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RESEARCH ARTICLE

IMPROVEMENT OF FAST DISINTEGRATING TABLETS USING RANITIDINE HCL

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ABSTRACT

The present study was designed towards the design and development of fast disintegrating tablets by direct compression technology using Ranitidine HCl as a model drug. Fast disintegrating tablet of Ranitidine HCl was formulated using two Superdisintegrants in different concentrations i.e. 30 mg and 35 mg. Kollidon CL and Sodium Starch Glycolate are used as Superdisintegrants. All the batches were prepared by direct compression method using the Single punch tablet compression machine using 13 mm diameter. Disintegration time and drug release were taken as the basis to optimize the immediate release tablet. Prepared tablets were evaluated for thickness, hardness, friability, uniformity of weight, disintegration time and dissolution study. Tablets containing 30 mg Kollidon CL showed the faster disintegration time (25-30 Secs) and percent of drug release (90% in 15mins) as compared to other superdisintegrating agent.

KEYWORDS: Ranitidine HCl, Superdisintegrants, Direct Compression, Fast Disintegrating Tablet.

INTRODUCTION:

One significant advance in this direction is the development of fast disintegrating oral dosage form that disintegrate fast/rapidly before swallowing, upon contact with recipient tongue or buccal mucosa with little amount of water or with saliva[1]. The target of these new oral disintegrating dosage forms have generally been pediatric, geriatric, bedridden and developmentally disabled patients and also pa-tients with persistent nausea, who are in traveling, or who have little or no access to water are also good candidates Topical developments in novel drug delivery systems (NDDS) aspire to formulate a dosage form of drug molecules for convenient administration and to achieve better patient compliance [2]. Fast disintegrating tablets have all the advantages of solid dosage forms, such as excellent stability, precise dosing, easy manufacturing, small packaging size and easy handling by patients. Fast disintegrating tablets also have the advantages of liquid formulations, such as easy administration and no risk of suffocation resulting from physical obstruction by a dosage form [3, 4, 5]. Because the tablets disintegrate inside the mouth, drugs may be absorbed in the buccal, pharyngeal, and gastric regions. Thus, rapid drug therapy intervention and increased bioavailability of drugs are possible. Because the pre-gastric drug absorption avoids the first-pass metabolism, the drug dose can be reduced if a significant amount of the drug is lost through the hepatic metabolism. Because fast disintegrating tablets dissolve or disintegrate in the patient's mouth, the drug will be partially dissolved in close proximity to the taste buds. After swallowing, there should be nominal or no residue in the mouth. A pleasant taste inside the mouth becomes critical for patient acceptance. Unless the drug is tasteless or does not have an undesirable taste, taste-masking techniques should be used. An ideal taste-masking technology should provide drugs without grittiness and with good mouth feel. The amount of taste-masking materials used in the dosage forms should be kept low to avoid too much increase in tablet size. The taste-masking technology should also be compatible with FDT formulations. For example, if drug particles are coated to minimize unpleasant taste, the coating should not be broken during compression or dissolved during wet granulation. Taste masking of bitter tasting drugs is critical to the success of the FDT formulations [2]. Because FDTs are designed to have a quick dissolution/disintegration time, the tablet porosity is usually maximized to ensure fast water absorption into the tablets. The key properties of the tablets are fast absorption or wetting of water into the tablets and disintegration of associated particles into individual components for fast dissolution. This requires that excipients should have high wettability, and the tablet structure should also have a highly porous network. Because the strength of a tablet is related to compression

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pressure, and porosity is inversely related to compression pressure, it is important to find the porosity that allows fast water absorption while maintaining high mechanical strength.

