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FORMULATION AND EVALUATION OF DOLASETRON MESYLATE MUCOADHESIVE TABLET BY USING MORINGA GUM AND XANTHAN GUM AS POLYMERS

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ABSTRACT

Dolasetron mesylate, a derivative of carbazole, is a selective and competitive antagonist of serotonin 5-HT3 receptors. 5-HT3 receptors are present in the central and peripheral nervous system and are associated with various physiological and pathological processes mediated by serotonin. 5-HT3 receptor antagonists may be effective in mitigating the abuse of a variety of psychotropic substances, such as alcohol and cocaine. Dolasetron Mesylate blocks the actions of chemicals in the body which can cause nausea and vomiting. Dolasetron Mesylate is used to prevent nausea and vomiting which can be caused by surgery or drugs to treat cancer (chemotherapy or radiation). Dolasetron Mesylate is not indicated for the prevention of nausea or vomiting caused by factors other than cancer treatment or surgery. Aim of the present work is to formulate and Evaluate Dolasetron mesylate mucoadhesive tablets by using Moringa gum and Xanthan gum as a polymer. Moringa gum was used as thickening agent and Xanthan gum was used as polymers. The tablets were formulated by direct compression method and were evaluated for various pre-compression & post-compression parameters, such as hardness, thickness, friability, weight variation, drug content uniformity studies, swelling index studies, dissolution study, in-vitro dissolution studies.

Key words: -Dolasetron mesylate, mucoadhesive tablets, moringa gum, xanthan gum

INTRODUCTION

Oral mucoadhesive tablets belong to modern dosage forms, which allow controlled drug release after buccal application. They are used for the treatment of oral cavity disorders or for systemic administration of drugs with high

first-pass effect or drugs instable in gastrointestinal tract [1]. Other desired characteristics of a mucoadhesive dosage form include high drug loading capacity, controlled drug release (preferably unidirectional release), good mucoadhesive properties, smooth surface, tastelessness, and convenient application [2]. Mucoadhesive drug delivery systems interact with the mucus layer covering the mucosal epithelial surface, and mucin molecules and increase the residence time of the dosage form at the site of absorption. The drugs which have local action or those which have maximum absorption in gastrointestinal tract (GIT) require increased duration of stay in GIT. Thus, mucoadhesive dosage forms are advantageous in increasing the drug plasma concentrations and also therapeutic activity. In this regard, this review covers the areas of mechanisms and theories of mucoadhesion, factors influencing the mucoadhesive devices and also various mucoadhesive dosage forms [3].

Advantages of Mucoadhesive Drug Delivery Systems:

Drugs administration via oral mucosa offers several advantages

- Ease of administration.
- Stopping therapy is simple.
- Allows localization of the drug in the oral cavity for an extended period of time.
- Can be administered to unconscious patients.
- Offers an excellent route for systemic administration of drugs with a high first pass metabolism, thus offering greater bioavailability.
- A significant dose reduction can be achieved by reducing the dose related side effects.
- Drugs that show little oral bioavailability can be easily administered.
- Offers a passive drug absorption system and requires no activation.
- The presence of saliva guarantees a relatively large amount of water for the dissolution of the drug, unlike the rectal and transdermal ways.
- Systemic absorption is rapid.
- This pathway offers an alternative for the administration of various hormones, narcotic analgesics, steroids, enzymes, cardiovascular agents, etc.
- The oral mucosa is highly perfused with the blood vessels and offers greater permeability than the skin.

Mucoadhesive Drug Delivery [4]

The oral cavity is innerly lined with a stratified squamous epithelium. The nonkeratinized epithelium occupies about 60% of the total oral cavity, including the, lingual and sublingual mucosa, and is interesting for the systemic release of drugs. Although it is not keratinized, the oral mucosa contains intercellular lipids which are responsible for its

physical barrier properties, resulting in low permeability for larger drugs. Especially for peptides and proteins. The transfer of peptides with molecular weights greater than 500-1000 Da through the Mucoadhesive mucosa would require the use of an absorption enhancer. Another limitation in the administration of drugs is the activity of the mucous enzyme, in particular of the proteases [5]. The reduced retention of the dosage form on the Mucoadhesive surface due to the constant rinsing with saliva can be overcome by using bioadhesive formulations. The influence of food intake and chewing on the residence time of mucoadhesive formulations is not yet clear. Thiolated polymers can be used simultaneously as a bioadhesive carrier and protease inhibitor. drug delivery using bioadhesive dosage forms offers a new route of drug delivery. This pathway has been used successfully for the systemic delivery of various drug candidates. administration of the drug can prevent problems such as first pass metabolism and degradation of the drug in the hostile gastrointestinal environment [6]. The activity of Lower saliva enzyme, formulation easy to removable, patient acceptance is better as well as compliance is other important meritorious aspects of adhesive systems. In addition, the administration of medications offers an easy and safe method for the use of drugs, since the absorption of the drugs can be quickly stopped in case of toxicity by removing the dosage form from the oral cavity. It is an alternative way to administer drugs to patients who cannot be administered orally. Therefore, adhesive mucosa dosage forms for oral administration are recommended, including adhesive tablets, adhesive gels and adhesive patches. Bioadhesive polymers not only cause adhesion effects, they can also control the release rate of the drug. From a technological point of view, an ideal oral dosage form should have three properties [7].

