

# Formulation and Evaluation of orally disintegrating tablets of Ondansetron Hydrochloride using Natural Superdisintegrants

Nitin Bansal\*, Govind Sharma,

College of Pharmacy, IPS Academy, Indore (M. P.), India.

\*Corres.author: [nitinbansal.mpharm@gmail.com](mailto:nitinbansal.mpharm@gmail.com)

Contact No: +91-9013277793

**Abstract: Purpose:** To develop orally disintegrating tablets of ondansetron HCl using natural Superdisintegrants.

**Method:** Tablets containing the drug were prepared by dry granulation method using different concentrations of superdisintegrants such as modified gum karaya, modified natural agar, crosscarmellose sodium and sodium starch glycolate. The formulations were evaluated for weight variation, hardness, friability, drug content, wetting time, in vitro disintegration time and in vitro dissolution study.

**Results:** The results showed that modified gum karaya and modified natural agar produce rapid disintegration of tablets. The optimized formulation showed acceptable physical characteristics. The optimized batch produced complete drug release within 6 minutes. The incorporation of clove oil provided additional properties such as symptomatic relief from nausea and vomiting, good mouth feel and taste masking. Kinetic analysis showed that drug release from optimized formulation was adequately described by first order release kinetics.

**Conclusion:** Modified gum karaya and modified natural agar can be used as an alternative superdisintegrants to commonly available synthetic and semisynthetic superdisintegrants due to their low cost, biocompatibility as well as easily availability.

**Keywords:** Ondansetron hydrochloride, orally disintegrating tablets, karaya gum.

## INTRODUCTION

In pharmaceutical sciences, disintegration usually means the process by which a solid dosage form breaks up when it comes in contact with aqueous medium absorption and thus promotes rapid release of drug for faster absorption<sup>[1]</sup>. A rapid disintegration process is the prerequisite for a good bioavailability<sup>[2]</sup>. Polysaccharides<sup>[3]</sup> such as karaya gum (KG) derived from *Sterculia urens* (Family sterculiaceae) and Natural agar (NA) derived from red algae *Gelidium amansii* have been investigated for its potential as a tablet disintegrant by heating modification. KG has been reported as an effective bulk laxative and adhesive agent for dental fixtures while NA has been used in

pharmaceuticals as a sustained-release agent in gels, beads, microspheres, and tablets. Modified polysaccharides<sup>[4,5]</sup> has been evaluated for its disintegrant properties. Water absorbing properties and swelling properties of gum have also been studied. Modified agar and karaya gum is a cheap, biodegradable and directly compressible polysaccharide.

In cancer chemotherapy<sup>[6,7]</sup>, drug induced nausea and vomiting may occur so regularly that anticipatory vomiting occurs when patients return for treatment before the chemotherapeutic agent is given. If not controlled, the discomfort associate with drug induced emesis may cause a patient to refuse further chemotherapy. In this condition ondansetron

hydrochloride is a drug of choice. Orally disintegrating tablets<sup>[8]</sup> provides immediate action, convenient dosing and improves patient compliance. Clove oil<sup>[9]</sup> provide symptomatic relief from nausea and vomiting, good mouth feel and freshness feeling as well as due to its mild local anesthetic effect it suppresses slight bitter after taste of drug.

## EXPERIMENTAL WORK

### Materials

Ondansetron hydrochloride was procured from Schon pharmaceuticals Ltd. Indore. Gum karaya was obtained as gift sample from Nutriroma, Hyderabad. Sodium starch glycollate was obtained as gift sample from DMV-Fonterra excipients B.V. Natural agar, Crosscarmellose sodium and Mannitol were purchased from Loba chemicals, Mumbai.

### Modification of Polysaccharides<sup>[10]</sup>

Modification of Polysaccharides (karaya gum and natural agar) was done by suspending 5gm of Polysaccharides in 100 ml of distilled water. The suspension is stirred at 500 rpm using magnetic stirrer for 24 hours. Obtained swollen mass is dried at 40°C for 72 hours. Dried product is collected and crushed in

pestle mortar to obtain coarse, non-free flowing particles of modified Polysaccharides having optimum water absorbing and swelling properties.

### Drug-Excipients Interaction Studies<sup>[11]</sup>

Drug-Excipients Interaction (1:5) study was carried out using thin layer chromatography at 55°C for 3 week. Study of effect of clove oil on  $\lambda_{max}$  (maximum wavelength) of drug was carried out on UV spectrophotometer.

### Preparation of Ondansetron orally disintegrating tablets

Orally disintegrating tablets were prepared by dry granulation technique. For it all excipients were weighed as per mentioned quantity individually and transferred into mortar pestle one by one for proper mixing (Table 1). Ondansetron HCl was added to the mixture and mixed well. Required quantity of clove oil solution in ethanol was properly mixed. The prepared mixture was dried at room temperature and passed through sieve. Screened powder was collected and evaluated for pre compression parameters. Prepared granules were transferred to compression process using hand operated single punch machine to formulate tablets.

