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Formulation and Evaluation of Fast Disintegrating Orodispersible Tablets of Ondansetron Hydrochloride

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Abstract:
The demand for mouth dissolving tablets has been growing, during the last decade especially for geriatric and pediatric patients because of swallowing difficulties. The purpose of this research was to mask the intensely bitter taste of Ondansetron HCl and to formulate a orodispersible of the taste-masked drug. Taste masking was done by complexing Ondansetron HCl with Kyron T-134 in different ratios. Drug- resin complex were optimized by considering parameters such as optimization of resin concentration, optimization of swelling time, optimization of stirring time, optimization of pH and optimization of temperature on maximum drug loading. The effects of variables were observed in preparation of drug resin complex (resinate), the other variables were kept constant. The resinate was evaluated for taste masking, characterized by and infra red spectrometer. In vitro drug release study of taste masked tablet showed that more than 90 % of the drug release within 20 minutes. Thus, results conclusively demonstrated successful masking of taste and rapid disintegration of the formulated tablets in the oral cavity.
Keywords: *Ondansetron hydrochloride, Kyron T-134, resinate, Orodispersible.*

INTRODUCTION:

The concept of fast disintegrating drug delivery system emerged from the desire to provide patients with conventional means of taking their medication. More than 50% pharmaceutical products are orally administered for several reasons and undesirable taste is one of the important formulation problems in oral dosage form. Taste of a pharmaceutical product is an important parameter for governing compliance. Thus taste masking of oral pharmaceuticals has become an important tool to improve patient compliance and the quality of treatment especially in pediatrics and geriatrics.

Ondansetron Hcl in most commonly used as anti emetic. It is a very bitter drug and slightly soluble in water. The main objective of the present work is to formulate taste masked dispersible tablets of Ondansetron HCl. The dispersible tablets can be swallowed without water in the form of dispersion. They increase the patient compliance as well as provide quicker onset of action.

Such a tablet may be swallowed in the form of dispersion, as it is expected to disintegrate quickly when in contact with saliva. When it comes in contact with acidic environment of the stomach, the complex will be broken down quickly and releasing the drug, which may then be absorbed in usual way.

ODTs made by direct compression are robust and can be easily packaged and handled. However, *in vivo* disintegration time is longer (30-60 seconds) and good taste and mouthfeel are harder to achieve. For unpleasant tasting drugs, current direct compression methods require a separate taste-masking process for the active ingredient. Processes are used for taste-masking include ion exchange resin, wet granulation, roller compaction, spray-drying, and coating. Taste-coating may be based upon time or pH dependent dissolution of the coating polymer.

MATERIALS AND METHODS:

Ondansetron Hydrochloride was obtained as a gift sample from Akums Drug Pharmaceutical Ltd, Utrakhand. Resin Kyron T-134 was gifted by Corel pharmaceuticals Ltd. Other chemicals used were of analytical grade.

Masking the bitter taste of API*:* As an API is a highly bitter drug, it has to be taste masked in order to formulate as an orally disintegrating tablets. So as to mask/reduce the bitter taste of API by using Ion exchange resin process. In this process complexed with weak cation exchange resins like Kyron-$t_{134,}$ Drug molecules attacked to the resin are released by exchanging with approximately charge ions, followed by diffusion of free drug molecules out of resin.

Compatibility studies of drug and excipients*:* Compatibility study of Ondansetron hydrochloride ODT was determined by the using FTIR spectroscopy. And there is as such no interaction and the pure drug is not altered functionally with superdisintegrant and other excipients.

Formulation of oral disintegrating tablet of taste masked API: Direct compression is ideal process for powders which can be mixed well and do not require further granulation steps. Direct compression is the simplest and least expensive tableting process. Direct compression uses conventional blending and tableting equipment as well as commonly available excipients. ODTs made by direct compression are robust and can be easily packaged and handled.