They should:

- keep the position in the mouth for a few hours;
- the drug is released in a controlled manner.

As for the first requirement, it is necessary to establish strong adhesive contact with the mucosa using mucoadhesive polymers as excipients. If the mucoadhesive excipients can control the release of the drug, the second requirement can also be met. Preparing a system that has uniform adhesion and a waterproof backing layer can achieve the third goal.

METHOD AND TECHNIQUE [8]

1.Preformulation studies:

The formulation study is an investigation of the physical and chemical properties of a single pharmacological substance when combined with excipients. It is the first step in the rational development of dosage forms.

Preformulation begins when a recently synthesized drug shows sufficient pharmacological responses in animal models to justify human evaluation. Therefore, these studies should focus on the Physico-chemical properties of the

new compound which could affect the drug's performance and the development of an effective dosage form. A thorough understanding of these properties can ultimately provide a rationale for the design of the formulation or support the need for molecular changes.

Physical Characterization of Drug Sample[9]

The drug obtained from IPCA Lab as a gift sample was physically characterized according to the following methods:

Description

The sample of Dolasetron mesylate was subjected to the following tests for its characterization:

a) Nature of the drug sample

The drug sample was observed visually and viewed under the Compound microscope 10x for the determination of its nature.

b) Solubility studies

Solubility is an important parameter for preformulation studies because it affects the dissolution of the drug. The bioavailability of the drug is directly influenced by the dissolution and absorption of the drug orally; the size of the particles, the shape and the surface area can influence the dissolution characteristics of the drug, therefore the solubility of the drug during the preformulation.

c) Method

100 mg of the drug was added to 100 ml of phosphate buffer solution (PBS) pH 6.8 and stirred for 24 hours until an excess of undissolved drug was present and stored at 20 ° C. The undissolved drug was filtered through the Whatman filter paper from the drug solution, an aliquot 1 ml and subsequently diluted and therefore the drug was quantified by spectrophotometry. An average of 3 of these readings was calculated[10].

d) Melting point of the drug sample

The melting point is one of the important methods of identifying the drug sample. The melting point of the given drug sample was performed using a capillary method. A small amount of pure drug was placed in a Thiel tube and the sealed Thiel tube at one end was suspended in a liquid paraffin bath. The oil was heated and the temperature at which the drug simply melted and the melting point of the drug was observed [11].

2.Identification tests

1.Preparation of Standard Calibration Curve of Dolasetron mesylate.

Preparation of the stock solution: 100 mg of Dolasetron mesylate were transferred to the 100 ml volumetric flask. Then about 50 ml of pH 6.8 phosphate buffer solution (PBS) were added and the resulting solution was sonicated for 5 minutes. In addition, the required amount of PBS pH 6.8 was used to adjust the volume of the solution to 100 ml and the resulting solution obtained was 1000 µg / ml. 1 ml of this solution was pipetted and further diluted with pH 6.8 phosphate buffer solution (PBS) until a 10 µg / ml solution was obtained [12].

2.UV scanning of drug.

10 µg/mL solution of Dolasetron mesylate was prepared in phosphate buffer solution (PBS) pH 6.8 and scanned for maximum absorbance (λ_{max}) in UV Double beam spectrophotometer between range 200 to 400 nm, against PBS 6.8 pH as blank. The λ_{max} was determined in triplicate [13].

1. Preparation of serial working solution

From the stock solution 0 ml, 0.5 ml, 1 ml, 2 ml, 4 ml, 6 ml, 8 ml, 10 ml, 12 ml, 15 ml, 20 ml and 25 ml were transferred to the 10 ml volumetric flask and the volume The final was carried out at 10 ml with PBS pH 6.8 to obtain a concentration of 2 to 25 µg / ml respectively. Finally, the absorbances of the prepared solutions were measured against the blank (PBS pH 6.8) at 310 nm using a visible UV spectrophotometer and the calibration curve was plotted. Similarly, a further dilution was performed to obtain from 0.5 µg / mL to 25 µg / mL to understand the beer limit [14].

2. Preparation of Phosphate Buffer pH 6.8

Accurately weighed quantities of 28.80 g of Disodium Hydrogen Phosphate and 11.45 g of Potassium Dihydrogen Phosphate were dissolved in 900 mL of distilled water and then pH was adjusted to 6.8 with sodium hydroxide solution and diluted with distilled water to produce 1000 mL. The pH was adjusting with a digital pH meter [15].