**Table 1: Composition of prepared batches**

Tablet Ingredients (mg)*	A1	A2	A3	A4	F1	F2	F3	F4	S1	S2	S3	S4	C1	C2	C3	C4
Ondansetron HCl	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Modified Karaya Gum#	2.5	5	7.5	10	-	-	-	-	-	-	-	-	-	-	-	-
Modified Natural Agar#	-	-	-	-	2.5	5	7.5	10	-	-	-	-	-	-	-	-
Sodium Starch Glycollate	-	-	-	-	-	-	-	-	2.5	5	7.5	10	-	-	-	-
Croscarmellos e Sodium	-	-	-	-	-	-	-	-	-	-	-	-	2.5	5	7.5	10
D-Mannitol	87.5	85	82.5	80	87.5	85	82.5	80	87.5	85	82.5	80	87.5	85	82.5	80
Total weight(mg)	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100

\*Each formulation contain sufficient amount of 0.01% solution of clove oil in ethanol

#Heat modification of KG and NA produces Modified KG and Modified NA with disintegrant properties.

## Evaluation of Tablets

### Physical Characterization<sup>[12]</sup>

The fabricated tablets were characterized for weight variation (n=20), hardness (n=6, Monsanto hardness tester), and % friability (n=20, Roche friabilator, Electrolab, Mumbai, India).

### Wetting Time

A piece of paper folded twice was placed in Petri dish having internal diameter of 5.5 cm containing 6 ml of purified water. A tablet was placed on the paper and the time required for complete wetting was measured. The time required for complete wetting of tablet was noted as wetting time.

### In-vitro Disintegration Time<sup>[13]</sup>

The *in-vitro* disintegration time was determined by placing one tablet in basket of dissolution apparatus type I (as per USP) and hold in 200 ml of distilled water in a 250 ml glass beaker. The time required for complete disintegration of the tablet with no particulate mass remaining in the basket is measured in seconds.

### Assay of tablets

Twenty tablets from each batch were weighed and powdered. Powder equivalent to 10 mg of Ondansetron hydrochloride was accurately weighed

and transferred into a 100 ml volumetric flask and dissolved in a suitable quantity of 0.1 N HCl. The prepared solution was diluted up to 100 ml with 0.1 N HCl and sonicated for 60 min. 1.0 ml of the resulting solution was diluted to 10 ml with 0.1 N HCl to get a concentration in the range of 10 µg/ml. A portion of the sample was filtered through 0.45 µm membrane filter and analyzed by Shimadzu UV-1601 UV/Vis spectrophotometer at 310 nm.

### Dissolution studies<sup>[14]</sup>

Release of the prepared tablets was determined up to 10 min using U.S.P. XXIV (type II) dissolution rate test apparatus. 900 ml of 0.1 N HCl was used as dissolution medium. The paddle was adjusted at 50 rpm and the temperature of  $37 \pm 0.5^\circ\text{C}$  was maintained throughout the experiment. Samples of 10 ml were withdrawn at known time intervals and were replaced with same volume of fresh dissolution media after each withdrawal. The samples were analyzed for drug contents by measuring absorbance using UV 1601 spectrophotometer.

### Stability study<sup>[15,16]</sup>

Formulations were subjected to stability study according to ICH guidelines at  $40^\circ\text{C}/75\% \text{ RH}$  over a 45 days period.

**Table 2: Evaluation of prepared batches**

Batch	Hardness	Friability*	DT <sup>a</sup>	WT <sup>b</sup>
A1	3	0.22 ±0.02	22 ±2	25 ±2
A2	3	0.35 ±0.01	17 ±1	22 ±3
A3	2-3	0.45 ±0.03	14±1	19 ±2
A4	2	0.64 ±0.02	11 ±2	15 ±3
F1	3	0.39 ±0.02	44 ±2	52 ±3
F2	2-3	0.52 ±0.01	39 ±3	46 ±4
F3	2-3	0.65 ±0.03	34 ±2	42 ±2
F4	2	0.80 ±0.02	30 ±2	36 ±2
S1	3-4	0.50 ±0.02	60 ±3	73 ±2
S2	3	0.58 ±0.01	52 ±2	62 ±3
S3	2-3	0.65 ±0.03	44 ±3	50 ±2
S4	2	0.72 ±0.02	35 ±4	42 ±3
C1	3-4	0.48 ±0.02	72 ±3	75 ±2
C2	3	0.68 ±0.01	54 ±2	60 ±3
C3	2-3	0.75 ±0.03	42 ±3	46 ±2
C4	2	0.84 ±0.02	28 ±4	36 ±3

\* Friability ( $\pm$  SD); <sup>a</sup>Disintegration Time; <sup>b</sup>Wetting Time.

Table 3: Kinetic Release Data of Different Model for Optimized Formulation (P3)

Model	R <sup>2</sup>
Zero Order	0.9530
First Order	0.9910

Analysis of drug release kinetics<sup>[17]</sup>

The release data were analyzed with the following release models: zero order (Eq. 1) and first order (Eq. 2).

