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Comparative Study of Four Different Brands of Ranitidine Available in Karachi

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Abstract

Ranitidine is used in peptic ulcer therapy and available as several brands in the market which makes it difficult to select the safe, effective and economic one. The aim of this study is to establish similarity among the different brands of ranitidine HCl tablets available in local market of Karachi, Pakistan. Four different brands of (150 mg) were selected for the study. Six quality control parameters: weight variation test, hardness test, thickness, friability, disintegration test and dissolution test were carried out specified by USP. Result revealed that all brands comply within limits for hardness, weight variation, thickness, friability, disintegration and dissolution. Disintegration time for all brands was within 15 minutes complying with the USP commendation. All brands showed Q-value more than 80% within 45 minutes. The present findings suggest that almost all the brands of ranitidine HCl that are available in Karachi meet the USP specification for quality control analysis and are interchangeable.

Keywords: Ranitidine HCl; Comparative study; Pharmaceutical formulations

Introduction

Comparative analysis is carried out to check, compare and evaluate the quality standards of commercially available local pharmaceutical brands of tablets with that of multinational pharmaceutical brands in Pakistan as prescribed by B.P. & U.S.P. Local and Multinational brands of drugs were evaluated comparatively for their physical and chemical parameters [1]. It is said that marketed oral drugs will generally possess favorable physiochemical properties with respect to absorption, metabolism, distribution, and clearance [2].

Ranitidine is Figure 1, an H_2 receptor antagonist that inhibits the acid production from stomach, it is used in the treatment of duodenal and gastric ulcer caused by helicobacter pylori infection, and for the treatment of gastrointestinal reflux disease [3]. It inhibits the secretion of acid which is stimulated by pentagastrin (an-enzyme), meal and histamine [3,4]. Histamine is a natural chemical that stimulates the stomach cells to produce acid [5]. Ranitidine is a new histamine H_2-receptor antagonist which does not contain imidazole group unlike cimetidine. On a weight basis, ranitidine is 4 to 10 times more potent than cimetidine in inhibiting stimulated gastric acid secretion in humans [4,6]. Ranitidine has a greater selectivity of action than cimetidine so avoiding certain unwanted effects such as interference with enzymatic degradation of a wide range of drugs metabolized by the liver [7]. Ranitidine acts by inhibiting parietal cell H_2 receptor competitively and suppress the normal secretion of acid which is stimulated by meal [8]. It is accomplished by two mechanisms blocking of histamine released by ECL cells present in the stomach by parietal cell H_2 receptor which in turns block the cascade of acid secretion and secondly blocking the other factors like acetylcholine and gastrin (enzyme) which have reduce but effect on H_2 receptors [6,9].

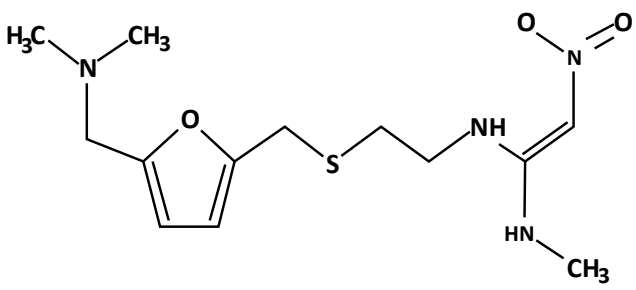

Figure 1: Ranitidine Molecular Structure ($C_{13}H_{22}N_4O_3S.Hcl$).

Like the H_1-antihistamines, the H_2 antagonists are inverse agonists rather than true receptor antagonists. The H_2-antagonists offer numerous benefits over antacids, including prolong duration of action i.e. 6-10 hours as compare to 1-2 hours for other antacids greater and bears efficacy and ability to be used prophylactically before meals to minimize the possibility of heartburn after food intake [9] (Figure 1).

