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Design and evaluation of rapid disintegrating tablets of risedronate sodium

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ABSTRACT

Recent advances in the field of Novel drug delivery systems have gained scientist attention to develop orodispersible tablets in order to enhance safety and efficacy of the drug. Osteoporosis is a diseases of bones which occurs due to lack of protein and minerals particularly calcium in bones. Presently available dosage forms lack to produce desired therapeutic effect. Orodispersible tablets of Risedronate sodium which helps in producing desired therapeutic effect within fraction of minutes. Risedronate sodium that inhibits osteoclast- mediated bone resorption and modulates bone metabolism. This has encouraged in the field of industry to develop new disintegrating formulations. The main aim of this article is to develop new ODT technologies and evaluation methodologies in order to enhance patient compliance.

Key words: Risedronate sodium, Orodispersible, Patient compliance, Evaluation methodologies.

1. INTRODUCTION

For most therapeutic agents used to produce systemic effects, the oral route still represents the preferred way of administration owing to its several advantages and ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance compared too many other routes [1]. Mainly drawback of solid dosage forms for some patients is the difficulty in swallowing or dysphasia is currently affecting 35% of general population. Drinking water plays an important role in the swallowing of oral dosage forms [2]. For these reasons tablets that can easily dissolve or disintegrate in the oral cavity have attracted a great deal of attention. To fulfill these medical needs, pharmaceutical technologists have developed a novel oral dosage form known as Orodispersible Tablets (ODTs) which disintegrate rapidly in saliva, usually in a matter of seconds, without the need to take water. Usually, Superdisintegrant are added to a drug formulation to facilitate the breakup of or disintegration of tablet content into smaller particles that can dissolve more rapidly than in the absence of disintegrants [3]. Drug dissolution and absorption as well as onset of clinical effect and drug bioavailability may be significantly greater than those observed from conventional dosage forms. Many substances like microcrystaline cellulose, crospovidone, Croscarmellose, sodium starch giycolate have been used in the formulation of fast disintegrating tablets [4].

Risedronate sodium or risedronic acid is a bisphosphonate used to strengthen bone, prevent osteoporosis and it has rare side effects. Osteoporosis mainly occures due to lack of calcium in bones.

2. MATERIALS AND METHODS

2.1. Materials

Risedronate sodium and crosspovidone were gifted by Okasa Pharma, Satara. Microcrystalline cellulose 102, Mannitol was received as a gift sample from India Sea Foods, Cochin, Kerala. Sodium starch glycolate (Maple Biotech Pvt. Ltd., Pune). Crosscaramellose sodium, Aspartame, Magnesium stearate and Talc analytical grade purchased from Raj Chemicals, Karad.

2.2. EXPERIMENTAL

2.2.1. Preparation of mixed blend of drug and excipients

All the ingredients were passed through mesh no.60. Required quantity of each ingredient was taken for each specified formulation and all the formulation was subjected to grinding to a

required degree of fitness [5]. The powder blend was evaluated for flow properties as follows:

2.2.1.1. Angle of Repose

Angle of repose was determined using funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained [6]. Radius of the heap(r) was measured and the angle of repose (q) was calculated using the following formula [7]:

Angle of repose= $\tan^{-1}$ (h/r)

2.2.1.2. Bulk density

Apparent bulk density (pb) was determined by pouring the blend into the graduated cylinder. The bulk volume and weight of the powder was determined [8]. The bulk density was calculated using the following formula,

Pb= M/v

2.2.1.3. Tapped density

The measuring cylinder containing a known mass of blend was tapped for a fixed time[9]. The minimum volume (vt) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density was calculated using the following formula

Pt=M/Vt

2.2.1.4. Compressibility index

The simplest way of measurement of free flow of powder is compressibility, a indication of the ease with which a material can be induced to flow is given by compressibility index(I) which is given as follws

I=Vo-Vt/Vbx

Vo is the bulk volume

Vt is the tapped volume

The value below 15% indicates good flow characteristics and the above 25% indicates poor flow characteristics [10].

2.2.1.5. Hauser, s Ratio

Hauser,s Ratio is an indirect index of ease of powder flow calculated by following formula**:**
Hauser, s Ratio= Pt/Pd

Where Pt is tapped density and Pd is bulk density [11]. Lower Haauser ratio (1.25) indicates better flow properties than higher one (1.2**)**

2.2.1.6. Preparation of Risedronate sodium tablets

Residronate sodium tablets were prepared by direct compression method. All the six formulations were showed in table 1.

2.2.2. Evaluation Tests

2.2.2.1. in-vitro Disintegration time

The in-vitro disintegration time was determined using disintegration test apparatus. A tablet was placed in each of the six tubes of the apparatus and one disc was added to each tube. The time in seconds taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds [12].

2.2.2.2. Wetting time

The method reported by was followed to measure tablet-wetting time [13]. A piece of tissue paper folded twice was placed in a small petridish (ID = 6.5 cm) containing 6 ml of simulated saliva pH 6.8, a tablet was put on the paper, and the time for complete wetting was measured [14]. Three trials for each batch were performed and standard deviation was also determined.

2.2.2.3. Drug content uniformity:

The drug content was determined by analyzing sample equivalent to 10 mg of drug in to simulated saliva and absorbance was taken against the blank at 235 nm using double beam UV- Visible Spectrophotometer [15].

