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A COMPREHENSIVE REVIEW ON FORMULATION AND EVALUATION OF FAMOTIDINE FLOATING TABLETS USING TAMARIND SEED GUM

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ABSTRACT

The goal of this project was to create a famotidine floating medication delivery device. Poor famotidine absorption in an acidic environment (upper GIT). The bioavailability when administered orally is close to 50%. The current study was conducted to look at the floating dose form of famotidine in an effort to get over these difficulties. Direct Compression was used to create floating tablets. Six formulations with varying ratios of the retardant (Na-CMC) and the gel-forming agent (HPMC K4M) were created. Its gas-generating substance (NaHCO3) combines with HCl to release CO2, which makes holes in the tablet, increases swelling, and keeps the tablet from disintegrating. The main structural polysaccharide in the primary cell wall of higher plants is xyloglucan. The looseness of a fine network of cellulose microfibrils regulates cell growth and expansion. These cellulose microfibrils are crosslinked by xyloglucan, giving them the flexibility needed for sliding. TSP (Tamarind Seed Powder) acts as TSG (Tamarind Seed Gum) and have good disintegrating and good adhesive property.

KEYWORDS: TSG, TSP, famotidine, adhesive, disintegrating property.

1. INTRODUCTION

Famotidine inhibits histamine H2-receptors. It is commonly used to treat stomach ulcers, duodenal ulcers, Zollinger-Ellison syndrome, and gastroesophageal reflux disease. The dose

for the treatment of benign gastric and duodenal ulcers is 40 mg daily by mouth at bedtime for 4 to 8 weeks. When gastroesophageal reflux disease is related to esophageal ulceration, a dose of 40 mg twice a day comparable amount of time is advised instead of the usual 20 mg by mouth twice daily for 6 to 12 weeks. It is recommended to take a dosage of 10 mg up to twice daily to alleviate the symptoms of non-ulcer dyspepsia or heartburn. The initial oral dose for Zollinger-Ellison syndrome is 20 mg every 6 hours, which is then raised as needed to a dose of up to 80 mg per day.[1] Drugs that have an oral sustained delivery window for absorption in a specific area of the gastrointestinal tract can be delivered using gastroretentive drug delivery devices that can be kept in the stomach. In order to ensure optimal bioavailability, these mechanisms aid in constantly releasing the medication before it enters the absorption window.[2] It has been suggested that combining antacids with a H2 receptor antagonist, such as famotidine or ranitidine, for the treatment of gastric diseases encourages the local transport of these medications to the receptor of the parietal cell wall. Additionally, local administration increases the bioavailability of stomach wall receptor sites and improves the effectiveness of medications to control acid secretion. Famotidine's systemic and local administration might be improved using this concept, effectively reducing stomach acid output.[3] Disintegration exhibited a significant contribution to improving therapeutic activity and raising patient compliance.[4] The rate of water absorption by superdisintegrants is often larger than the rate of swelling of disintegrants.[5] The most efficient medication is used nowadays in solid dosage forms with modest concentrations of 1–10% superdisintegrant.[6] Superdisintegrants expand, alter the tablet's volume, and disrupt the tablet when in contact with water. They are effective at low concentrations and have a larger capacity for dissolving. As an illustration, consider the following natural superdisintegrants: Gellan gum, Isapghula husk mucilage, Chikle gum, Locust bean gum, Lepidium sativum seed mucilage, Tamarind seed gum, Cassia fistula, and Jackfruit seed gum. Artificial superdisintegrant Modified starch (sodium starch glycolate), Primojel, Chitin, cross-linked PVP, cross-linked starch, cross-linked alginate, alginates, calcium silicate.[7] Consequently, the unique method of making superdisintegrant from tamarind seed gum is the focus of this work. Tamarindus indica L. family belongs to Leguminosae[8] (Fabaceae). Gum's carboxylic composition is crucial for the breakdown process.Tamarind seed gum was chemically altered to improve its ability to disintegrate.[9] Additionally, calcium chloride was used to complex the carboxymethylated gum in order to increase the ability of the gum. The formulation would simply dissolve with this, and improves quicker medication release. Drugs that: (a) act locally in the stomach; (b) are largely absorbed in the stomach; (c) are poorly soluble in alkaline pH; (d) have a

