ISSN: 0976-3031

Available Online at http://www.recentscientific.com

International Journal of Recent Scientific Research
Vol. 7, Issue, 10, pp. 13802-13806, October, 2016

International Journal of Recent Scientific Research

Research Article

FORMULATION DEVELOPMENT AND EVALUATION OF RAPIDLY DISINTEGRATING ANTACID TABLETS

Gadhve Manoj V., Garje Vaibhav N., Narad Vaibhav R., Gaikwad D.D and Jadhav S.J

Department of Pharmaceutics:-VJSM'S Vishal Institute of Pharmaceutical Education and Research, ALE, Pune. 412411

ARTICLE INFO

Article History:

Received 05th July, 2016
Received in revised form 08th August, 2016
Accepted 10th September, 2016
Published online 28st October, 2016

Key Words:

Rapidly disintegrating tablet, antacid, superdisintegrants, acid neutralizing capacity.

ABSTRACT

Aluminum hydroxide is an effective oral antacid. It is available in form of dried aluminum hydroxide gel consist largely of hydrated aluminium oxide together with varying quantities of basic aluminium carbonate & bicarbonate. Rapidally disintegrating tablets are those that dissolve or disintegrate quickly in the oral cavity, resulting in solution or suspension. The effectiveness of formulation was tested by Rosette-Rice test.

INTRODUCTION

Aluminium hydroxide and Magnesium trisilicate are used as a antacid to treat conditions caused by the acid that is produced by the stomach. The stomach naturally secretes an acid i.e. hydrochloric acid which cause the contents of the stomach to be acidic in nature. Antacid perform a neutralization reaction, principal mechanism of action is reduce the intragastric acidity. They directly neutralize acid, thus raising the gastric ph this also has the effect of inhibiting the activity of peptic enzymes. Antacid inhibit the conversion of pepsionogen to pepsin, which depends on the degree of acid neutralization.7

Oral disintegrating antacid tablet are solid single unit dosage forms that are to be placed in the mouth, allowed to disperse or dissolve in the saliva, and then swallowed without the aid of additional water. Formulated Oral disintegrating tablet should disintegrate in the mouth within seconds.

MATERIAL AND METHODS-[1-3]

Dried aluminium hydroxide gel and magnesium trisilicate are the main drug purchase from SD fine chem. Ltd. mumbai. The other excipient use are SSG, cross carmellose sodium, crospovidone, microcrystalline cellulose, magnesium stearate, mannitol, talc, saccharin sodium.

Formulation of Tablets-[13,6]

Rapidly disintegrating antacid tablet was formulated by using direct compression method.

Formula for rapidly disintegrating antacid tablet. Evaluation of formulated tablet

Preformulation Study

Angle of repose

Angle of repose has been used to describe flow properties of solids. A funnel with 10mm inner diameter of stem was fixed at height of 2cm over the platform.10gm sample was slowly passed through the wall of funnel until the tip of pile formed and touches to the stem of funnel. a rough circle was drawn around the pile base and radius of powder cone was measured. Angle of repose determined by following formula

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

Bulk density

Accurately weighed 5 gm of powder blend was transferred in 50ml graduated cylinder. Powder was carefully leveled without compact in and read the unsettled apparent bulk volume. Bulk density determined by following formula- Bulk density=Wt of powder in gm/Bulk volume Tapped density-Accurately weighed 5gm blend was transferred in 50ml graduated cylinder. Then the cylinder was, mechanically tapped by raising the cylinder and allowing it to drop under its own

**Corresponding author: Gadhve Manoj V*
Department of Pharmaceutics:-VJSM'S Vishal Institute of Pharmaceutical Education and Research, ALE, Pune. 412411

weight. Cylinder was tapped 500times.It is determined by following formula-

Tapped density= wt of powder/Tapped volume

Carr's index-The Carr's index of powder blend was determined by cords compressibility index. the formula for corr's index is
Carr'sindex(%)=TD-BD*100/Bulk density

Hausner's ratio-Hausner's ratio is a number i.e. correlated to flowability of powder. Formula for Hausner's ratio
Hausner's ratio=TD/BD

Post Compression Evaluation

General appearance-20Three tablets from each batch were randomly selected and organoleptic property such as colour, odour, taste, shape were evaluated.