3.Drug excipients compatibility studies

FTIR studies

Excipients are integral components of almost all pharmaceutical dosage forms. The successful formulation of a stable and effective solid dosage form depends on the careful selection of the excipients, which are added to facilitate administration, promote consistent release improve bioavailability of the drug and protect it from degradation [16]. The FT-IR spectrum of pure drug and physical mixture of polymers were analyzed to verify the compatibility between the pure drug and polymers using by KBr disc method. The procedure consisted of dispersing a sample (drug alone or mixture of drug and polymers in 1:1 ratio) in KBr and compressing into discs by applying a pressure of 5 tons for 5 min in a hydraulic press. The pellet was placed in the light path and the spectrum was obtained to identify functional group and bond of drug or its mixture. The IR absorption spectra of the pure drug and physical mixture were taken in the range of 500-4000 cm^{-1} [17].

4.Pre-compression parameter:

a) Angle of Repose

The angle of repose is the maximum angle of a stable slope determined by friction, cohesion and the shapes of the particles. When bulk granular materials are poured onto a horizontal surface, a conical pile will form. The internal angle between the surface of the pile and the horizontal surface is known as the angle of repose and is related to the density, surface area, and coefficient of friction of the material, particle size and shape. Material with a low angle of repose forms flatter piles than material with a high angle of repose. In other words, the angle of repose is the angle a pile forms with the horizontal plane [18]. Angle of repose was determined using funnel method. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the heap of the blends. Accurately weighed blend was allowed to pass through the funnel freely on to the surface. The height and diameter of the powder cone was measured and angle of repose was calculated using the following equation [19].

$$\theta = \tan^{-1} (h/r)$$

Where,

h = Height of pile, r = Radius of pile, and θ = Angle of repose

table .1 significance of angle of repose

Sr no	Angle of repose	Flow property
1	<25	Excellent
2	25-30	Good
3	30-40	Passable
4	>40	Poor

b) Determination of Bulk Density and Tapped Density

It is the ratio between a given mass of a powder and its bulk volume. Bulk density is calculated by using the Formula-

$$\text{Bulk Density} = \frac{\text{Mass of powder}}{\text{Bulk Volume of the powder}}$$

A given quantity of powder is transferred to a 100 mL measuring cylinder and is tapped mechanically till a constant volume is obtained. This volume is the bulk volume and it includes true volume of the powder and the void space

among the powder particles (g/cm^3) [20]. Tapped density is calculated by using the formula.

$$\text{Tapped density} = \frac{\text{Weight of powder}}{\text{Tapped volume of the powder}}$$

c) Carr's Compressibility Index

Compressibility index was determined by placing the dried granules in a measuring cylinder and the volume was noticed before tapping, after 100 tappings again volume was noticed.

table 2: relationships between percentage compressibility and flowability

% Compressibility	Flowability
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
23 – 35	Poor
33 – 38	Very Poor
> 40	Extremely Poor

d) Hausner's Ratio

Hausner's Ratio indicates the flow properties of the powder and it's the ratio of tapped density and bulk density. Hausner found that this ratio was related to interparticle friction and, as such, could be used to predict powder flow properties. Generally, a value less than 1.25 indicates good flow properties, which is equivalent to 20 % of Carr's index [21].

$$\text{Hausner's ratio} = \frac{Df}{Do}$$

D0 = Bulk density,

Df = Tapped density

table 3: significance of hausner's ratio

Sr.no	Hausner's Ratio	Property
1	0-1.2	Free flowing
2	1.2-1.6	Cohesive powder

5.Preparation of Mucoadhesive tablets [22,23]

The composition of different hole-adhesive formulations prepared using varying amounts of moringa gum (MG), xanthan gum (XG), direct compressible lactose (DCL) together with a fixed amount of Mg. Stearate, Talc and Ethylcellulose. The hole-adhesive double-layer tablets were prepared with a direct compression method which involves two steps. Initially, the drug, polymers (MG and XG) and diluents were mixed homogeneously [24]. This mixture was then ground in a mortar and pestle. And then it went through the sieve. Finally, the lubricant was added and mixed for 5 minutes. The mixture was then compressed with a 10-station tablet punching machine with 6 mm punches at a pressure of about 5-6 kg / cm2, then the upper punch was raised in mm and the ethyl cellulose support layer detailed as quantity, pressure, punches diameter, etc. it was inserted in the previous compact, so two layers were compressed. For all practical purposes, a batch size of 100 tablets was maintained for each formulation[25.]

Formulae of various mucoadhesive formulations of Dolasetron mesylate

table 4: actual values of ingredients taken for mucoadhesive tablet

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Dolasetron mesylate	8	8	8	8	8	8	8	8	8
Moringa gum	6	6	6	12	12	12	24	21	18
Xanthan gum	9	18	21	12	18	24	9	18	27
Direct compressible lactose	35.8	26.8	23.8	26.8	20.8	14.8	17.8	11.8	5.8
Mg. Stearate & Talc 1:2 (2%w/w)	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
Ethyl cellulose as Backing Layer	20	20	20	20	20	20	20	20	20
Total	80	80	80	80	80	80	80	80	80

6.Evaluation of Tablets

All the prepared Mucoadhesive tablets were evaluated for the following official and unofficial tests described in pharmacopoeia or in standard text books or research articles.

1. Appearance

The tablets were identified visually by checking the difference in colour against contrast backgrounds.

