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EFFECT OF PLANTAGO OVATA MUCILAGE USED AS NATURAL SUPERDISINTEGRANT ON RAPIMELTS TABLET OF METACLOPRAMIDE HCL

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ABSTRACT:
Formulation, development and optimization of rapimelts containing metoclopramide HCl using natural superdisintegrant to isolate mucilage from the plantago ovata husk powder by pregelatinization method. To prepare priliminary trial batches of repimelts using β cyclodextrin with different ratio of drug and polymer. To evaluate the drug polymer complex and finally which polymer and ratio of drug and polymer is better to formulate final formulation. To achieve taste masking of drug. To prepare preliminary trial batches of rapimelts using plantago ovata mucilage as natural superdisintegrant and crosspovidone as synthetic superdisintegrant by direct compression method. To evaluate the prepared rapimelts for various properties like friability, hardness, wetting time, water absorption ratio, disintegration time, drug content, drug etc. Identifying the key variables and their levels for applying factorial design and to optimize one formulation. To evaluate the final batches and find out the optimized batch based on statistical optimization using experimental design. To compare the optimized formulation with marketed preparation. To carry out stability studies of optimized batch as per ICH guidelines. The aim of the present investigation was to Formulate, designed, and evaluates plant agoovata mucilage used as a natural superdisintegrant was to developed and optimized rapimelts containing Metoclopramide HCL.
Keywords: Rapimelt , Superdisintegrant, Rapimelt Super disintegrate, Metaclopramide hydrochloride

INTRODUCTION

Dosage forms are the means by which drug molecules are delivered to sites of action within the body[1].

Tablets and capsules are the most popular and frequently dispensed medication dosage form because they are convenient for self-administration and easily handled by the patient; however, there are many other different dosage forms available for patients.

Ever wonder why there are so many different dosage forms whenever you walk into a pharmacy to get a medication filled or to pick up an OTC item? Here are a couple of reasons: coated tablets protect the active ingredient/ drug substance from the destructive influences of oxygen and humidity; enteric-coated tablets protect the active ingredient from destruction from gastric acid in the stomach after oral administration; capsules, coated tablets, effervescent granules, flavored suspensions and solutions conceal bitter, salty, or bad tastes; lozenges, troches, gummy bears, ODT tablets, thin strips, lollipops, suspensions, and solutions provide formulations for patients, often children, who cannot swallow tablets or capsules; controlled-release tablets, capsules, and suspensions provide rate-controlled medication release and action; ointments, creams, gels, patches, ear drops, eye drops, and nasal sprays provide optimal drug action from topical administration sites; ointments, creams, gels, suppositories, and enemas provide medication to patients who cannot take anything by mouth, either due to nausea/ vomiting or inability to swallow; and inhalers and nebulizers provide optimal drug therapy to the pulmonary system.

Listed below are various dosage forms, including dosage forms to be taken by mouth, to be applied to the affected area (topical administration), to be inhaled, and to be inserted rectally. Each dosage form has unique physical characteristics and its own advantages and disadvantages. The availability of various dosage forms provides patients and providers with multiple ways to ensure the patient is able to take the prescribed medication. Regardless of dosage form, the medicinal agent must safe, stable, and efficacious[2].

Pharmaceutical Excipients

The word *excipient*is derived from the Latin *excipere*, meaning 'to except', which is simply explained as 'other than'. Pharmaceutical excipients are basically everything other than the active pharmaceutical ingredient. Ideally, excipients should be inert, however, recent reports of adverse reactions have suggested otherwise.

What are excipients doing in medicines?

The best new therapeutic entity in the world is of little value without an appropriate delivery system [3].Today, medicines are available in many dosage forms including tablets, capsules, oral liquids, topical creams and gels, transdermal patches, injectable products, implants, eye products, nasal products, inhalers and suppositories. Pharmaceutical excipients are substances that are included in a pharmaceutical dosage form not for their direct therapeutic action, but to aid the manufacturing process, to protect, support or enhance stability, or for bioavailability or patient acceptability. They may also assist in product identification and enhance the overall safety or function of the product during storage or use[4].

Thousands of different recipients are used in medicines and make up, on average, about 90% of each product. They represent a market value of €3 billion (almost $4 billion) accounting for 0.5% of the total pharmaceutical market according to industry experts[5].