Thickness-20 Three tablets was measured vernier caliper. The extent to which the thickness of each tablet deviated from ±5% of the standard value was determined.

Hardness:-20 The tablet were tested for hardness by using calibrated hardness tester (Monsanto). It is nothing but the force required for the breaking of tablet.

Friability test:[4-6] The friability test was done by using the Roche friabilator (4 mines at 25 rpm). 20 tablets were selected for the test.

Uniformity of weight*:-40-67* the 20 tablets were selected, weighed individually and average deviation was determined. Not more than 2 tablets deviate from the average weight by more than 5%.

Wetting time: [12] the following procedure was used to measure tablet wetting time. A piece of tissue paper folded twice was placed in a small culture dish (i. d. = 6.5 cm) containing 6 ml of water. A tablet was placed on the paper, and the time required for complete wetting of the tablet was measured and reported.

Disintegration test:-[6] the disintegration test was carried out by using the disintegration apparatus. Six tablets were placed in each tube. Raise and lower the tube in such manner that complete up and down movement is repeated 28 and 32per minute. The tablet were disintegrated when no particle remains above the gauge, which readily pass through 10 mesh screen.

Preliminaery Antacid Test (PAT):[6] an accurately weighed quantity of the uniform mixture, equivalent to the minimum labeled dosage, was transferred into 100ml beaker. Sufficient quantity of water was added to obtain a total volume of 40 ml, mixed well on a magnetic stirrer at 300 ± 30 rpm for a minute. Then 10 ml 0.5 N HCl was added to the test solution while stirring on the magnetic stirrer at 300 ± 30 rpm for about 10 minutes. The pH of mixture was recorded. The sample should raise pH above 3.5 within 10 minutes. The samples which comply this test can be labeled as antacids.

Acid Neutralising Test (ANC): [7]

This test is used to check effectiveness of an antacid formulation. The ANC value of a formulation must be more than 5 mg per dose (minimum labelled dose), so that it can be considered as an antacid.

Preparation of test solution*:-* In this method, transferred an accurately weighed quantity of the uniform mixture, equivalent to the minimum labeled dosage, to a 250ml beaker and water was added to make a total volume of about 70 ml and mixed on the magnetic stirrer for1 min.

Procedure: Pipetted 30 mlo f1 NHCl and added in to the test solution prepared as per above mentioned procedure and kept for stirring with the magnetic stirrer. Stirredfor1 5min, accurately timed, after the addition of the acid, and titrated immediately, and within a period not exceeding an additional 5 minutes. The excess of HCl was titrated with0.5N NaOH to attaina stable pH of 3.5. The acid neutralizing capacity was calculated as each ml of 1 N HCl is equal to one meq of acid consumed. The whole experiment was conducted maintaining the solution temperature at $37^0C \pm 1^0C$. Calculated the number of meq of acid consumed and expressed the results interms of m Eqofacid consumed per dose of the substance tested.

Reheis test: [8]

It is a reaction velocity test indicating the time required to raise pH to 3.0 and thereby shows the speed of neutralization of the acid by the drug.

Rosette-Rice test:[9]

It is an acid neutralizing dynamic test. It is an *in vitro* method reflecting the efficacy of dose of antacid. The Rosette-Rice test attempted to stimulate the stomach, and to record the pH profile during acid neutralization. The pH profile during the neutralization reaction was followed by adding 70 ml of 0.1 N HCl and 30 ml of distilled water, to a 500 ml reaction beaker. When the temperature was maintained at 37°C, an equivalent weight of tablet sample was added introduced into the reaction beaker under continuous magnetic stirring. Then, 0.1N hydrochloric acid was continuously added at a rate of 2 ml / min, from a burette. A pH meter was attached to the reacting vessel, to record the pH during the neutralization reaction. The time taken to reach pH 3.0 and Rosette-Rice time (RRT) i.e. the time during which the pH maintained between pH 3.0 and 5.0, was noted and also the pH changes were recorded as a function of time.