Characterization and evaluation of the tablet blend: Physical properties such as bulk density, tapped density, compressibility index, and the angle of repose of blend were determined.

RESULTS AND DISCUSSION:

Preparation of resinate: The resinate was prepared by batch process, the weighed amount of resin was stirred for 10-15 minutes for swelling of resin then drug was added to it. In which Drug molecules attacked to the resin are released by exchanging with approximately charge ions, followed by diffusion of free drug molecules out of resin. The method described for the preparation of drug resin complex mentioned under experimental work was adopted.

Selection of Drug Resin ratio*:* For the selection of the proper drug resin ratio, the ratio of the drug resin was varied, keeping concentration of drug constant. The pH of the solution was maintained at 4. The result shows that drug resin in the ratio of 1:3 has better drug release and loading as compared to the other.

Evaluation test for optimized formulation: The Ondansetron ODT tablet was evaluated in which the hardness was found to be 2.9 $\pm$ 0.22 to 3.2 $\pm$ 0.32 kg/cm^2. And friability was found to be below 1% indicating good mechanical strength. The thickness of the tablets was found to be 2.77± 0.02 to 2.79± 0.03. All the tablets passed weight variation test, as percentage weight variation was within the pharmacopoeial limits i.e. ±10%. The drug content was found to be 99.21 to 100.13 %, indicating uniform distribution of drug in the tablets. The in-vitro dissolution time for all the formulation varied from 15-25.5 sec. the rapid disintegration was seen in the formulation.

Determination of swelling index: The optimized formulation (F6) of Ondansetron hydrochloride ODT showed very high percentage of swelling index than other formulations F1, F2, F3, F4, F5.

Table no 1: Evaluation of prepared oral dispersible tablet

Formulation	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Wetting time (sec)	Water absorption Ratio	DT (Sec)	Content uniformity (%)
F1	51±1.32	2.9±0.36	2.76±0.01	0.20±0.23	39±1.22	133±1.32	57±1.26	99.89±2.15
F2	50±1.12	3.0±0.52	2.79±0.02	0.24±0.13	72±1.92	109±1.39	96±1.32	100.19±2.19
F3	49±1.75	2.9±0.62	2.78±0.02	0.29±0.12	67±1.87	112±1.45	85±1.41	100.52±1.12
F4	48±1.13	3.0±0.65	2.77±0.02	0.30±0.21	59±1.34	120±1.69	78±1.25	99.49±0.96
F5	49±1.18	3.2±0.32	2.79±0.04	0.26±0.13	41±1.20	129±1.58	69±1.36	99.21±0.24
F6	51±1.12	3.2±0.21	2.77±0.06	0.22±0.14	82±1.18	102±1.49	101±1.28	99.54±0.89

Table no 2: Swelling index of all Formulations

S.No	Formulations	Swelling index (%v/v)
1	F1	34±2.3
2	F2	41±1.3
3	F3	52±1.9
4	F4	67±1.6
5	F5	74±1.3
6	F6	89±2.1