restricted absorption window; and (e) are unstable in the intestinal or colonic environment might benefit from floating drug delivery.have a restricted absorption window; and (e) are unstable in the intestinal or colonic environment might benefit from floating drug delivery[10] improves quicker medication release. Famotidine floating tablets using tamarind seed gum achieved an excellent bioavailability compared with other artificial superdisintegrants. The primary restrictions on famotidine's therapeutic efficacy are its low bioavailability (40–45%) and brief half-life (2.5–4 h). Multiple doses are required to maintain a steady plasma concentration of the medication for a satisfactory therapeutic response because of its short biological half-life. However, more frequent medication usage is linked to a higher risk of side effects such irregular heartbeat, constipation, exhaustion, sleeplessness, bleeding, depression, nausea, and insomnia. Consequently, the main goal of the current study was to create a maintenance therapy and lowering stomach acid output in ulcers, by formulating famotidine floating tablets by using tamarind seed gum as superdisintegrants. In this study, an attempt was made to make gum from crude Tamarind seed material, and utilising this as a binder, attempts were conducted to create a composite with cellulose rich sisal agave plant tibre. Methods for increasing the strength of the composite by humidification and compression were designed.

1.1 MATERIALS AND METHODS

Famotidine was received as a gift sample from Tonira pharma Ltd, Ankleshwar, India. HPMC K4M and MCC pH 102 were received as a gift sample from Signet Ltd, Mumbai, India. Na-CMC was received as a gift sample from Aqualon Ltd. Di basic calcium phosphate; Sodium bicarbonate and Hydrochloric acid were purchased from Merck Ltd. Magnesium stearate was procured from Mukesh pharma distribution. Talc was purchased from Nikita pharma, tamarinds eed gel was prepared in the laboratory.

1.2 Preparation of tamarind seed gum

1. Tamarind seeds were dried in the sun for a day or two before being broken into small pieces and powdered into a fine powder. Distilled water was used. Taken in a beaker with the necessary quantity of fine tamarind seed powder was used to create a solution with a 4% w/v concentration.
2. At room temperature, the powder could not be dissolved. As a result, the mixer was heated to 80°C to 100°C while the solution was constantly stirred to avoid layer development on the surface. The procedure needed a minimum of two hours. Filtration

was done hot, with glass wool used to remove the undissolved, which was mostly attributable to the seed's skin.

3. Approximately 25% of the dry weight component was present in the undissolved material. The final solution produced had a concentration of 3% w/v.
4. The produced gum solution demonstrated good flow properties as well as adhesiveness. The tension at the breaking point of the adhesive surfaces, where failure occurred solely at the adhesive junction, was used to assess the adhesive strength. The following is how the test was carried out. After drying in the sunshine, the gum was placed equally all over the surface of two sheets of Executive Bond paper, leaving the bottom margin ungummed (the bottom margin has a dimension h th of the entire surface) and cut into 30 cmx 3 cm pieces.
5. Initially, weights were added at 10 g intervals, but towards the breaking point, weights were introduced at fewer than 5 g intervals. The adhesive strength of gum solution was determined using a simple formula, and the experimental value was 117+/-11 Nrn^{-1}. By doing a comparable test, this number was compared to the adhesive strength of gums available on the market manufactured by standard corporations. This revealed that Tamarind seed gum was as good as commercially available gums and might be used as an alternative supply of glue, enhancing Tamarind seed's economic value.
6. Adhesive Strength = Weight at breaking point/ Width of adhesive surface

1.3 Preparation of famotidine floating tablets

1. The composition of various famotidine floating tablet formulations.
2. Famotidine, HPMC K4M, Na-CMC were passed through sieve no. 80 separately. Sodium bicarbonate was passed through sieve no. 44.
3. All the ingredients were mixed in proportion.
4. The powder blends were lubricated with Magnesium stearate (2% w/w) and Talc (1% w/w), and the lubricated blends were crushed into tablets using a single punch tablet machine utilizing 9.5 mm flat faced round tooling (Rimek mini press II)
5. To produce tablets with hardness between 4.5 and 5 kg/cm2, the compression force was altered. Six formulations were created and assigned FT1 through FT6 codes.