Common excipients used in tablets

The list of purposes for which excipients are used, as defined in international pharmacopoeias, is extremely long. Many excipients have more than one use, which can be an advantage since it reduces the number of excipients needed and minimises the risk of interactions between them.

Tablets are the most widely used dosage form. Their manufacture can be a complex process and considerable ingenuity and formulation expertise are required to produce a product that will be stable during storage, transport and handling, yet will release its active pharmaceutical ingredient as required once ingested[6].

Adverse reactions to Excipients

Ideally, an excipient is pharmacologically inactive, non-toxic, and does not interact with the active ingredients or other excipients. However, in practice few excipients meet these criteria. Toxicity may relate to compounds used as excipients in the final dosage form or to residues of compounds (such as solvents) used during the manufacturing process.

Colouring agents

Owing to their widespread and relatively large use in food, a number of colours in current use have been associated with adverse effects, although in a relatively small number of people[7].The role of food additives in hyperactive behaviour has been debated for many years. In 2007 a study was published linking the use of six colours (tartrazine, quinoline yellow, sunset yellow, carmoisine, ponceau 4R and allura red) with behavioural problems in children. However, after reviewing the results of the study, the European Food Standards Agency concluded that no change in legislation was needed[7].

Identifying reactions to excipients in practice

When presented with a patient who has an adverse reaction, it is important to be aware that reactions may not always be due to the active ingredient. They are more likely to occur if the patient has an existing sensitivity to similar ingredients, or is on multiple medicines, or when the quantity of excipients may be high relative to body weight, for example in premature babies[8]. Excipients present in their current and past medication history should also be considered. This will help to rule out which ingredients may be causing the adverse effects[8].

Materials and Methods

Examination of drug by determining melting point:

Melting point of Metoclopramide HCl was determined by Melting Point Apparatus.

Metoclopramide HCl was filled in capillary tube and capillary tube as well as thermometer was kept in Melting Point Apparatus. The point at which Metoclopramide HCl melts is recorded from thermometer.

Examination of drug by UV spectrophotometer 38,39:

U.V. scan of Metoclopramide HCl in following media:

- In phosphate buffer pH 6.8
- In 0.1N HCl pH 1.2

-Resulting solutions of 20 µg/ml in 0.1N HCl pH 1.2 and 20 µg/ml prepared in

-Phosphate buffer pH 6.8 were scanned between 200 nm to 400 nm using Double beam UV-visible spectrophotometer.

Materials

ANALYTICAL METHOD DEVELOPMENT

Standard calibration Plot of Metoclopramide HCl in phosphate buffer pH 6.8 and 0.1N HCl pH 1.2

- **Standard (Stock) solutions**:

An accurately weighed 10 mg of Metoclopramide HCl was dissolved and diluted to 100 ml with phosphate buffer pH 6.8 and 0.1N HCl to produce 100µg/ml stock solutions.

- **Preparation of Sample solutions:**

Different dilution of stock solution were prepared using Phosphate buffer pH 6.8 and 0.1N HCl to obtain solution having concentration 4, 8, 12, 16, 20 µg/ml in both the media and absorbances were measured at obtained λmax of 273nm.

Isolation of Plantago ovata mucilage

The husk of Plantago ovata was powdered and passed through a no. 80 screen. The powder was soaked in distilled water for 24 h and boiled for a few minutes, so that complete gelatinization takes place and dried in an oven at a temperature less than 60°C. After drying gelatinized material was collected, and size reduced.

FORMULATION AND DEVLOPMENT

Preparation of Rapimelts by Direct Compression Technique

Rapimelts of Metoclopramide HCl were prepared by direct compression method according to the formula given in table. All the ingredients were passed through 60 mesh sieve separately. The drug and mannitol were mixed by small portion of both and blended to get a uniform mixture. Rest of the ingredients were weighed and mixed in geometrical proportion with Metoclopramide-Mannitol mixture and tablets were directly compressed using 9 mm sizes flat round punch on 10 stations, B tooling Rotary Tablet Compression Machine.

Preliminary study

- **Taste masking of Metoclopramide HCl by complexing with β-**

cyclodextrin14 Preparation :

Solid complexes of Metoclopramide HCl−β-CD were prepared in 1:1, 1:2 and

1:3 molar ratios by kneading methods.