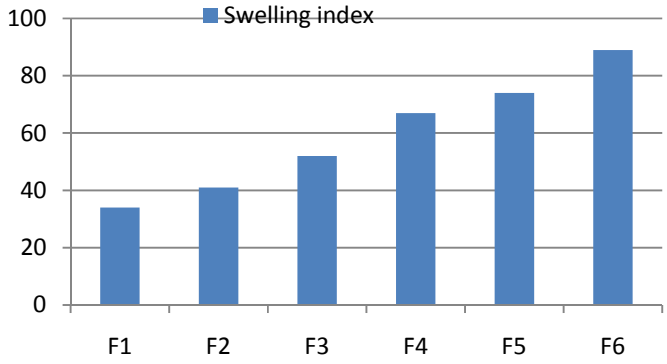

Fig no 1: Graph of swelling index of all formulations

Table no 3: Cumulative percentage drug release of ODT

S. No.	Time (min)	CUMULATIVE % DRUG RELEASE					
		F1	F2	F3	F4	F5	F6
1	0	0	0	0	0	0	0
2	5	81.12±2.41	81.29±0.27	89.61±0.23	89.94±0.98	90.86±0.69	91.12±1.31
3	10	87.51±2.28	89.56±0.98	92.45±0.49	92.55±1.32	93.25±0.87	92.82±1.26
4	15	90.89±2.22	91.04±0.92	93.28±0.78	93.98±1.29	94.13±1.23	93.49±1.20
5	20	91.63±0.98	93.59±0.27	96.32±0.84	96.13±1.25	94.37±1.41	94.79±1.12
6	25	93.53±0.42	95.79±1.23	97.7±0.93	97.86±0.97	98.22±1.29	98.99±0.98

Table no 4: Accelerated stability studies for optimized formulation of ODT

S.No	Parameters	Time in month	
		0 (Initial)	One month
1	Hardness(kg/cm^2)	2.9±0.36	2.9±0.10
2	Disintegration time (sec)	47±1.26	45±0.673
3	Drug content(%)	100.19±2.9	100.12±0.83
4	In-vitro drug release (%)	98.99±0.98	99.62±0.32

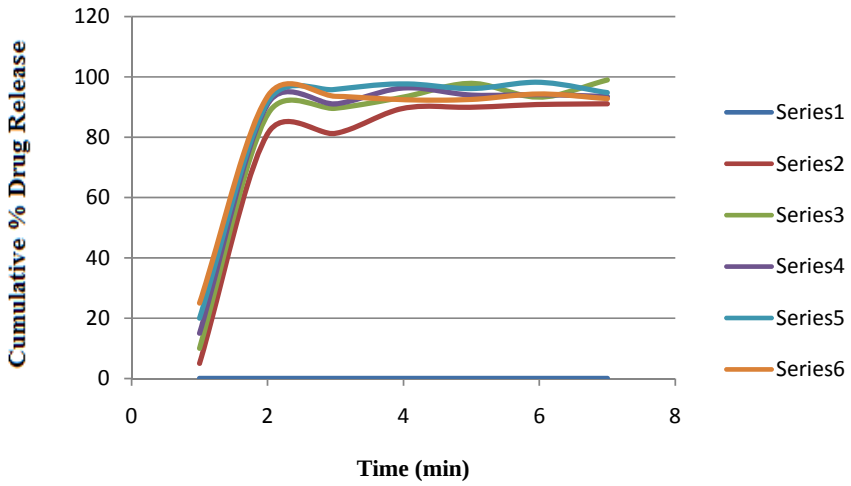

Fig no 2: Cumulative percentage drug release of ODT

Dissolution study: The dissolution of Ondansetron Hcl tablets (4 mg Ondansetron Hcl) was carried out in paddle type dissolution apparatus. The dissolution medium was 900ml of Gastric Simulated Fluid (without enzyme) pH 1.2 maintained at 370C ± 10 C. The paddle was rotated at 50 rpm for 20 min. The sample of 10ml was withdrawn after every 5 min. and its absorbance was measured at 310nm. Dissolution study of tablets revealed that more than 90% of drug released within 15 min.

Accelerated stability studies: The stability of this optimized formulation was known by performing stability studies for one month at accelerated conditions of 40±2^{0}C/75±2% RH on optimized formulation. The formulation was found to be stable, with insignificant change in the hardness, disintegration time, and drug content and in-vitro drug release**.**

CONCLUSION:

The studies of various formulation trials (F1-F6) were carried out with different concentrations of disintegrants, lubricants. From the various formulations it was concluded that the formulation batch of F6 was finalized as the optimized formula. Which (F6) showed satisfactory results with various physicochemical evaluation parameters like Disintegration time, Dissolution profile, and swelling index. And subjected to accelerated stability studies the Oral disintegrating tablets were found to be stable.

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