1.4 Evaluation of famotidine floating tablets using tamarind seed gum

Blends' flow characteristics (before to compression) were described in terms of their Angle of repose.[12] Bulk density and tapped density[13], Carr's index[14] and Hausner's ratio.[14]

1.5 Physical evaluation of famotidine floating tablets using tamarind seed gum

Two tablets were chosen at random from each formulation, and organoleptic qualities such colour, odour, taste, and shape were assessed. Vernier callipers were used to gauge the thickness and diameter of 10 tablets. Using 20 tablets each, the manufactured floating tablets' weight variation, hardness (as measured by the Monsanto tester), and friability (10 tablets each) were assessed (Roche type friabilator).[7]

1.6 In vitro buoyancy studies

Drug dissolution from solid dosage forms was represented using a kinetic model, where the amount of drug dissolved is a function of test time. Drug release data was evaluated using Higuchi's square root and the Zero order 9 to determine the precise mechanism of drug release from the tablets. The goodness of fit test was used as the foundation for choosing the most suitable model. Regression analysis was performed on the data using the MS EXEL statistical programme.

According to the Rosa et al. approach, in vitro buoyancy tests were carried out on each of the six formulations.The tablets from each formulation that were randomly chosen were maintained in a 100 ml beaker that contained simulated stomach juice with a pH of 1.2 in accordance with USP. A tablet's time to rise to the surface and float was measured as its floating lag time (FLT). Total floating time was calculated as the amount of time the dose form was continuously on the medium's surface (TFT).

1.7 Drug content estimation

The drug content in each formulation was determined by triturating 10 tablets and powder equivalent to 10 mg was added in 0.1N HCl followed by stirring. The solution was filtered through a 0.45 µ membrane filter, diluted suitably and the absorbance of resultant solution was measured spectrophotometrically at 265 nm using 0.1N HCl as blank.

1.8 In vitro buoyancy studies

In order to evaluate buoyancy, researchers looked at how effectively the tablet floated on the dissolving media over time. It keeps its integrity for 8 to 10 hours without disintegrating. Visual observation was used to calculate the overall floating duration and the floating lag time (the interval between inserting the tablet in the medium and buoyancy starting).[13]

1.9 In vitro dissolution studies

Using the USP Dissolution Testing Apparatus 2 from the United States Pharmacopeia (USP), the release rates of famotidine from floating tablets were calculated (paddle method). 900 cc of 0.1N HCl were used for the dissolving test, which was conducted at 37° 0.5°C and 50 rpm. Every hour, a sample (10 ml) of the solution was taken out of the dissolving equipment and replaced with new dissolution media. The samples were filtered through a 0.45 membrane filter and diluted with 0.1N HCl to the proper concentration. Using a UV/Visible spectrophotometer, the absorbance of these solutions was determined at 265 nm. To calculate the release profile, the cumulative percentage of drug release was plotted versus time.

2.0 In vitro drug release kinetic studies

Drug dissolution from solid dosage forms was represented using a kinetic model, where the amount of drug dissolved is a function of test time. Drug release data was evaluated using Higuchi's square root and the Zero order 9 to determine the precise mechanism of drug release from the tablets. The goodness of fit test was used as the foundation for choosing the most suitable model. Regression analysis was performed on the data using the MS EXEL statistical programme.[16]

Table no.1 composition of famotidine floating tablets of TSP.

Ingredients	F1	F2	F3
Famotidine	40	40	40
HPMC	90	90	90
K4M	50	50	50
MCC	10	10	10
TSP	15	15	15
CMC	-	-	6
Sodium bicarbonate	78	78	78

Tables 2: Results of precompression flow properties of famotidine floating blends of TSP.