$Q_t = k_0 t$  ..... (1)

$\ln Q_t = \ln Q_0 - k_1 t$  .....(2)

Where  $Q_t$  is the amount of drug released in time  $t$ ,  $Q_0$  is the initial amount of drug in the tablet and  $K$  is a constant. The drug release data obtained were subjected to the above drug release models in order to establish their release mechanism and kinetics. Criteria for selecting the most appropriate model were based on regression coefficient  $R^2$  value. Regression coefficient  $R^2$  value nearer to 1 indicated the model fitting of the release mechanism.

RESULTS & DISCUSSION

Results

Table 2 indicates the results hardness, friability, disintegration time and wetting time study performed on the tablet formulations. The data show that hardness ranged from 2.0 to 4.0 while friability ranged from

0.22 to 0.84 %. The drug content in all the batches was in the range of 98 to 102% (i.e., a variation of  $\pm 2\%$ ).

ODT's prepared using natural polysaccharides showed good disintegration time as well as in vitro release. Drug-excipient interaction study showed no significant effect of clove oil on absorbance of ondansetron. Formulations A4 produce disintegration time of 11 seconds and released complete drug within 6 minutes. In vitro release of different formulations was comparable with marketed formulation. Stability study showed that formulations were stable over a period of time. The drug content of all the formulations was found to be between 98 - 102% which was within the acceptable limits as per USP XXVII. The *in vitro* dissolution profile (Fig.1) indicated faster and maximum drug release from formulation A 4. The results of the analysis of drug release kinetics for optimized formulation A 4 based on various models are shown in Table 3.  $R^2$  value nearest to 1 was obtained with First order equation with value of 0.9910.

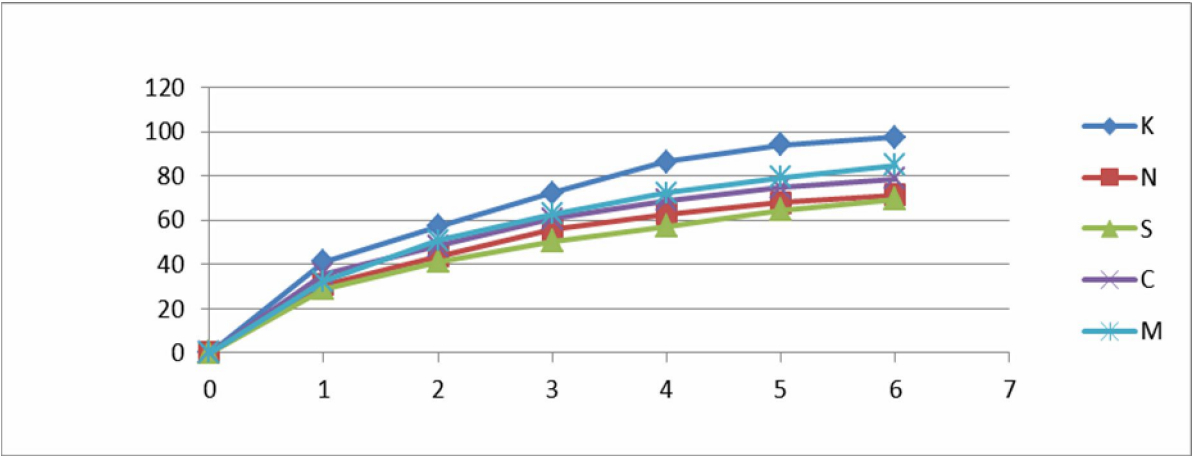


Fig. 1 Percent drug release of various formulations containing different superdisintegrants  
#K=modified karaya gum (A4), N= modified natural agar (F4), S= sodium starch glycollate (S4), C= crosscarmellose sodium (C4), M= marketed tablet

## DISCUSSION

Tablets were prepared using different natural and semisynthetic superdisintegrants, directly compressible diluent, mannitol and a Flavoring agent, clove oil. Additions of clove oil provide symptomatic relief from nausea and vomiting, good mouth feel and freshness feeling as well as due to its mild local anesthetic effect it suppresses slight bitter after taste of drug.

Modification of hydrophilic polysaccharides leads to three-dimensional swelling to an equilibrium value upon interaction with aqueous solution which further leads to entrapment of a significant portion of water within their structure. Drying at this stage leads to evaporation of water leaving behind a porous structure. This structural modification does not allow the formation of gelatinous mass of the modified polysaccharides in water. However, the individual particles shall facilitate water uptake due to the porous structure, undergo independent swelling thus facilitating the process of faster disintegration in tablets containing natural polysaccharides.

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## CONCLUSION

It can be concluded that sequentially controlled wetting and drying modifications of gum karaya and natural agar leads to formation of modified form having superdisintegrant property. Orally disintegrating tablets of Ondansetron HCl can be successfully formulated by using modified polysaccharides as alternative superdisintegrants. Clove oil provides symptomatic relief from nausea, mouth freshness as well as taste masking due to local anesthetic action.

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