2. Thickness and Diameter

Twenty tablets were randomly selected from formulations thickness and diameter was measured individually by using a vernier caliper. It was expressed in millimeter and average was calculated [26].

3. Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling and during transportation. The hardness of the tablets was determined by using Monsanto type hardness tester. It was expressed in Kilogram per centimeter square (kg/cm^2). 3 tablets were randomly selected from each formulation and hardness of the same was determined. The average value was also calculated [27].

4. Friability

Twenty tablets were weighed as per IP and placed in the Roche friabilator and apparatus was rotated at 25 rpm for 4 minutes. After revolutions, the tablets were dedusted and weighed again. The difference in weight not is more than

0.8 %. The percentage friability was computed using formula [28].

$$\% F = \{(Wi-Wf) / Wi\} X 100$$

Where,

% F = Friability in percentage.

Wi = Initial weight of tablets.

Wf = Weight of tablets after the revolution.

5. Weight variation [29,30]

The weight variation test was performed by weighing 20 tablets individually, the average weight was calculated and the weight of the single-tablet was compared with the average weight. Calculating the average weight, comparing the individual weight of the tablet with the average weight. The tablets comply with the IP 2014 test if no tablet differs by more than double the percentage deviation or if no more than two of the individual weights must deviate from the average weight by a deviation of 7.5%.

6. Drug content uniformity

This test is used to monitor the batch-to-batch variation in drug content. The active substance requires uniform distribution throughout the tablet formulation. Five tablets of each formulation were weighed and pulverized. The amount of powder equivalent to 8 mg of medicine. The equivalent weight drug was transferred to a standard 100 ml volumetric flask and using a buffer solution at pH 6.8 as the extraction solvent. The drug was extracted with intermittent shaking for 24 hours and the samples were analyzed by spectrophotometry (Jasco) at 310 nm. The drug content was estimated to triplicate [31].

7. Surface pH study

The surface pH of the oral tablets (n = 3) was determined to investigate the possibility of side effects in vivo. Since the acidic or alkaline pH can cause irritation to the oral mucosa, the pH has been kept as neutral as possible. A combined glass electrode was used for this. The tablet was inflated keeping it in contact with 1 ml of distilled water (pH 6.8 ± 0.05) for 2 hours at room temperature. The pH was measured by bringing the electrode into contact with the tablet surface and allowing it to equilibrate for 1 minute [32].

8. Swelling Studies

The degree of swelling was measured in terms of the percentage of weight gain per tablet. The swelling behaviors of all formulations were studied. One tablet of each formulation was stored in a Petri dish containing phosphate buffer solutions of pH 6.8 at 37 ± 0.5 ° C. At fixed time intervals (0.5, 1, 2, 3, 4 and 5hr); the tablets were carefully removed from the petri dish. The tablet was cleaned to remove excess water using filter paper, and then weighed. The weight

of the swollen tablets was calculated. The swelling index was determined by the following equation [33].

$$S.I = \{(Ws - WI) / WI\} X 100$$

Where,

S.I = swelling index,

Ws = weight of swollen tablet and WI = initial weight tablet.

The experiment was carried out in triplicate.

9. In vitro Dissolution studies [34,35]

The dissolution test was performed using a USP type II apparatus. The head was rotated at 50 rpm. Dolasetron mesylate tablet in 0.1 N HCl was used as dissolution medium (900 ml) and kept at 37 ± 0.5 ° C. 5 ml samples were taken at predetermined intervals (0.5, 0.75, 1, 1.5, 2, 3, 4, 5, 6, 7 and 8 hour) was filtered and replaced with 5 ml of fresh dissolution medium. The collected samples were adequately diluted with dissolution liquid when necessary and analyzed for drug at 265 nm by U V. Each dissolution study was performed three times and means values were taken [36].

DRUG PROFILE:

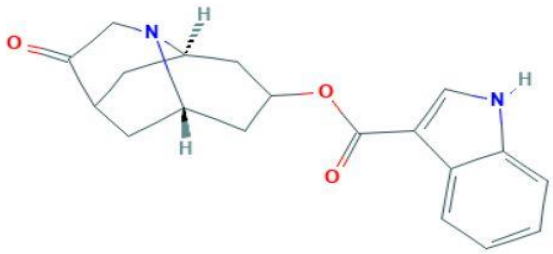
DOLASETRON MESYLATE:

Category: Antiemetic

Molecular Formula: $C_{19}H_{20}N_2O_3$

Molecular weight: 324.380 g/mol

Structural formula:



Chemical Structure of Dolasetron Mesylate

Chemical Name: [(3S,7R)-10-oxo-8-azatricyclo [5.3.1.03,8] undecan-5-yl]1H-indole-3-carboxylate

Description*:* A white or almost white, odorless crystalline powder.

Melting Point: 160 °C

Solubility of Dolasetron Mesylate [37]:

Sparingly soluble in water and alcohol; soluble in methanol; slightly soluble in isopropyl alcohol and dichloromethane; very slightly soluble in acetone, chloroform and ethyl acetate.