Blends	Angle of repose (θ)	Carr's Index (%)	Hausner's ratio	Flow Property
FT1	20.03°±0.625	13.96±0.361	1.15±0.002	Excellent
FT2	20.78°±0.686	14.19±0.383	1.17±0.005	Excellent
FT3	20.29°±0.639	14.07±0.372	1.16±0.003	Excellent

Table 3: Results of post compression flow properties of famotidine floating tablets.

Formulation	Thickness (mm)	Hardness (kg/cm)	Friability (%)	Weight Variation (mg)	Drug Content (%)
FT1	3.72±0.019	5.13±0.234	0.63±0.081	302.89±2.821	98.42±0.234
FT2	3.52±0.037	5.00±0.367	0.71±0.062	302.32±2.892	99.24±0.267
FT3	3.42±0.043	4.98±0.291	0.59±0.078	299.91±0.998	99.45±0.231

Table 4: Results of In vitro buoyancy study of famotidine floating tablets of TSP.

Formulation code	Buoyancy lag time (sec)	Total floating time (hrs)
FT1	20 ±1.356 s	>12 hrs
FT2	06 ±2.475 s	>10 hrs
FT3	16 ±1.587 s	>10 hrs

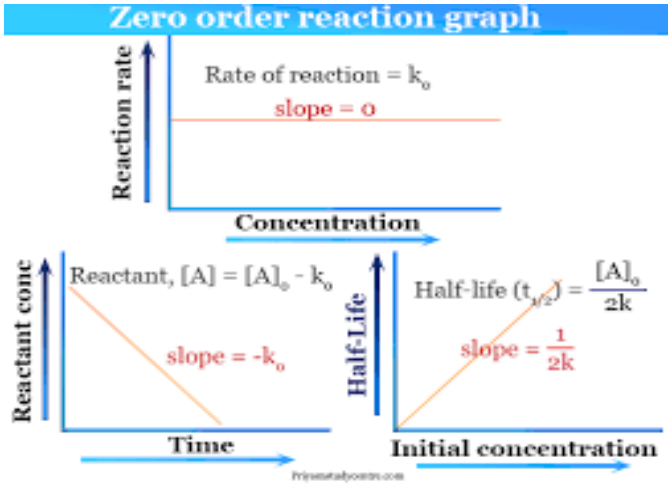

Fig. 2: Famotidine follows zero order reaction.

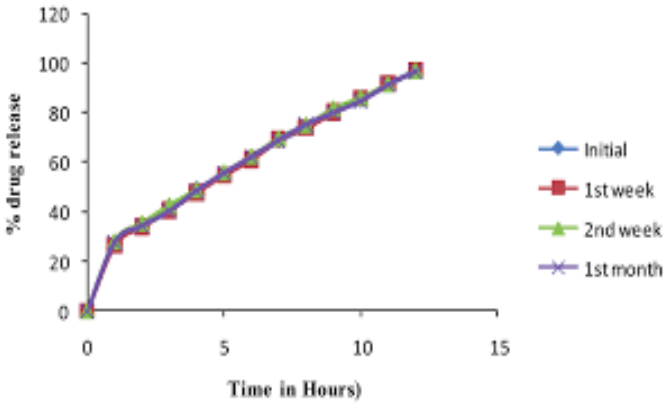

Fig. 3: Famotidine floating tablet using TSP %drug release.

CONCLUSION

This review discovered that TSP used to have significant cellulose adsorption, as demonstrated by several prior investigations. Additionally, it has been demonstrated that the fundamental traits of tamarind seed XG and plant cell wall XG are comparable. The TSG and

TSP increases the adhesiveness of the tablet and act as self disintegrating agent and increases the bioavailability of the tablet. Due to the presence of sodium bicarbonate increases the floating ability of the tablet. Further research to be done on TSG and TSP to formulate some novel drug delivery by using natural polymers and gums compared with the synthetic polymers or gums.

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