORMULATION OF ONDANSETRON ORODISPERSIBLE TABLETS

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ABSTRACT

In order to assist patients having difficulty of swallowing and for better patient compliance orodispersible tablets are prepared. Ondansetron, 5-HT 3 receptor antagonist used as antiemetic is tried for orodispersible tablet formulation in present study. Objective of study undertaken is to mask bitter taste of ondansetron and develop fast orally disintegrating tablets. It is found that judicious selection of proportion of sucralose, polyplasdone XL 10, sodium starch glycolate and cross carmellose sodium along with trusil orange, peppermint and trusil strawberry flavours are suitable for orodispersible tablet of ondansetron.

Keywords: Ondansetron, orodispersible Tablet, Superdisintegrants, Flavoring agents.

INTRODUCTION

New and novel oral drug delivery systems that dissolve or disperse quickly in a few seconds after placement in the mouth without water can alleviate the problem of swallowing tablets [1]. The desired criteria for the Fast dissolving tablet they should have a pleasing mouth feel, leave minimal or no residue in the mouth after oral administration and not require water to swallow, but it should dissolve or disintegrate in the mouth in a matter of seconds [2,3]. Elderly patients may have to consume medicines on a regular basis to maintain their quality of life and they may find difficult to swallow with water [4,5]. Children also develop difficulty to ingest tablet or capsule with water due to their underdeveloped muscular and nervous system [6]. Patients with the problem of swallowing of tablets can be tackled by formulating fast and rapid disintegrating and dissolving in saliva dosage forms for oral administration without administering water [7]. Orodispersible tablets are uncoated tablets placed in the mouth where they disperse rapidly before being swallowed [8]. The drug candidates suitable for such systems include cardiovascular agents, neuroleptics, analgesics, antiemetics, antiallergics, antiemetics and for erectile dysfunction [9]. Ondansetron HCl is a potent antiemetic drug indicated for the treatment and/or prophylaxis of postoperative or chemotherapy- or radiotherapy-induced emesis, and is also used in the early onset of alcoholism [10].

Ondansetron is a drug of choice but possessing bitter taste hence the primary objective is to mask bitter taste by formulating as orally disintegrating tablet by compression method.

MATERIALS

Ondansetron raw material was obtained from Safetab Life Science, Puducherry. Pearlitol, Polyplasdone XL10 (Crosspovidone), Colloidal silicondioxide, talc, magnesium Stearate, Suralose, Sodium starch glycolate, cros carmellose sodium, Trusil orange flavor, peppermint and trusil strawberry flavor were obtained from Safetab Life Science, Puducherry. All other chemicals, solvents and reagents were used of either pharmacopeial or analytical grade.

METHODS

Preparation of oral disintegrating tablet by direct compression method

All the ingredients in Table: 1 was passed through 40 mesh sieve separately. The drug and the excipients are blended for 10 minutes to get a uniform mixture by using Octagonal blender. Then pearlitol, talc, magnesium stearate were added to the blended material and mixed. The powder mix was compressed on Cadmach compression machine by using 7.2 mm standard concave punches. The

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dose of Ondansetron is 8 mg and the formula is used for 1000 tablets [11]. Thus four formulations (Table: 1) F1, F2, F3 and f4 were prepared and studied in this work.

COMPATIBILITY STUDIES

The compatibility of drug and excipients under experimental condition was conducted using FTIR studies. In the present study, the potassium bromide disc (pellets) method was employed.

EVALUATION OF ONDANSETRON ORODISPERSIBLE TABLETS

Pre-compression Parameters

The powder blends of F1, F2, F3 and F4 were evaluated for bulk density, tapped density and flow properties. The bulk density of a powder is the ratio between a given mass of a powder and its bulk volume. A given quantity of the powder is transferred to a measuring cylinder and is tapped using tap density apparatus till a constant volume is obtained. This volume is the bulk volume (v) and it includes the true volume of the powder and void space among the powder particles. Bulk density is determined by Weight of powder/ untapped volume. True density is calculated by using a formula True Density = Weight of the powder / True volume. The loss on drying test is designed to measure the amount of water and volatile matter in a sample when the sample is dried under specified conditions. As the monograph indicates such a specification as not more than 0.50 % at 105 ^{o} c, for 3 hours within the limit.

The prepared tablets F1, F2, F3, and F4 were evaluated for weight variation, hardness, friability, and drug content studies (Table 2). In weight variation test, twenty tablets were selected at random, and average weight was calculated. The individual weight of the tablets was weighed and the weight was compared with an average weight. The Monsanto hardness testing apparatus was used in the determination of the hardness of the tablet. Five tablets were randomly picked and analyzed for hardness. The force of fracture was recorded. The friability of the tablets was determined using Roche's Friabilator. 20 tablets were weighed and charged into the friabilator and subjected to 100 revolutions. The tablets were made free dust weighed. The disintegration time [12] (D.T) of a tablet was determined using disintegration test apparatus per I.P specifications (Figure: 1).