2.2.2.4. Taste evaluation:

The 10 healthy human volunteers held the disintegrated particles in the mouth for 30 seconds and the taste sensation felt was recorded[10]. Volunteer's opinion for bitterness levels were recorded by giving different score values i.e. 0: no bitterness, 1: acceptable bitterness, 2: slight bitterness, 3: moderate bitterness, 4: strong bitterness. Descriptive statistics mean and standard deviation were calculated for all variables.

2.2.2.5. Stability studies:

Stability studies were carried out at 40 ± 2^0C / 75 ± 5% RH for a period up to 30 days for selected formulations according to ICH guidelines (Table 4).

2.2.2.6. Dissolution studies:

Dissolution studies were carried out in 0.1N Hcl buffer [16]. All the dissolution profile is shown in fig no 1. Risedronate sodium dissolution was carried out at 235nm by uv spectrophotometric method.

3. RESULTS AND DISCUSSIONS

The present invention was undertaken to formulate Risedronate sodium into orally disintegrating tablet formulation using direct compression technique for the treatment of orally Osteoporosis disease.

Table – 1: Formulation.

Ingredients	F1	F2	F3	F4	F5	F6
Risedronate Sodium	5	5	5	5	5	5
Mannitol	59.5	57	59.5	57	59.5	57
MCC 102	25	25	25	25	25	25
SSG	2.5	5	-	-	-	-
CCS	-	-	2.5	5	-	-
CP	-	-	-	-	2.5	5
Aspartame	5	5	5	5	5	5
Magnesium Stearate	2	2	2	2	2	2
Talc	1	1	1	1	1	1

MCC: Microcrystalline cellulose**, SSG:** Sodium starch glycolate**, CCS:** Crosscaramellose sodium, **CP :** Cross povidone

Table - 2: Results for pre and post compression studies.

Parameters	F-1	F-2	F-3	F-4	F-5	F-6
Angle of repose	25.33	26.50	29.80	26.56	32.53	28.67
Bulk density	0.364	0.380	0.389	0.410	0.428	0.36
Tapped density	0.531	0.546	0.533	0.601	0.611	0.52
Carr's index	28.45	31.20	27.27	31.50	28.57	26.53
Hausner ratio	1.42	1.40	1.35	1.46	1.40	1.38
Thickness(mm)	5.03	5.01	5.02	5.04	5.03	5.01
Hardness(kg/cm^2)	4.75	4.1	4.2	4.5	4.5	3.8
Friability (%)	0.05	0.06	0.04	0.05	0.05	0.03
Disintegration Time(sec)	25-40	25-50	10-15	10-15	15-20	20-25
Wetting time(sec)	20	25	20	18	15	16

Table – 3: Assay and dissolution results.

Parameters	F-1	F-2	F-3	F-4	F-5	F-6
Content uniformity (%)	101.5	85.86	90.75	95.5	99.8	87.85
Drug release (%)	80.5	89.87	91.43	94.67	98.93	86.3

Table - 4: Stability data of formulation F5 at 40 ± 2^{0}C / 75± 5% RH

Time in days	Physical changes	Percentage of drug content*±SD	Moisture content	Percentage of drug release * ± SD (99.5% of release label claim in 10 min).
1st day (initial)	Round, yellow color uncoated tablets with plain on both side.	99.51±0.48	0.82	99.5%
30th day	No changes	99.35±0.11	0.78	99.2%
60th day	No changes	98.12±0.13	0.80	99.3%
90th day	No changes	97.81±0.28	0.78	99.2%

* SD- Standard deviation

and from that, F1, F2 with SSG at concentration of 2.5%, 5% respectively were not satisfactory with the disintegration time and hardness (Table 2). F4 with crosscaramellose 2.5% produced satisfactory

results with DT (disintegration time) of 23 sec. F5 crospovidone with produced a satisfactory results with DT of 25 sec and hardness 4.5 Kg\cm^2. Out of six formulation F4&F6 were satisfactory with their hardness and DT. Stability studies were performed for initial, 30 days and 60 days period (Table 4) and solubility study of the API also performed which showed solubility in 0.1 N HCl was more than in water. Content uniformity and dissolution profile values were shown in table 3.

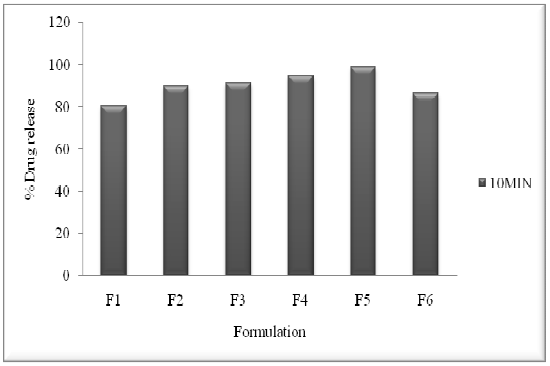

Figure -1: Dissolution Profile of Risedronate Sodium IR Tablets

4. CONCLUSION

From all the above observations it was concluded that the formulation F5 found to be better formulation in terms of rapid disintegration and maximum percentage drug release when compared with all other formulations. Prepared tablets disintegrate within few seconds without need of water; thereby enhance absorption leading to increase bioavailability. Thus the present study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and increased patient compliance.

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