Storage: Store in well-closed, light-resistant containers.

Mechanism of Action

a) As an Antiemetic

Dolasetron mesylate, a derivative of carbazole, is a competitive antagonist of serotonin 5-HT3 receptors. 5-HT3 receptors are present in the central and peripheral nervous system and are associated with various physiological and pathological processes mediated by serotonin. Peripheral nervous system-related effects are believed to result in inhibition of the 5-HT3 receptor-induced depolarization of vagal afferent nerves and inhibition of myenteric neurons and 5-HT3 receptor mediated nociceptive responses [38].

b) As Alcohol Addiction Inhibitor

Recent evidence suggests that 5-HT3 receptor antagonists may be effective in mitigating the abuse of a variety of psychotropic substances, such as alcohol and cocaine. The ability of 5-HT3 antagonists to influence alcoholic behavior has been demonstrated in numerous animal studies. For example, the 5-HT3 receptor antagonists MDL 72222 and ICS 205-930 eliminate the discriminatory stimulating effects of alcohol in pigeons and rats. In addition, the 5-HT3 receptor antagonists Zatosetron and MDL 72222 block the anxiolytic effects of alcohol by reducing the response to hut avoidance in pigeons. Therefore, data from these animal studies suggest that agents that antagonize 5-HT3 receptors also modify some of the behavioral effects of alcohol [39].

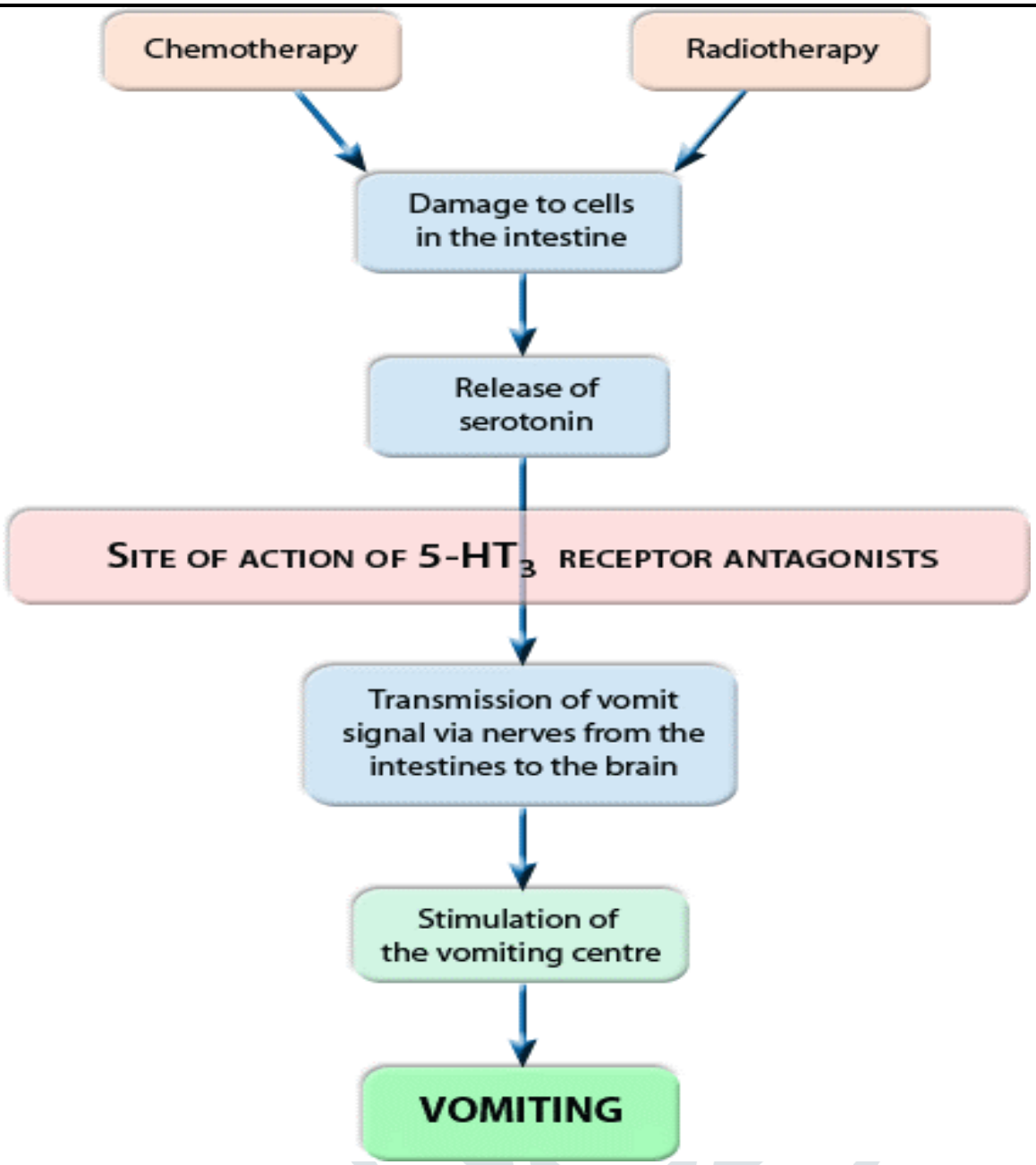


fig. 1: mechanisms of action of dolasetron mesylate [40]

Duration of Therapy

Since Dolasetron Mesylate is not an approved drug for alcohol abuse, there is no stated duration of therapy. But daily and uninterrupted administration of Dolasetron Mesylate can be continued until the patient has established a basis for permanent self-control. Depending on the individual patient, therapy may be necessary for months or even years.