In-vitro Dissolution Study

The dissolution of Ondansetron orodispersible tablets F1, F2, F3 and F4 was performed by using rotating paddle Dissolution Test Apparatus type II USP XXIII. The dissolution medium was 900 ml of 0.1 N hydrochloric acid at 37± 2 ^{o} C.

The paddle was rotated for 10 minutes, aliquots of dissolution medium were withdrawn at 2 minutes interval, the volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium and the amount of drug dissolved was estimated spectrophotometrically (Figure: 2) [13,14].

Stability Testing

The stability studies of F4 tablets were carried out according to international conference on Harmonization (ICH) guidelines. The tablets of the scaleup batch were packed on alu-alu with aluminium foil (thickness of 20 microns) and HDPE containers. Each alu-alu pack contains 10 tablets of F4 and each container contains 30 tablets. Alu-alu packing and container packing was evaluated for 45 days at 25℃/ 60 % RH and 40℃/75% RH for its physical changes and in drug content (Table: 3) [15].

RESULTS AND DISCUSSION

In the present study the IR spectra for drug and its formulation with various polymers & other excipients is taken to establish the physical characterization of drug and its formulation. The IR spectra study indicates that there is no interaction of the drug with polymers and other excipients used. The loss on drying was found to be 0.3 %. The bulk density was found to be 0.57 gm/cm^3 and tapped density was 0.68 gm/cm^3.

Figure 1. D.T in Secs of F1, F2, F3 and F4

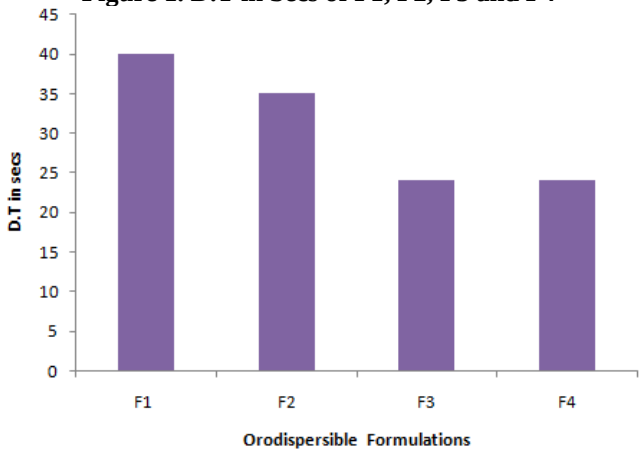

Figure 2. In vitro Release Profile of ndansetron Orodispersible tablets

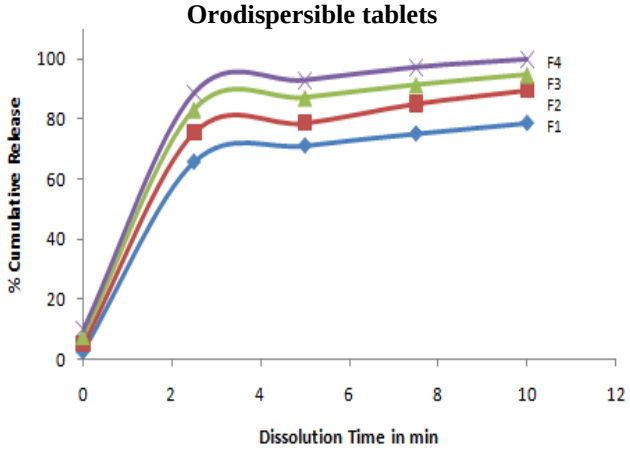

Table 1. Composition of Ondansetron Oral Disintegrating Tablet

S.No	Ingredients	Formulations Kg/1000 Tablets			
		F1	F2	F3	F4
1	Dried granules Ondansetron	0.0081 kg	0.0081 kg	0.0081 kg	0.0081 kg
2	Pearlitol	0.129 kg	0.129 kg	0.129 kg	0.129 kg
3	Colloidal silicon dioxide	0.004 kg	0.004 kg	0.004 kg	0.004 kg
4	Talc	0.004 kg	0.004 kg	0.004 kg	0.004 kg
5	Magnesium stearate	0.004 kg	0.004 kg	0.004 kg	0.004 kg
6	Sucralose	0.0024 kg	0.0096 kg	0.0096 kg	0.0096 kg
7	Polyplasdone XL 10	0.013 kg	0.013 kg	0.013 kg	0.005 kg
8	Sodium starch glycolate	-	0.012 kg	0.014 kg	0.012 kg
9	Cros carmellose sodium	-	-	0.014 kg	0.014 kg
10	Trusil flavor orange	0.746 g	0.746 g	0.746 g	0.746 g
11	Peppermint flavour	0.2 g	0.2 g	0.2 g	0.2 g
12	Sunset yellow lake	0.746 g	0.746 g	0.746 g	0.746 g
13	Trusil Strawberry flavour	0.746 g	0.746 g	0.746 g	0.746 g