In addition, low compression pressure causes fast dissolving dosage forms to be soft, friable, and unsuitable for packaging in conventional blisters or bottles. A strategy to increase tablet mechanical strength without sacrificing tablet porosity or requiring a special packaging to handle fragile tablets should be provided [2]. H2 receptor antagonist, ranitidine HCl occurs as a white to pale-yellow granular substance with a bitter taste and a sulfur-like odor [7]. It is widely prescribed in active duodenal ulcers, gastric ulcers, Zollinger-Ellison syndrome, gastroesophageal reflux disease, and erosive esophagitis. The recommended adult oral dosage of ranitidine is 150 mg twice daily or 300 mg once daily. The effective treatment of erosive esophagitis requires administration of 150 mg of Ranitidine 4 times a day [8, 9, 10]. As we know Ranitidine HCl is bitter in taste so to provide this drug in a more accessible and patient compliant form and to overcome such problems, in the present study it was decided to mask the bitter taste and formulate into a rapid disintegrating tablet. The physicochemical properties of Ranitidine HCl are water soluble drug having plasma half life of 2-3 hrs, make it suitable candidate to formulate buccal disintegrating tablets [11].

MATERIALS AND METHODS:

MATERIALS:

Ranitidine HCl, Kollidon CL, Sodium Starch Glycolate were supplied by Incepta Pharmaceuticals, Dhaka. All the ingredients received were of pharmaceutical grade and were used as received. Other materials and solvents used were of analytical grade.

Some super disintegrants:

1. **Sodium Starch Glycolate (Explotab, primogel)** used in concentration of 2-8 % & optimum is 4%. **Mechanism of Action**: Rapid and extensive swelling with minimal gelling. Microcrystalline cellulose (Synonym: Avicel, celex) used in concentration of 2-15% of tablet weight and water wicking [12].

2. **Cross-linked Povidone (crospovidone) (Kollidon)** used in concentration of 2-5% of weight of tablet. Completely insoluble in water. **Mechanism of Action**: Water wicking, swelling and possibly some deformation recovery. Rapidly disperses and swells in water, but does not gel even after prolonged exposure. Greatest rate of swelling compared to other disintegrants. Greater surface area to volume ratio than other disintegrants [12].

METHODS:

PREPARATION OF TABLET: Fast disintegrating tablets of Ranitidine HCl was prepared according to Table No 1. All the excipients without Magnesium stearate and Aerosil were mixed uniformly followed by addition of magnesium stearate and Aerosil [13]. The prepared powder blend was evaluated for various parameters like bulk density, tapped density, angle of repose, compressibility index and Hausner ratio. All the formulation showed the good blend properties for direct compression and hence tablets were prepared by using direct compression technology. After evaluation of powder blend the tablets were compressed with single punch compression machine using 13mm punches.

EVALUATION OF TABLET:

All the tablets were evaluated for different parameters as thickness, hardness, friability, uniformity of weight, disintegration time, wetting time and *in vitro* dissolution study (Table 2). **Thickness:** Thickness of tablets was determined using vernier caliper. Five tablets from each batch were used and an average value was calculated. **Hardness:** For each formulation, the hardness of six tablets was determined using the Veego, India hardness tester. **Friability**: Twenty tablets were weight and placed in the Veego, India and apparatus was rotated, after revolution the tablets were dusted and weighed. **Uniformity of weight:** Twenty tablets were randomly selected from each batch individually weighed, the average weight and standard deviation of 20 tablets was calculated [14]. **Disintegration test:** The *in vitro* disintegration studies were carried out using Digital Tablet Disintegration Test Apparatus (Veego). One tablet was placed in each of the six tubes of the basket assembly and disk was added to each tube. This assembly was then suspended in one-liter beaker containing water maintained at 37±2 0C. The basket was then moved up and down through a distance of 5 to 6 cm. at a frequency of 28 to 32 cycles per minutes. The time required for complete disintegration of the tablet was recorded [15]

Table.1: Formulation of fast disintegrating tablet of Ranitidine HCl

Ingredients (mg)	F1	F2	F3	F4
Ranitidine HCl	300	300	300	300
Kollidon CL	35	30	-	-
Na Starch Glycolate	-	-	35	30
Aerosil	10	10	10	10
Magnesium Stearate	5	5	5	5
Starch 1500	130	135	130	135
Total weight mg	**500**	**500**	**500**	**500**

Dissolution Studies: The release rate of Ranitidine HCl from fast disintegrating tablets was determined using IP Dissolution Test Apparatus Type II (basket type). Tablets were placed in a dry basket at the beginning of each test. Lower the basket in the dissolution medium and apparatus was run at 50 rpm, The dissolution test was performed using 900 ml of 0.1 M HCL, at 37± 0.50C and 50 rpm. Ten-milliliter aliquots were withdrawn at time intervals of five minute. This was maintained at same temperature, was added to the bulk. The samples were filtered through Whatman filter paper no. 41. Absorbance of these solutions was measured at 322 nm using UV spectrophotometer Shimadzu. Cumulative percentage drug release was calculated using an equation obtained from a standard curve [16].