Indications

Dolasetron Mesylate blocks the actions of chemicals in the body which can cause nausea and vomiting. Dolasetron Mesylate is used to prevent nausea and vomiting which can be caused by surgery or drugs to treat cancer (chemotherapy or radiation). Dolasetron Mesylate is not indicated for the prevention of nausea or vomiting caused by factors other than cancer treatment or surgery [41].

Dolasetron Mesylate Pregnancy Warnings

Dolasetron Mesylate has been assigned to pregnancy category B by the FDA. Animal studies failed to reveal evidence of fetal damage.

Adverse Reactions

Most common: confusion, dizziness, fast heartbeat, fever, headache, respiratory weakness,

Less common: decreased urination frequency, decreased urine volume, difficulty urinating (drip), painful urination

Dosage

The usual adult dose for radiation-induced nausea / vomiting is 8 mg orally every 8 hours.

RESULTS AND DISCUSSION

1.Preformulation studies:

Before starting formulation development, detailed studies of preformulation are essential. Therefore, a qualitative analysis of the drug was performed, including the physical characterization and development of the analytical method and also the evaluation of the tablet mixture, including the determination of the apparent density, the compressibility index, the Hausner's relation and the angle of rest [42].

Physical characterization of drug sample [43]:

The results of physical characterization of the drug candidate are as follows:

a) Description

The received sample of Dolasetron mesylate was found to be white crystalline and odorless powder.

b) Melting Point

The average melting point of Dolasetron mesylate was determined by the Thiel test tube method in triplicate and the average was found at 276° C, which is in good agreement with the reported melting point range 278 ° C.

c) Solubility

The solubility of the received sample of Dolasetron mesylate was examined in various solvents. Average of triplicate readings was computed. The results thus obtained were as follows.

table 5: solubility of the dolasetron mesylate

Sr. No.	Solvent	Solubility in mg/mL
1	0.1 N HCL	5.629 mg/mL
2	Phosphate Buffer pH 6.8	3.163 mg/mL
3	Distilled Water	505mg/L

Solubility was found to be in the order, 0.1 N HCL Phosphate buffer pH Distilled Water.

d) PH of solution:

PH of solution in water was determined with a 2 %w/v solution of drug in water in electronic pH meter. The pH was found to be pH 3.4.

2.Evaluation of Precompression parameters of powder blend [44]:

Powder blends of all formulations were evaluated for Angle of repose, Bulk density, Tap density, Compressibility index and Hausner's ratios. The results obtained are given in Table.6 (n=3).

a) Angle of repose

The angle of repose of all formulated batches was found to be between $21^0.86' \pm 0^0.78'$ and $27^0.57' \pm 0^0.18'$. The values indicate that, powder blends are free flowing.

b) Bulk density and Tap density

The apparent bulk densities of all formulated batches were found to be in between 0.6819±0.227 g/mL and 0.8172±0.12 g/mL. The values of tapped density were found to be in between 0.7511±0.154g/mL and 0.909±0.150g/mL. Bulk and Tap densities were found in acceptable limit, which indicates that, the porosity is minimum and hence the powder blend may form a good compact where compressed under force.

c) Compressibility Index

The values of compressibility index range from 11.84±2.738 % to 13.82±2.008% indicating that, the powders where found to be acceptable range.

d) Hausner's ratio

The Flow property was also insured by measuring the Hausner's ratio. The values of were found to be in between 1.013±0.501 to 1.130±0.124which indicates free flowing powder property.

table 6: rheological properties of powder blend of f1 to f9

Batch	Angle of Repose (°)*	Bulk Density* (g/mL) ± S.D	Tapped Density* (g/mL) ±S.D	Compressibility Index*(%) ±S.D	Hausner's Ratio* ±S.D
F1	25.63±0.2	0.817±0.101	0.909±0.21	10.76±0.79	1.120±0.28
F2	25.27±0.5966	0.767±0.203	0.866±0.13	11.47±0.72	1.129±0.24
F3	24.36±0.1163	0.730±0.253	0.825±0.21	11.53±0.72	1.130±0.24
F4	25.34±0.923	0.768±0.285	0.864±0.15	11.08±0.67	1.124±0.15
F5	24.13±0.4072	0.736±0.252	0.819±0.13	10.18±0.55	1.013±0.14
F6	24.56±0.8375	0.725±0.252	0.809±0.12	10.46±0.51	1.117±0.08
F7	21.86±0.7873	0.783±0.281	0.874±0.22	10.35±0.62	1.116±0.23
F8	24.03±0.2801	0.774±0.144	0.866±0.22	10.63±0.32	1.193±0.38
F9	27.57±0.7831	0.681±0.222	0.751±0.14	09.10±0.42	1.101±0.23

Average of three values (n=3) ±Standard Deviation.