Table 2. Physical parameters of orodispersible tablets of Ondansetron

S.No	Batch No	Weight Variation in mg Limits (300 mg ± 2 %)	Friability in % Limits (NMT1.0%)	Hardness in kg/cm^2	Thickness in mm Limits (4.00 ± 0.20 mm)	Drug content
1	F1	298	0.7	2	4.00	3.86
2	F2	300	0.7	2	4.00	3.88
3	F3	300	0.6	1.5	4.20	3.88
4	F4	300	0.6	1.5	4.20	3.90

NMT = Not more than

Table 3. Stability study data of F4 in alu-alu packing

S.No	Storage condition & Period	Appearance	Average Weight In mg	Hardness In Kg/cm^2	Drug Content in mg/tablet	Disintegration In sec	Dissolution In %
1	Initial(control)	Normal	300	1.5	3.90	24	99.72
2	4 th week						
	25^{o}C/60 % RH	Normal	300	1.5	3.90	24	99.72
	40^{o}C/ 75% RH	Normal	300	1.5	3.90	24	99.72
3	8 th week						
	25^{o}C/60 % RH	Normal	300	1.5	3.88	25	98.80
	40^{o}C/ 75% RH	Normal	300	1.5	3.86	25	97.24
4	12 th week						
	25^{o}C/60 % RH	Normal	298	1.5	3.86	26	97.12
	40^{o}C/ 75% RH	Normal	298	1.5	3.80	27	96.54

The values of pre compression parameter were within prescribed limits and indicated good free flowing property. All the post compression parameters were evaluated and present in Table: 2 the results are within IP acceptable limits. In all the formulations, the hardness test indicated good mechanical strength ranges from 1.5 kg/cm^2 to 2 kg/cm^2. The friability range is 0.6 to 0.7 % to be well within the approved range (<1%) indicated that had good mechanical resistance. The weight variation was found in all designed formulations in the range of 298 to 300 mg. All the tablets passed weight variation test as prescribed in I.P 2007. The thickness was almost uniform in all the formulations and values ranged from 4.00 to 4.20 mm.

Rapid disintegration from 24-40 sec was observed in all four (F1-F4) formulations. Based on the disintegration time, formulation F4 is found to be promising and successful having 24 sec D.T. (Figure: 1).

In vitro dissolution studies on the formulations F1, F2, F3, and F4 were carried out in 900 ml of 0.1N hydrochloric acid at 37± 2^{o}C. The percent drug dissolved in 2.5 min (minutes), 5 min, 7.5 min, and 10 min are shown in Figure: 2. this data reveals that overall, the formulations F1 to F4 show faster drug release (Figure: 2).According to Figure: 2, F4 shows 78.62 % in 2.5 min, 89.61 % in 5 min, 94.67 % in 7.5 min and 99.72 % in 10 minutes dissolution profile. According to Figure 1, D.T of

F4 is 24 secs less than half minute. Physical parameters of F4 from Table: 2 show that F4 is robust, of suitable shape and size and passing all official requirements for a suitable orodispersible tablet. Trusil flavor orange, peppermint flavor, trusil strawberry flavor along with sweetening agent, pearlitol are able to mask the bitter of Ondansetron hydrochloride and F4 is observed for its taste, flavor and mouthfeel. Thus F4 is most promising and suitable orodispersible tablet in present study. F4 is further subjected to stability study in alu-alu packing and container packing. The results of alu-alu packing is depicted in Table: 3. The results of container packing is almost the same of alu-alu packing except in dissolution study which is only showing a little variation at second decimal place. These stability studies are as per ICH guidelines F4 is stable in all aspects and there is no change. Thus F4 is a successful orodispersible tablet of Ondansetron.

CONCLUSION

The present study concludes that pearlitol as sweetening agent along with trusil flavour orange peppermint flavor and trusil strawberry flavor are able to mask the taste of Ondansetron hydrochloride. Superdisintegrants sucralose, polyplasdone XL10, sodium starch glycolate and cross carmellose sodium in judicious combination are suitable for orodispersible tablet of Ondansetron hydrochloride. Direct compression method employed may be able to reduce the manufacturing cost of tablet.

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