

Formulation and Evaluation of Mouth Dissolving Tablets of Ranitidine HCl

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Abstract: Ranitidine HCl is an H₂ antihistaminic drug mainly used for treatment of peptic ulcers and is absorbed 50% orally. The drug undergoes hepatic metabolism, so the attempt has been made to administer it as mouth dissolving tablet to increase its oral bioavailability. The tablets were prepared by using sublimation method using ammonium bicarbonate as sublimating agent. The tablets were evaluated for hardness, wetting time, dispersion time, disintegrating time. The other tablets prepared by using sodium starch glycolate and cross carmellose sodium as superdisintegrant. It was concluded that the tablets prepared by super disintegrant addition have better disintegrating properties and release profile when compared to the tablets prepared by sublimation method.

Keywords: Mouth dissolving tablets, Sublimation, Ranitidine HCl, Super disintegrant.

Introduction

The concept of mouth dissolving drug delivery system emerged with an objective to improve patient's compliance. These dosage forms rapidly disintegrate and/or dissolve to release the drug as soon as they come in contact with saliva, thus obviating the need for water during administration, an attribute that makes them highly attractive for paediatric and geriatric patients. Difficulty in swallowing conventional tablets and capsules is common among all age groups, especially in elderly and dysphagic patients¹.

Difficulty in swallowing (Dysphagia) is a common problem of all age groups, especially elderly and pediatrics, because of physiological changes associated with these groups of patients. Solid dosage forms that can be disintegrated, dissolved, or suspended by saliva in the mouth resulting in easy swallowing can provide significant benefits to the pediatric and geriatric population, as well as other patients who prefer the convenience of easily swallowable dosage forms. This

tablet disintegrates instantaneously when placed on tongue, releasing the drug that dissolves or disperses in the saliva².

Ranitidine is E)-N-[2-[[5-(dimethylamino methyl) furan-2-yl]methylsulfanyl]ethyl]-N'-methyl-2-nitro - ethene-1,1-diamine, and used in treatment of peptic ulcers. Ranitidine is a histamine H₂-receptor antagonist. An H₂-receptor antagonist, often shortened to H₂ antagonist, is a drug used to block the action of histamine on parietal cells in the stomach, decreasing acid production by these cells. The H₂ antagonists are competitive inhibitors of histamine at the parietal cell H₂ receptor. They suppress the normal secretion of acid by parietal cells and the meal-stimulated secretion of acid³. The drug is 50% absorbed orally but it undergoes hepatic metabolism.

In present study an attempt has been made to formulate it as fast dissolving tablets to increase its oral bioavailability. The tablets were prepared by two

methods sublimation and superdisintegrant addition using sodium starch glycolate and crosscarmellose sodium as the Superdisintegrants.

Material and Methods

Ranitidine HCl, sodium starch glycolate and crosscarmellose were obtained as gift sample from Alkem labs Raigarh Maharashtra. Ammonium bicarbonate, lactose, sodium sachharin and aerosil were purchased from central drug house New Delhi,

Formulation of fast dissolving tablets

The fast dissolving tablets of ranitidine were prepared using the subliming agent, ammonium bicarbonate, sodium starch glycolate and crosscarmellose sodium as superdisintegrants, lactose as a diluent, sodium saccharin as sweetening agent, aerosil as hardness imparting agent in different concentrations (see Table 1). Formulations F1 - F3 prepared by using ammonium bicarbonate, F4 - F6 using sodium starch glycolate, F7- F9 using cross carmellose sodium. The drug was mixed with different excipients in a glass pestle mortar and compressed using CADMACH SMS25 single punch tablet machine at a fixed compression force of 400kgf. Formulations F1 – F3 was kept in oven at 60°C for 1 hour so that the sublimating agent sublimizes from tablets leaving pores in tablets.