3.Evaluation Post compression parameters of formulations [45,46]

Tablets of all batches were evaluated for thickness, hardness, friability, weight variation, drug content uniformity and results were tabulated in Table 7

a) Thickness and Diameter

Twenty tablets of the formulations were randomly selected and the thickness was individually measured using a vernier caliper (Mitutoyo, Japan). It was expressed in millimeters and the average was calculated. The thickness values of all formulations were found in the range from 2.263 ± 0.305 mm to 2.493 ± 0.20 mm and the diameter was found in the range from 5.98 ± 0.1 mm to 6.006 ± 0.20 mm. There was no marked variation in the thickness of the tablets within each formulation, indicating a regular process.

b) Hardness

This was determined by using Monsanto hardness tester. 10 tablets of each formulation were evaluated and mean hardness values. Hardness values of all formulation were found to be in the range of 4.333±0.152 Kg/cm^{2}to 5.233±0.152 Kg/cm^2 which indicates good mechanical strengths of the tablets. The values of hardness obtained reveal that, formulated tablets have good mechanical strength and sufficient hardness to withstand mechanical shocks during various stages of handling in manufacture, packaging and shipping.

c) Friability

The friability of the prepared formulations was determined by the Roche Friabilator and the total weight losses were calculated in terms of percent friability. Generally, the value of percent friability must not be greater than 1.0 %. Friability values for all formulations were found to be in the range between0.313±0.004%to 0.501±0.008%. The values of friability obtained reveal that, formulated tablets have good mechanical strength and sufficient to withstand mechanical shocks during various stages of handling in manufacture, packaging and shipping [47].

d) Weight Variation

Twenty tablets of each formulation were evaluated. The mean values of each formulation along with the percent deviation are recorded in Table .7 None of the tablets fall outside the 7.5 % deviation of tablet weight. The readings obtained for Weight variation of the tablets indicated that the tablets of all the formulation passed the weight variation test. Which were found to be in the range of 0.0793±0.001g to 0.079±0.001 gm [48].

e) Drug Content uniformity studies

The drug content uniformity was calculated for all the formulations of mucoadhesive tablets. The study was carried out in triplicate. Table. 7 shows the results of the drug content uniformity (theoretical content) in each formulation with S.D. values. The values for the determination of content uniformity of all formulations were within the range

5.40±0.664 % to 6.97±0.993 %. These values are found satisfactory, which ensured good uniformity of the drug content in tablets [49].

f) Surface pH Study

The surface pH of all formulations was obtained between the range of 6.166±0.0577 to 6.433±0.058 which was nearer to salivary pH (pH5-7) suggesting that the prepared tablets can be used without the risk of mucosal irritation and discomfort. Table 7 shows the results of the surface pH of each formulation with S.D. values [50].

table 7: evaluation parameters of formulations

FC	Thickness * (mm) ± S.D.	Hardness* /cm²) ± S.D.	Friability (%)	Average weight variation* (mg) ± S.D.	Drug content* (mg) ± S.D.	pH* ± S.D
F1	2.403±0.25	4.600±0.36	0.438±0.18	0.279±0.02	6.97±0.93	3.5±0.57
F2	2.406±0.31	5.033±0.10	0.375±0.14	0.270±0.03	6.18±0.41	3.7±0.50
F3	2.493±0.20	4.333±0.15	0.501±0.13	0.278±0.01	5.72±0.63	3.6±0.20
F4	2.453±0.15	5.200±0.17	0.313±0.11	0.278±0.05	6.71±0.27	3.7±0.57
F5	2.343±0.15	4.676±0.36	0.378±0.17	0.273±0.04	5.97±0.34	3.9±0.10
F6	2.263±0.30	5.230±0.15	0.312±0.14	0.279±0.05	5.53±0.60	3.3±0.52
F7	2.353±0.11	4.600±0.17	0.376±0.12	0.277±0.06	6.51±0.23	3.6±0.52
F8	2.346±0.15	4.833±0.35	0.375±0.13	0.278±0.02	6.84±0.18	3.3±0.57
F9	2.423±0.25	5.066±0.23	0.376±0.11	0.277±0.01	5.40±0.64	3.4±0.57

Average of three values (n=3) ±Standard Deviation

g) Swelling Index Studies [51,52]

The swelling index was calculated for all hole-shaped tablet formulations. The study was conducted in triplicate. Table .8 shows the results of studies on swelling indices in each formulation with S.D. values. The swelling increases with the increase of the contact period because the polymers gradually absorb the water due to the hydrophilicity of the polymer. The outermost hydrophilic polymer moisturizes and swells and forms a gel barrier on the outer surface. the swelling index of the tablets containing Moringa gum (X1) and xanthan gum (X2) as a mucoadhesive polymer increased from 1 to 6 hours. It has also been found that increasing the polymer content increases the swelling rate of the tablet formulations containing moringa gum and xanthan gum. Moringa gum as a matrix carrier increased from 1 to 6 hours. Increases in the polymer content were found to increase the swelling rate of the tablet formulations and the swelling order was found [53].