Stability Studies: [10-11]

Stability of a drug has been defined as the ability of a particular formulation, in a specific container, to remain within its physical, chemical, therapeutic and toxicological specifications The stability studies for the optimized formulation (Formulation F7) were performed for 3 months at 5°C, room temp and 40°C. The physical and chemical evaluations were performed routinely. The parameters like physical appearance, disintegration time, % drug content, and Acid neutralization capacity were tested routinely during these studies.

RESULT AND DISCUSSION

Results for the Preformulation Evaluation

Description

Table 1 Description of the drugs.

Name of drug	Description of the drug
Dried aluminium hydroxide gel	It is a white, light, amorphous powder containing some aggregates; odorless; tasteless.
Magnesium trisilicate	It is a fine, white on early white powder, odorless, tasteless powder, free from grittiness; slightly hygroscopic.

Solubility

Table 2 Solubility of the drugs in different solvents.

Name of solvent	Name of the drug	
	Dried aluminium hydroxide gel	Magnesium trisilicate
Water ,Methanol	Insoluble	Practically insoluble
Methanol	Insoluble	Practically insoluble
pH 6.8 phosphate buffer	Insoluble	Insoluble
0.1 N HCl	Soluble	Soluble
0.1 N H_2SO_4	Soluble	Soluble

pH of drug solution

Table 3 pH of drug solutions

Name of the drug	pH of drug solution
Dried aluminium hydroxide gel	9.4
Magnesium trisilicate	6.3

Evaluation of Pre-Compression Parameters of Powder Blend Prepared For Direct Compression

Table 4 Results of pre-compression parameters of powder blend

Formulation	Bulk density (g/mL)	Tapped density (g/mL)	Angle of repose (ϕ)	% Carr's index (CCI)	Hausner's ratio
F1	0.2629	0.3367	31.4443	21.0106	1.2659
F2	0.2688	0.3278	27.5907	18.0107	1.2196
F3	0.2680	0.3289	27.9317	18.4986	1.2269
F4	0.2645	0.3300	30.1816	19.8415	1.2475
F5	0.2666	0.3246	26.9165	17.8666	1.2175
F6	0.2659	0.3289	28.4039	19.1489	1.2368
F7	0.2673	0.3322	29.7166	19.5187	1.2425

Evaluation of Tablets / Post-Compression Parameters

Results for the General appearance

Table 5 Results of general appearance evaluation of formulations of step 1.

Parameters	Formulation code						
	F1	F2	F3	F4	F5	F6	F7
Colour	White	White	White	White	White	White	White
Odour	Sweet	Sweet	Sweet	Sweet	Sweet	Sweet	Sweet
Taste	Sweet	Sweet	Sweet	Sweet	Sweet	Sweet	Sweet
Shape	Round	Round	Round	Round	Round	Round	Round

Uniformity of weight (weight variation test)

Table 6 Results of weight variation test of formulations of step 1.

Parameters	Formulation code(in mg)						
	F1	F2	F3	F4	F5	F6	F7
Total weight of 20 tablets	10766.1	10932.4	10920.9	10855.1	10923.8	10929	10962.7
Average weight	538.305	546.62	546.045	542.755	546.19	546.45	548.135
Weight variation	538.305 ±1.652%	546.62 ±1.862%	546.045 ±2.079%	542.755 ±1.576%	546.19 ±1.444%	546.45 ±1.948%	548.135 ±3.149%

Hardness: Table7 Results of hardness test of formulations of step 1.