RESULTS AND DISCUSSIONS:

Evaluation of Rapidly Disintegrating Tablet, Thickness: Thickness values for of all tablets were in the range of 3.00-3.03 mm. **Uniformity of Weight:** Weight variation values for prepared tablets were found within the specifications. **Hardness:** The hardness was uniformly maintained and it was found to be within 8.00-9.15 kgf. **Friability:** Percent friability was less than 1% in the entire formulations and the values obtained lies within 0.20- 0.35. **Disintegration test and Drug release** Tablets from each batch showed immediate disintegration. Disintegration time decreases with increase in concentration of super disintegrants. Disintegration time was given in Table No. 2. Among tablets prepared using 35mg and 30 mg Kollidon CL, tablet containing 30mg Kollidon CL showed the faster disintegration time (25-30 Secs) and % drug release (90 % in 15 mins). Among tablets prepared using 35mg and 30 mg Sodium starch glycolate, tablet containing 30 mg Sodium starch glycolate showed the faster disintegration time (28-32 Secs) and % drug release (78% in 15 mins). The decreasing order of superdisintegrating agents in term of disintegration time was as follows: **Kollidon CL > Sodium starch Glycolate.** Release of drug of various batches shown in Figure-1.

Table 2: Evaluation of Ranitidine HCl fast disintegrating tablets

Batch No.	Avg. weight (mg)	Avg. Thickness (mm)	Avg. Hardness (kgf)	Disintegration Time (Secs)	%Assay (W/W)	Friability (% w/w loss)
F1	500.2	3.02	8.12	30-33	99.19	0.20
F2	501.00	3.00	9.15	25-30	99.19	0.29
F3	500.85	3.01	8.00	31-34	99.50	0.30
F4	501.60	3.03	9.11	28-32	99.80	0.35

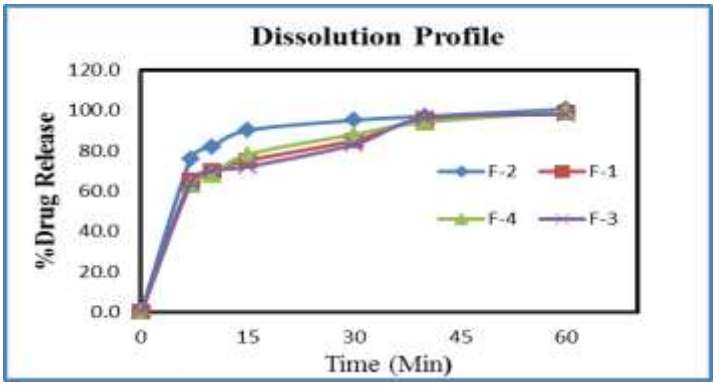

Figure 1: Release profiles of Fast disintegrating tablets of Ranitidine HCl.

CONCLUSION:

From the above result it was concluded that for the preparation of ranitidine fast disintegrating tablet, the combination of two different superdisintegrating agents were used to achieve maximum percent drug release and minimum disintegration time. Finally Kollidon CL showed the better results as compared to the other superdisintegrating agents for the preparation of tablets. Fast disintegrating tablets emerge from the desire to provide patient with more conventional means of taking their medication**.** It is difficult for many patients to swallow tablets and hard gelatin capsules. Hence they do not comply with prescription, which results in high incidence of non-compliance and ineffective therapy. Particularly the difficulty is experienced by pediatric and geriatric patients. Such problems can be resolved by means of fast disintegrating tablet.

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