Drug content

Twenty tablets were weighed and powdered. An amount of the powder equivalent to 150 mg of famotidine was dissolved in 100ml of pH 6.4 phosphate buffer, filtered, diluted suitably and analyzed for drug content at 228nm using UV-Visible spectrophotometer (UV 160- Shimadzu, Japan).

Tablet Hardness

The strength of tablet is expressed as tensile strength (Kg/cm²). The tablet crushing load, which is the force required to break a tablet into halves by compression. It was measured using a tablet hardness tester⁴ (Pfizer Hardness Tester).

Friability

Ten tablets were weighed and placed in a Roche friabilator and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, dedusted and reweighed. The percentage friability of the tablets was measured as per the following formula⁵.

Percentage friability =

$$\frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Wetting Time

The method reported by Yunxia et.al. was followed to measure tablet-wetting time.

A piece of tissue paper folded twice was placed in a small petry dish (ID 6.5cm) containing 6ml of pH 6.8 (simulated saliva fluid). A tablet was put on the paper and

the time for complete wetting was measured⁶. Three trials for each were performed.

In vitro dispersion time

In vitro dispersion time was measured by dropping a tablet in a 10ml measuring cylinder containing 6ml of buffer solution simulating saliva fluid (pH 6.4)⁷.

Table 1: Composition of formulations F1-F9 (250mg).

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ranitidine HCl	150	150	150	150	150	150	150	150	150
Ammonium bicarbonate	20	40	60	-	-	-	-	-	-
Sodium starch lycolate	-	-	-	20	40	60	-	-	-
Cross carmellose sodium	-	-	-	-	-	-	20	40	60
Aerosil	2.5	3	3.5	2.5	3	3.5	2.5	3	3.5
Sod. saccharin	5	5	5	5	5	5	5	5	5
Lactose	72.5	52	31.5	72.5	52	31.5	72.5	52	31.5

Disintegration time

Three tablets per batch were evaluated for disintegration time by employing a modified dissolution apparatus⁹. Instead of the disintegration apparatus described in JP XII, a modified dissolution apparatus (JP XII paddle method) was employed. Water (900 ml), maintained at 37 ± 0.5 °C was stirred with a paddle at 100 rpm. Disintegration time was recorded when all the fragments of the disintegrated tablet passed through the screen of the basket⁸.

Dissolution test

Dissolution test was carried out in 900 ml of pH 6.4 phosphate buffer in dissolution apparatus USP II at 50 rpm. An aliquot of dissolution medium was withdrawn at regular interval and absorbance was measured at 228 nm. An equal volume of phosphate buffer was added to maintain the sink condition. Dissolution was carried out for all the formulations¹⁰.