• F3> F2> F1 contain a constant quantity of Moringa gum, i.e., 10%, and a variable quantity of xanthan gum, i.e., 45%, 30% and 15%.

• F6> F5> F4 contain a constant quantity of Moringa gum, that is 20%, and a variable quantity of xanthan gum, that is 45%, 30% and 15%.

• F9> F8> F7 contains a constant quantity of Moringa gum, that is 30%, and a variable quantity of xanthan gum, that is 45%, 30% and 15%.

The study revealed that, amount of matrix carriers in the formulations influences the swelling behavior. Also, all the formulations containing matrix carriers swell considerably without losing the shape or integrity of the tablets. The percent swelling behaviors of all formulated tablets were calculated and observed ranging from 29.831±0.649 % to 87.393±0.185 % and the results clearly indicate that swelling capacity increases by increasing the contact of the polymer [55,56].

table 8: swelling index studies data

Formulation code	Time (Hrs)					
	0.5	1	2	3	4	5
F1	29.83±0.64	41.17±0.56	52.94±0.36	65.12±0.55	67.64±0.69	73.94±0.30
F2	36.97±0.36	46.21±0.96	56.30±0.52	57.64±0.85	72.68±0.15	77.31±0.60
F3	41.34±0.34	48.53±0.69	59.07±0.64	71.73±0.68	75.10±0.42	81.43±0.52
F4	30.14±0.30	42.25±0.54	53.13±0.41	65.69±0.54	68.20±0.36	74.06±0.84
F5	39.08±0.69	46.63±0.68	57.13±0.78	68.91±0.64	71.10±0.28	78.56±0.68
F6	42.19±0.46	51.05±0.89	60.33±0.65	72.99±0.94	76.37±0.46	82.27±0.80
F7	31.10±0.80	43.27±0.25	53.78±0.14	66.38±0.35	69.32±0.20	74.36±0.26
F8	40.34±0.79	47.06±0.45	57.98±0.64	70.58±0.84	74.19±0.39	80.63±0.48
F9	43.27±0.56	52.94±0.30	61.34±0.39	73.10±0.13	77.31±0.70	83.19±0.10

CONCLUSSION

The mucosa is an attractive site for the delivery of therapeutic agents and may be ideal for compounds not suitable for oral delivery. Excellent accessibility, high patient acceptance, compliance and robustness are interesting features of the oral mucosa. The development of a bioadhesive dosage form for administration of the drug through the mucosa is of interest with respect to the drug undergoing first pass metabolism. Dolasetron mesylate is a selective 5HT3 receptor antagonist. Serotonin 5HT3 receptors are located on the terminals of the vagus nerve at the periphery and centrally in the zone of activation of the chemoreceptors in the area of the prostema. Chemotherapeutic agents are

believed to cause nausea and vomiting by releasing serotonin from enterochromaffin cells into the small intestine and the released serotonin activates the vomiting reflex. Therefore, Dolasetron mesylate works by blocking the serotonin receptor on 5HT3 receptors. Dolasetron mesylate buccal tablets are designed to release the drug to the mucosal site in a one-way pattern for a long period of time without blushing the drug from saliva. The present research was planned for the formulation and development of Dolasetron mesylate hole-adhesive tablets with 2 factors, namely Moringa gum and Xanthan gum in 3 different levels. For the formulation of hole-adhesive tablets, MG and XG are used in 3 different levels with direct compressible lactose as a diluent. Fixed amount of ethyl. Cellulose used as a support layer. Spectral FTIR studies confirmed the absence of drug / polymer / excipient interactions. The formulation variables include the nature and quantity of polymers and diluents with different physico-chemical properties, mucoadhesive resistance, swelling index studies, in vitro permeability studies and stability. The results of all laboratory experiments together with the recorded observations.

The tablets were compressed with a 6 mm circular punch and die on a 10-station rotary punching machine (Cemach machines limited the tablet press R and D). Prestressing parameters such as rest angle, bulk density, shunt density, compressibility index and host ratio within the prescribed limits. The prepared oral adhesive tablets were evaluated for post-compression parameters such as hardness, weight variation, thickness, friability, swelling index, uniformity of the drug content, surface pH, and mucoadhesive resistance. The in vitro permeability of Dolasetron mesylate was influenced by the nature and quantity of polymers and by the physical-chemical properties of the diluents used. All prepared oral tablets were found to follow an abnormal non-Fickian release. The formulation was stable with respect to the content of the drug, permeation in vitro during the stability study period. The present study has conclusively shown that Dolasetron mesylate oral tablets can be successfully developed using 2 factors, i.e., MG and XG at 3 different levels. The prepared tablets gave promising results in terms of mucoadhesive resistance and in vitro permeation of the dosage form.

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