Evaluation of Drug-Polymer Complex

- **% Yield:** It is calculated using following formula

Percentage yield = [Wp/Wt] × 100

Where, Wp= actual weight of taste masked particles obtained and

Wt= total weight of drug + polymer

(metoclopramide HCl and β-cyclodextrin).

B. Evaluation Tests for Rapimelts

- **Pre Compression Evaluation**

Pre compression evaluation studies were carried out for following parameter

i.e. Bulk density, Tapped density, Hausner's ratio, Carr's index, Compressibility index. These parameters were evaluated on a laboratory scale for preparation of tablets with good flow properties of powder material.

- **Bulk density (Do)**

It is the ratio of bulk volume to the total mass of the powder taken. It was measured by pouring the weighed powder into a 25 ml graduated cylinder and the volume was noted. It is given by:

- **Do = M/Vo**

Where, 'M' is the mass of powder,

'Vo' is the Bulk Volume of powder; it is expressed in g/ml.

- **Tapped density (Dt)**

It is the ratio of mass of the powder to the tapped volume of the powder. The tapped volume was measured by bulk density apparatus in which the powders were tapped for predetermined number of taps until the volume became constant.

It is given by formula:

- **Dt = M/Vt**

Where, 'M' is the mass of powders

'Vt' is the tapped volume of powders; it is expressed in g/ml.

- **Carr's index**

It is the %compressibility index. It is given by

I = (Dt-Do/Do) x 100

Where, 'Dt' is tapped density

'Do' is bulk density; it is expressed in terms of percentage.

Limit: <16- Excellent flow,

16-20-Good flow,

>20-poor flow.

- **Hausner's ratio**

It is the ratio of tapped density to untapped density. It is given by

H = Dt/Do

Where, 'Dt' is the tapped density of powders

'Do' is the untapped density of powders.

Limit: <1.25- Good flow

1.25-1.5- Fair to Passable

>1.5- Poor flow

Angle of Repose

The angle of internal friction is a measure of internal stress distribution and is the angle at which an applied stress diverges as it passes through the bed. It is the least slope at which a powder will slide down an inclined plane surface. It is denoted by **Ɵ**. Angle of repose was determined using fixed funnel method.

The blend was poured through funnel fixed at a height of 2cm, until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and angle of repose was calculated using the formula

tan-1 Ɵ = h/r

The values of angle of repose obtained can be interpreted as follows:

Post Compression Evaluation

- **Weight variation**

As per U.S.P. procedure, 20 tablets were selected randomly from the lot and weighed individually on digital weighing balance to check for weight variation. Weight variation specification as per U.S.P is shown ahead.

- **Tablet Thickness**

Micrometer was used for the measurement of thickness of tablet. Ten tablets were taken and their thickness recorded. The mean value was calculated and standard deviation was determined.

- **Hardness**

Hardness or tablet crushing strength (fc) means the force required to break a tablet in a diametric compression was determined using Pfizer/Monsanto tablet hardness tester. It is expressed in kg/cm2. The hardness of Rapimelts is kept lower than conventional tablet because increase in hardness delays the disintegration of tablet. Five tablets from each batch were randomly selected and average hardness was calculated and standard deviation was determined.

- **Friability**

Friability of the tablet was determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at height of 6 inches in each revolution. Tablets, 10 were preweighed and placed in the friabilator and the equipment was rotated at 25 rpm for 4 min. Tablets were dusted and weighed again. % Friability should be less than 1% The friability (F) is given by the formula.

% F = (loss in weight/Initial weight) × 100

- **Wetting Time**

A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small petridish (ID = 10 cm) containing 6 ml of Phosphate Buffer pH 6.8. A

tablet was placed on the paper, and the time for complete wetting was measured. Five tablets from each batch were analyzed. The mean value was calculated and standard deviation was determined.

- **Content Uniformity**

Content uniformity was determined as per USP specifications for 10 tablets from each batch. Tablet was dispersed in 50 ml of phosphate buffer pH 6.8 and sonicated for 30 min. Volume was made up to 100 ml with phosphate buffer pH 6.8 and filtered using Whatman filter paper. Filtrate was analyzed for Metoclopramide HCl content by measuring UV absorbance at 273nm. To pass the test, all the 10 tablets must show drug content in the range of 85- 115%. Not more than 1 tablet sholud show the drug content in the range of 75-125%.