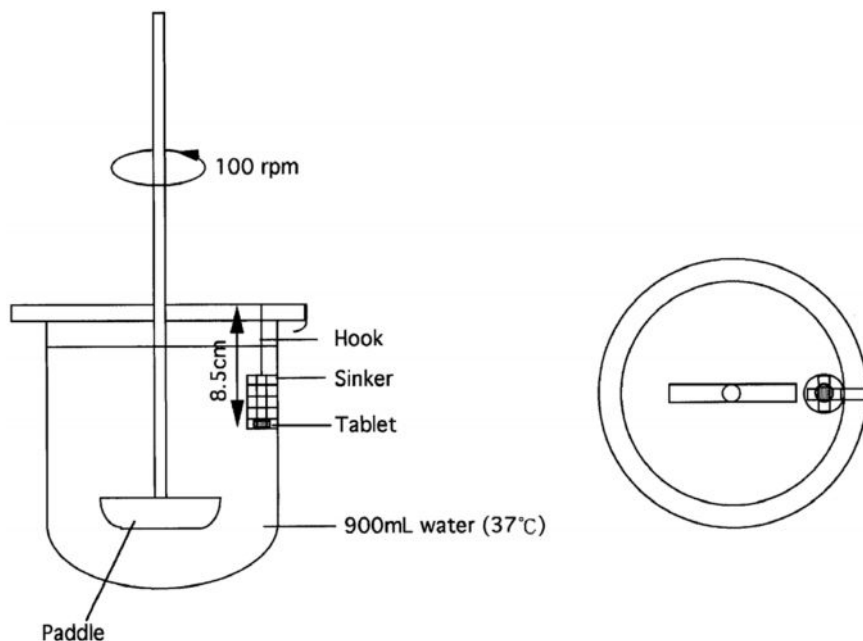


Fig.1. Schematic view of modified dissolution apparatus for disintegration test (from Reference⁹)

Table 2: Comparative result evaluation parameters of formulations F1-F9

Parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
Drug content (%)	97.34	98.14	98.43	99.10	98.29	99.67	98.84	98.89	98.46
Hardness*	3.1 $\pm$ 1.1	3.5 $\pm$ 1.5	4.3 $\pm$ 1.9	3.2 $\pm$ 1.4	3.7 $\pm$ 1.2	4.1 $\pm$ 1.3	3.1 $\pm$ 1.8	3.8 $\pm$ 1.7	4.5 $\pm$ 1.4
Friability(%)	0.467	0.532	0.765	0.323	0.465	0.658	0.423	0.543	0.765
Wetting time*(sec)	64 $\pm$ 1.2	49 $\pm$ 1.1	37 $\pm$ 11.6	58 $\pm$ 1.8	41 $\pm$ 1.4	25 $\pm$ 1.3	55 $\pm$ 1.1	37 $\pm$ 1.5	22 $\pm$ 1.2
In vitro dispersion time(sec)	52	45	32	48	31	21	45	32	20
Disintegration time(sec)	55 $\pm$ 1.3	43 $\pm$ 0.67	34 $\pm$ 0.98	50 $\pm$ 1.4	38 $\pm$ 1.9	25 $\pm$ 0.35	48 $\pm$ 1.1	36 $\pm$ 1.7	23 $\pm$ 1.3
In vitro drug release at 30 min(%)	96.03	97.93	98.43	95.10	98.29	100.10	95.84	97.89	99.86

*All values are expressed as mean $\pm$ SD, n=3

Result and Discussion

The tablets were prepared by two methods i.e. sublimation and super disintegrant addition and finally evaluated for different parameters. The comparative result of all the evaluation parameters is listed in table. 2.

The drug content was found to be within range of 97.34 to 99.67 indicating uniform distribution of the drug in the formulated tablets as per pharmacopoeial specification. The hardness of the tablets was found to be 3.1 ± 1.1 to 4.5 ± 1.4 , indicating good mechanical strength with an ability to withstand physical and mechanical stress conditions while handling. It was found that the hardness of the tablets increased on increasing the amount of aerosil in formulations. Friability of tablet was found less than 1% indicating good mechanical resistance.

The wetting time of the formulations was in the range 22 ± 1.2 to 64 ± 1.2 . The wetting time was decreased on increasing the concentration of ammonium bicarbonate in formulations (F1 – F3). This may be due to the formation of pores in formulations on increasing concentration of volatilizing agent. Similar results were obtained on increasing the concentration of cross

carmellose sodium and sodium starch glycollate in formulations F4 – F9.

In vitro dispersion time was found to be 22 to 52 seconds, which may be attributed to faster uptake of water due to the porous structure formed (F1 – F3). In F4 – F9 thus facilitating the super disintegrant to bring about faster disintegration. The *invitro* drug release after 30 minutes was between 96.03 to 100.10 % indicating better drug release and improved bioavailability.

The formulations (F4-F9) prepared by super disintegrant addition were having lesser wetting time, disintegration time, invitro dispersion time and better drug release as compared to the formulations prepared by sublimation technique (F1-F3). So it was concluded that super disintegrant addition method was excellent as compared to sublimation method in formulation of mouth dissolving tablets.

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