Ranitidine is widely used in short term treatment of duodenal ulcer and in the management of hypersecretory conditions [4,10,11]. The dose recommended by WHO for ranitidine is 150 mg tablet containing ranitidine base, given as the hydrochloride salt [4,11]. Twice-daily treatment with ranitidine 150 mg is a valuable therapy for GERD in a typical family practice setting and reduces the frequency and severity of symptoms within the first 24 to 48 hours of treatment [12]. Another study conducted in Oman showed that different brands of ranitidine

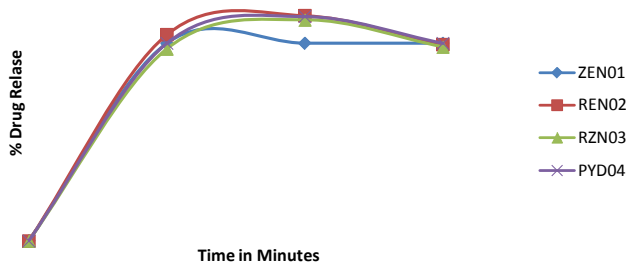

Figure 2: %Drug Release of various brands Vs. Time.

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available in market that pharmaceutical equivalent with a slight difference in manufacturing process [13].

The aim of the study is to evaluate equivalence of different ranitidine HCl tablets brands of available in Karachi. Comparison of the quality aspects of ranitidine will help for the selection of best brand of drug by the pharmacist or doctors. This study aims to provide the proof of safety, effectiveness of the drugs can be used.

Methodology

Test performed in order to conduct a comparative study between four different brands of active ranitidine, available in market of purchased and coded as ZAN01 (multinational brand taken as standard) and three local brands given serial no as REN02, RZN03, PYD04 and tested for following physiochemical parameters in order to conduct a comparative study among the brand leader of multinational company and other local company brands. Following test parameters are performed to evaluate the physicochemical parameters of available brands of ranitidine:

Weight variation

Variation in weight was checked on A.N.D Electronic Balance FX-400. Weight variation between tablet with respect to dose and weight must be within BP limits. For which 20 tablets of each brand is selected randomly. In-process uniformity of weight is a test parameter which ensures evenness of dosage units through compression. The percentage weight variation from average tablet weight was calculated. In order to pass weight variation test, the tablet should be within the limits of the percentage deviation allowed by BP. Upper and lower control limit for weight variation is calculated as per following formula:

Upper control limit: Mean+ 3x Standard Deviation

Lower control limit: Mean- 3x Standard Deviation

And Maximum and minimum weight variation limit in percentage was calculated as per following formula:

Max wt. variation %=(Maximum weight-Average weight)/Average weight×100

Min wt. variation %=(Average weight-Minimum Weight)/Average weight×100

Thickness

The degree of compaction of 20 tablet of each brand is assessed by measuring the thickness of tablets, by using VERNIER CALIPER.

Hardness

This test is conducted on 10 tablets of each brand to determine the strength of tablet when applied mechanical stress. A tablet must be hard enough to endure stress. Hardness of all the brands is checked on MH-1, Hardness Tester of Galvano Scientific. The hardness value of each tablet was evaluated and average value was calculated and compared.

Friability

Friability test has been performed on 10 tablets of each brand of ranitidine by subjecting to a uniform tumbling motion for specified period of time i.e. 25 rotation/minute for 4minutes in FB–1004 CURIO Company and the weight loss is determined. Friability test is done to check if a tablet abrades during transportation by taking initial and final weight and determining the weight loss.

Disintegration

Disintegration Testing is one of the quality control test done to determine whether capsules or tablets are disintegrating within the approved time when placed in a fluid medium. Disintegration test for all brands s was done on CURRO MODEL NO DS-0702. A 900 ml beaker was filled with distilled water and temperature was maintained at 37 ± 2°C. From each brand, 6 tablets of each brand were selected randomly and placed into the basket rack assembly and connected to the disintegration apparatus. The disintegration time for each brand is compared with the Pharmacopoeial limit specified by BP.

Dissolution

This test determines the amount of active ingredient released from oral solid dosage form, i.e. tablet or a capsule, using medium with known volume. Tablet dissolution was conducted on model no. GDT-7L of Galvano Scientific. It is carried out to determine the bioavailability of drug invitro dissolution tests were performed with the paddle apparatus I in 900 ml 0.1 N HCL dissolution media at 100 rpm for 60 minutes. The tablets were placed in the vessels at the beginning of each test and the stopwatch was started simultaneously. In order to minimize evaporation vessels are covered during the run with plastic covers. The temperature in the vessels was maintained at 37 ± 0.5°C throughout every dissolution run. Manually samples are removed using 5 ml syringes fitted with stainless tubing to make certain reproducibility of the sampling site. Samples are filtered. In vitro dissolution testing parameters used for are described in Table below:

Price variation study

Per unit retail price of the different brands of Ranitidine HCl under study was noted and the average price of all brands compared.