Formulation code	Hardness (Kg / cm^2)			
	A	B	C	Mean ± S. D.
F1	3.5	4.0	4.0	3.8333 ± 0.2357
F2	5.0	5.0	5.5	5.1667 ± 0.2357
F3	4.5	5.0	5.0	4.8333 ± 0.2357
F4	4.0	4.0	4.5	4.1667 ± 0.2357
F5	5.0	5.5	5.5	5.3333 ± 0.2357
F6	4.5	4.5	4.0	4.3333 ± 0.2357
F7	4.0	4.5	4.0	4.1667 .2357

Disintegration time (sec) in 0.1N HCl

Table 8 Disintegration time in distilled water of formulations of step 1.

Formulation code	Disintegration time (Sec) in 0.1 N HCl
F1	38
F2	15 min 17 sec
F3	8 min 11 sec
F4	92
F5	21 min 22 sec
F6	207
F7	**64**

Hardness

Table 9 Results of hardness test of formulations of step 2.

Formulation code	Hardness (Kg / cm^2)			
	A	B	C	Mean ± S. D.
F1	3.5	4.0	4.0	3.8333 ± 0.2357
F4	4.0	4.0	4.5	4.1667 ± 0.2357
F7	4.0	4.5	4.0	4.1667 ± 0.2357

Thickness

The thickness of tablets was measured by using Vernier callipers.

Table 10 Thickness of various formulations of step 2.

Formulation code	Thickness (mm)			
	A	B	C	Mean ± S. D.
F1	3.361	3.35	3.339	3.35 ± 0.008981
F4	3.331	3.291	3.35	3.324 ± 0.024589
F7	3.324	3.328	3.329	3.327 ± 0.002160

Friability

Table 11 Results of friability test of formulations of step 2.

Formulation code	% Friability			
	A	B	C	Mean ± S. D.
F1	1.17	1.09	1.04	1.10 ± 0.05354
F4	0.8503	0.8132	0.8295	0.831 ± 0.01583
F7	0.995	0.962	0.977	0.978 ± 0.01349

Wetting time

Table 12 Wetting time of formulations of step 2.

Formulation code	Wetting time (Sec)			
	A	B	C	Mean ± S. D.
F1	68	65	67	66.66 ± 1.2472
F4	144	151	146	147.0 ± 2.9439
F7	96	88	93	92.33 ± 3.2998

Content uniformity (Assay of drug)

Table 13 % drug content of formulations of step 2.

Formulation code	Drug content (%)	
	Dried aluminium hydroxide gel (Mean ± S. D.)	Magnesium trisilicate (Mean ± S. D.)
F1	98.66 ± 0.4871	99.15 ± 0.3149
F4	100.84 ± 1.0325	100.98 ± 0.8662
F7	99.26 ± 0.5143	100.17 ± 0.5272

Preliminary antacid test (PAT)

Table 14 Results of preliminary antacid test of formulations of step 2.

Formulation code	pH of mixture (after 10 min)			
	A	B	C	Mean ± S. D.
F1	4.59	4.64	4.66	4.63 ± 0.02943
F4	4.61	4.53	4.63	4.59 ± 0.04320
F7	4.58	4.61	4.66	4.6166 ± 0.03299

Acid neutralizing capacity test (ANC)

Table 15 Acid neutralization capacity (ANC) of formulations of step 2

Formulation code	Acid neutralization capacity (ANC) in mEq / dose			
	A	B	C	Mean ± S. D.
F1	10.70	10.70	10.75	10.7166 ± 0.02357
F4	11.0	10.85	11.05	10.9666 ± 0.08498
F7	11.10	11.20	10.95	11.0833 ± 0.1027

Reheis test

Table 16 Reheis time of formulations of step 2.

Formulation code	Reheis time (RT) in min
F1	4 min and 10 seconds
F4	7 min and 5 seconds
F7	4 min and 55 seconds

Rosette-Rice test

Table 17 Rosette-Rice time profile of formulations of step 2.