- **In-Vitro Dispersion Time**

In vitro dispersion time was measured by dropping a tablet in a 10 ml measuring cylinder containing 6 ml of buffer solution simulating saliva fluid (pH 6.8) at 37+0.5ºC, 5 tablets were randomly selected and time required for complete dispersion of a tablet was measured. Average dispersion time and standard deviation was determined.

- **In-Vitro Disintegration Time**

Disintegration time for Rapimelts was determined using USP disintegration apparatus in Phosphate buffer pH 6.8, volume 900 ml at 37°C temperature. To comply the test all tablets should disintegrate within 3 minutes.

- **In-Vitro Dissolution test for drug release**

In vitro dissolution test of Metoclopramide HCl Tablet was done by following two methods:

· **In 0.1N HCl:** Dissolution was carried out using USP dissolution test apparatus type 2 (paddle) at 50 rpm in 300 ml of 0.1 N HCl (pH 1.2) as dissolution media, maintained at 37+0.5ºC. 3 ml of sample was withdrawn from the dissolution medium at the specified regular intervals, filtered through Whatmann filter paper and assayed spectrophotometrically at λmax 273 nm.

In phosphate buffer pH 6.8: Dissolution placed on magnetic stirrer, maintained at 50rpm and 37+0.5ºC. 3ml of sample was withdrawn from it at the specified regular intervals, filtered through Whatmann filter paper and assayed spectrophotometrically. An equal volume of pre warmed (37 ºC) fresh mediun is replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test.

Results

Metoclopramide HCl was found to be 183˚ C which was similar to that of standard values thus indicating the purity of the drug and all other laboratory observations were almost similar to the reported values.

Table 1:

Sr. No	Evaluation Parameter	Results
1.	Organoleptic properties;state. Color, odour, Taste, Fracture	Solid, Off White-Lightish Brown, Characteristic, Bland, Smooth.
2.	pH	7.4
3.	Solubility	Soluble in hot water forming colloidal solution insoluble in organic solvent
4.	Swelling index	25.7 ml
5.	Total ash	1.68%
6.	Moisture content	1.7%
7.	Bulk density and tapped density	0.62 to 0.74
8.	Angle of repose	32.70
9.	Carr's index	198.3
10.	Hausner's ratio	1.19
11.	%yield	95%
12.	Particle size analysis	15-65 µm
13.	Estimation of total mucilage content	77.57%
14.	Total microbial count	<100cfu/g

Discussion

The aim of the present investigation was to Formulate, designed, and evaluates plant agoovata mucilage used as a natural superdisintegrant was to developed and optimized rapimelts containing Metoclopramide HCL. To purpose of the study isolate mucilage from the plantago ovata husk powder by pregelatinization method and prepared priliminary trial batches of repimelts using β cyclodextrin with different ratio of drug and polymer. Evaluate the drug polymer complex and finally which polymer and ratio of drug and polymer is better to formulate final formulation. To achieve taste masking of drug. prepare preliminary trial batches of rapimelts using plantago ovata mucilage as natural superdisintegrant and crosspovidone as synthetic superdisintegrant by direct compression method. Rapimelts tablet of metoclopramide Hcl tablets by determination of range of technological parameters. Dissolution profile suggested that tablet prepared with Plantago ovate mucilage were capable of releasing up to 90 % drug within 15 minutes in phosphate buffer 6.8 pH, by an appropriate combination of excipients it is thus possible to obtain Rapimelts tablet of metoclopramide Hcl tablets using simple and conventional technique.

Conclusion

To purpose of the study isolate mucilage from the plantago ovata husk powder by pregelatinization method and prepared priliminary trial batches of repimelts using β cyclodextrin with different ratio of drug and polymer. Evaluate the drug polymer complex and finally which polymer and ratio of drug and polymer is better to formulate final formulation. To achieve taste masking of drug. prepare preliminary trial batches of rapimelts using plantago ovata mucilage as natural Superdisintegrant and crosspovidone as synthetic superdisintegrant by direct compression method. Rapimelts tablet of metoclopramide Hcl tablets by determination of range of technological parameters. Dissolution profile suggested that tablet prepared with Plantago ovate mucilage were capable of releasing up to 90 % drug within 15 minutes in phosphate buffer 6.8 pH, by an appropriate combination of excipients it is thus possible to obtain Rapimelts tablet of metoclopramide Hcl tablets using simple and conventional technique.

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