Statistical analysis

Data were recorded coded and analyzed statistically using Microsoft Excel and various parameters are evaluated and compared (Tables 2 and 3).

Results and Discussion

Pakistan is one of the developing country that is striving for survival of its economy and cost of living is increasing day by day, in such a scenario people use to show un-affordability towards the use

Parameter of Method	
Apparatus	I
Dissolution Medium	0.1 N HCL
Analytical Instrument	UV-VIS Spectrometer
Wavelength	315nm
Agitation	50 RPM
Degassing	Yes
Volume	900ml
Temperature	37°C
Sampling Time	0, 15, 30, 45, Minutes
Tolerances	NLT 80%(Q) of the labeled amount in 45 min

Table 1: *In vitro* dissolution testing parameters.

SNO	Serial No	Code No	Batch No	Price/10 Units PKR
1	ZAN01	6520	CZBBR	88
2	REN02	47498	RP026	59.45
3	RZN03	42567	1673	56
4	PYD04	42514	027	54

Table 2: Label Information.

SNO	Brand	Mean Weight ± SD mg	Mean Thickness ± SD n mm	Mean Hardness ± SD kg	Friability ± SD in %	Disintegration in min
1	ZEN01	303.2 ± 2.16	5.54 ± 0.069	5.33 ± 0.4	0%	10 min 27 sec
2	REN02	216.2 ± 5.42	4.23 ± 0.067	4.48 ± 0.26	0%	6 min 6 sec
3	RZN03	211.9 ± 2.45	4.26 ± 0.142	7.4 ± 0.4	0%	14 min 35 sec
4	PYD04	257.4 ± 5.8	4.25 ± 0.051	4.01 ± 0.244	0%	11 min 4 sec

Table 3: Mean Weight, thickness, hardness, friability and disintegration of all available brands in Karachi.

of medicine. Here the diet used is usually spicy and other factors like stress is also available that leads to several acidity cases, since they are young. So in such circumstances use of drug like ranitidine becomes necessary to avoid the complications but here the cost of that medicine may affect the compliance level.

This study is based on the comparison of available ranitidine brands in market that are available for consumer use. Four brands of drug was taken that are coded accordingly, batch number and price are mentioned in Table 1 each brand taken was having 150 mg of ranitidine.

Price variation of all the brands are checked and compared indicating a fact that all the local brands are less in price as compare to brand leader while having similar or better physicochemical property. Local brand has taken less time to dissolute and are having all other parameters similar to brand leader, but having low price than ZAN01, indicating the fact that they are physicochemical equivalent with brand leader having cost of Rs 88/10 tablets.

All tablet contain 150 mg active but are of different weight probably because of different excipients use for the manufacturing that are increasing the bulk or weight of the tablet, while others are avoiding this and are having weight less than 250 mg having weight variation up to 7.5% while the brand leader falls in 5% range of deviation from average weight. The other point that should come under light is the disintegration time shown in Table 2, a local brand having serial no REN02 has the least disintegration time that is 6min and 6 sec as compare to the brand leader having disintegration time 10 min 27 sec, while one local brand of same cost has maximum dissolution time that is 14 minutes 35 sec.

All the brands having Q value within the limits that is not less than 80% as given in USP. Dissolution is measured as one of the most significant quality control tests performed on pharmaceutical dosage forms and is now emerging as a tool for calculating bioavailability. Figure 1 explains the % dissolution of available brands at different time interval that are 0,15,30, and 45 mintes, that are about 100% indicating the bioavailability of all the brands.

Conclusion

Hence it is concluded from above discussion that all the available brands in local market of Karachi Pakistan are having physicochemical parameters within the specified quality control range and can be interchange if found any non-compliance due to cost issue.

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