Time (in min)	pH of mixture of formulation		
	F1	F4	F7
0	5.08	4.71	4.96
5	4.54	4.18	4.39
10	3.94	3.62	3.76
15	3.48	3.27	3.39
20	3.14	2.98	3.06
25	2.95	2.83	2.89
30	2.84	2.75	2.81
35	2.80	2.71	2.75

Table 18 Results of Rosette-Rice time of formulations of step 2.

Formulation code	Rosette-Rice time (RRT) in min
F1	23 min 37 seconds
F4	19 min 18 seconds
F7	21 min 32 seconds

The Rosette-Rice time of formulations F1, F4 and F7 was found to be 23 min 37 seconds, 19 min 18 seconds and 21 min 32 seconds respectively.

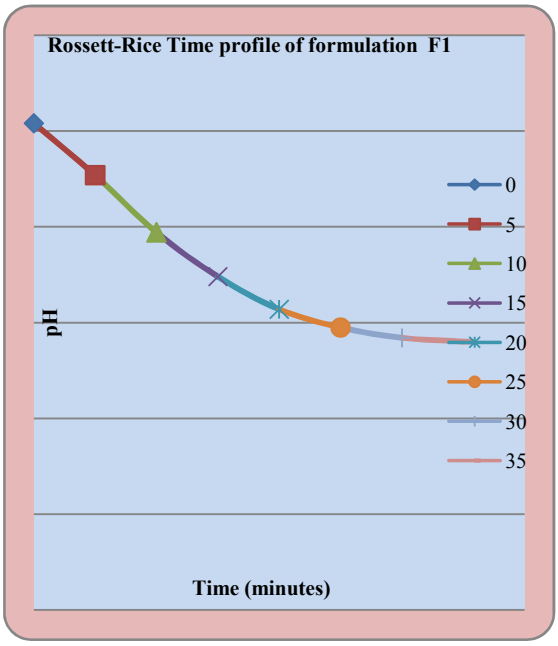

Figure 19 Rosette-Rice time profile of formulation F1.

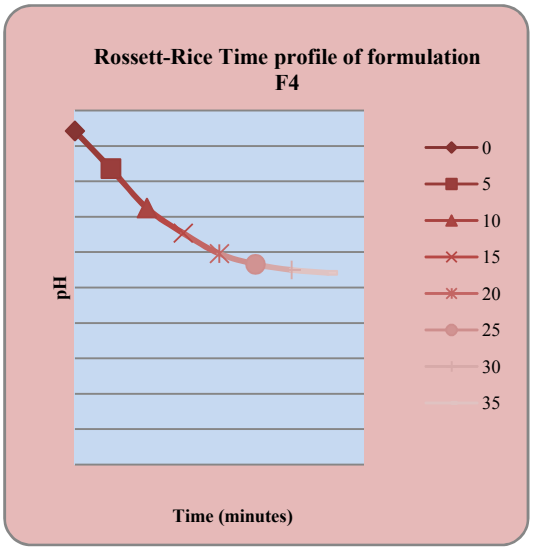

Figure 19 Rosette-Rice time profile of formulation F4

Stability studies

Table 20 Results obtained after three months of stability studies.

Formulation parameters tested		Initial results	At 5°C ± 2°C	At 25°C ± 2°C / 60 % RH	At 40°C ± 2°C / 75 % RH
Colour		White	-	-	-
Odor		Sweet	-	-	-
Mouth feel		Pleasant	-	-	-
Taste		Sweet	-	-	-
In-vitro disintegration time (Sec) in Distilled Water		58.00	57.00	58.66	58.33
In vitro disintegration time (Sec) in 0.1N HCl		61.33	61..66	61.33	59.00
% drug content	Dried aluminium hydroxide gel	99.26	98.87	98.54	98.04
	Magnesium trisilicate	100.17	99.84	99.55	99.12
Acid neutralization capacity in mEq		11.0833	10.914	10.757	10.583

CONCLUSION

In the present work, the rapidly disintegrating tablets containing dried aluminium hydroxide gel and magnesium trisilicate were successfully formulated using suitable excipients to delivery of drug via oral route. The drugs (dried aluminium hydroxide gel and magnesium trisilicate) and excipients like sodium croscarmellose, crosspovidone, sodium saccharin, sodium starch glycolate, microcrystalline cellulose (pH 101), mannitol, magnesium stearate and talc are compatible with each other. different formulations were prepared and coded as F1, F2, F3, F4, F5, F6 and F7.All the formulations have tested for preliminary requirements of rapidly disintegrating tablets and only those formulations (i.e. F1, F4 and F7) conforming the requirements of rapidly disintegrating tablets were subjected to the evaluation of post-compression characters. All three formulations have shown good post-compression characters: but formulation F7was proved superior due to its less disintegration time. The optimized formulation F7 was subjected to stability studies as per ICH Guidelines.

Hence, rapidly disintegrating tablets containing dried aluminium hydroxide gel and magnesium trisilicate may be an

advantageous alternation for other oral conventional tablets, chewable tablets and suspensions of dried aluminium hydroxide gel and magnesium trisilicate formulation and improved the compliance in patients (old age) finding difficulty to swallow tablets in the treatment of acid peptic disorders.

References

1. RoweRaymond C., SheskyPaul J., and QuinnMarian E, Handbook of Excipients, Published by Pharm. press. New York, (2009), 6th edition, pp. – 120-133, 206-210, 404-409, 424-428, 608-609, 663-665, 728-730.
2. Aulton M. E., Pharmaceutics science of dosage form and design, 3rd edition, 2007, pp. – 355 – 357.
3. Martin, Physical pharmacy and pharmaceutical sciences, 5th edition, 2006, pp. - 553-558.
4. Indian Pharmacopoeia, Government of India 2007, Ministry of Health and Family Welfare, Delhi: Published by the controller of Publications, Vol - I, 5th edition, pp. – 182 – 183.
5. KonapureSagar A., et al, "Mouth dissolving tablets" an innovative technology, *International Journal of Applied Biology and Pharmaceutical Technology*, Volume: 2: Issue-1: Jan-Mar -2011, 496 – 503.
6. HiraniJaysukh J, RathodDhaval A, VadaliaKantilal R, Orally Disintegrating Tablets: A Review, Tropical *Journal of Pharmaceutical Research*, April 2009; 8 (2), 161-172.
7. United States Pharmacopoeia, USP/NF 2009, The Official Compendia of Standards, Asian Edition, Volume I, pp. – 139 - 140.
8. Paradkar A. R., Studies on ShankhaBhasma – I Antacid activity evaluation of ShankhaBhasma, *Indian journal of pharmaceutical sciences, Sep – Oct* 1997, 254 – 256.
9. Gainotti Alessandro et.al, the effect of residual water on antacid properties of sucralfate gel dried by microwaves, AAPS PharmSci Tech 2006; 7 (1), E1 - E2.
10. Banker G. S. and Rhodes C. T., Modern pharmaceutics, 3rd Edition, NewYork: Marcel Dekker, INC; 1996, pp. - 205.
11. Stability Testing Guidelines: Stability Testing of New Drug Substances and Products, The European Agency for the Evaluation of Medical Products, London 2003, 1 - 21.
12. SinghShailendra Kumar, MishraDina Nath, JassalRishab, SoniPankaj, Fast disintegrating combination tablets of omeprazole and domperidone, Asian *Journal of Pharmaceutical and Clinical Research*, Vol.2 (3), July-September 2009, 74-82.
13. Lachman L., Lieberman H. A., Kanig J. L., The theory and practice of Industrial pharmacy, Varghese Publishing House Bombay; special Indian edition, 2009, pp. -66 - 70, 296 -303, 430 - 440.

****

How to cite this article:

Gadhve Manoj V *et al*.2016, Formulation Development and Evaluation of Rapidly Disintegrating Antacid Tablets. *Int J Recent Sci Res.* 7(10), pp. 13802-13806.