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IN-VITRO COMPARATIVE STUDY OF THREE DIFFERENT BRANDS OF FAMOTIDINE40 MG TABLETS AVAILABLE IN LOCAL PHARMACIES OF KARACHI

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Abstract:

Famotidine 40 mg film coated tablet by invitro comparative study , together with the official and non official compendial test. Famotidine is an aggressive inhibitor of histamine H2-receptors. The pivotal clinically critical pharmacologic activity of Famotidine is to hold of gastric discharge. Both the acid concentration and volume of gastric secreation are concealed by famotidine, while changes in pepsin discharge are relative to volume generation. Famotidine is more potent than other class of drugs like.the drug is intended to release after oral administration for immediate release so we execute testing analysis to illustrate the procedure, the major test for analyzing the effectiveness of drug comprises, dissolution , assay, disintegration time, thickness and weight variation in three brands available in market of Karachi Pakistan. The weight variation test shows outcomes within the limits and all brands dissolves within 30 minutes, every brand showed the drug dissolution more than 75 % within the 30 minutes ,all outcome showed good effectiveness and producing outcomes within the limits and complying the USP recomendation.

Key Words: *Compendial test, immediate release, competitive inhibitor, famotidine, tablets*

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INTRODUCTION:

Famotidine was developed by Yamanouchi Pharmaceutical Co(1) It was licensed in the mid-80s by Merck & Co(2)and is marketed by a organization between Merck and Johnson & Johnson. The imidazole ring of cimetidine was replaced with a 2-guanidinothiazole ring. Famotidine proved to be 9 times extra strong than ranitidine, and 32 times more potent than cimetidine.(3) .Famotidine is a viable histamine H2-receptor antagonist. Its main pharmacodynamic effect in humans is inhibition of gastric acid secretion (4) Famotidine is the most dominant, specific H2-receptor opponent yet existing for ulcer treatment. On a power premise, famotidine is roughly multiple times more viable than ranitidine and multiple times more compelling than cimetidine. Moreover, it expands the gastric mucosal blood stream, bringing about an expanded haemostatic impact.(5) **F**amotidineisN'(aminosulfonyl)-3-[[[2-[(diaminomethylene)amino]-4-thiazolyl]methyl]thio]propanimidamide.

The molecular formula of famotidine is C8H15N7O2S3 and its molecular weight is 337.45. Famotidine is freely soluble in glacial acetic acid, it is a white to pale yellow crystalline compound, slightly soluble in methanol, soluble in water very faintly, and almost insoluble in ethanol(6) Different techniques have been accounted for assessment of famotidine, which comprise of spectrophotometric strategies, spectrophotometric and spectrofluorimetric strategy and investigation by stream infusion .In the present correspondence, a basic spectrophotometric strategy has been made for the evaluation of famotidine from pharmaceutical arrangements (7) For invitro study dissolution tests important they have to advocate in vivo study situation The use of phosphate buffers which do not recount to gastrointestinal lumenal fluids may elucidate the summary in vitro-in vivo correlations obtained for modified release dosage forms(8) It has been uncovered that expanding ionic quality and cradle limit of disintegration media builds prescription discharge rate.(8) catogries in a few pharmaceutical industry, tablet disintegration examination is distinctively used to give genuine in vitro medication discharge data for both quality control purposes, i.e.,solid measurement structure to evaluate group to-bunch consistency, for example, tablets, and medication advancement, i.e., to conjecture profiles fortress in vivo medication discharge . (9)(10) For immediate release tablets, The drug is proposed to be discharged quickly after administration or the tablet is disintegrated in fluid before admission and consequently regulated as solution(10) Generally the more noteworthy the weight connected the harder the tablet., although the attributes of granulation have additionally bearing hardness .a tablet duarability might be resolved using friabilator. For the restorative specialist in the tablet to turn out to be completely accessible for retention the tablet should initially break down and release the medication into the body liquid for disintegration the amount fill in the die determine the heaviness of the tablet the volume of fill is changed in accordance with the initial few of tablets to yield the ideal weight and steady. (11)

Instruments:

Following are the instruments used for analysis of all three brands of famotidine 40 mg tablet. Electronic balance FX 400,Vernier caliper(VC-TY56), Disintegration tester 121-L Galvano scientific,GDT-7L Galvano scientific dissolution tester, p H meter(GH-09) and UV – Visible spectrophotometer Shimadzu(1800)

MATERIALS AND METHODS:

For the comparative study of famotidine 40 mg tablet, Jinnah university for women ,provided the opportunity to conduct the pharmacopeial test, included weight variation test ,disintegration time test ,assay ,thickness and dissolution test at their research lab. All brands were purchased from different pharmacies available in Karachi and all the reagents were provided by Deajung chemical Korea.

Weight Variation Test. Most of the pharmacopeia include a simple weight test on a specified number of tablets, individual weight and the airthmatic mean were calculated. The permitted limit of weight variation in USP not more than 2 tablets differ from the mean by more than 5% and in B.P the permitted limit of weight variation are essentialy the same as that of the USP. For performing weight variation test select 20 tablets of famotidine 40 mg and each tablet weight were recorded in mg, average weight were also noted by using electronic balance.

Thickness Test. The thickness test is nonofficial test and it could be considerd as an additional control to tablet dimension and it increase reproducibility. Calibrated vernier caliper were used to determined the thickness of the tablets. Adjusting the ten individual tablets, sandwiched between the jaw of vernier caliper, record the thickness results in mm.

Disintegration Time. The disintegration test is useful as a quality assurance tool for conventional dosage forms. The disintegration test is carried out by using disintegration tester which was consist of a basket rack holding 6 tubes, open at the top and

bottom, the bottom of the tube was covered by 40 mesh screen, the basket was immersed in a bath of suitable liquid held at 37 °C preferably in a 1 liter beaker. By using disintegration tester 6 tablets were placed in tubes containing baskets and cover it with discs and disintegration time were determined by visualizing each tablet to break and completely dissolved, showing the time in sec or minutes.

Pharmaceutical Assay. Spectrophotometer is suitable for measuring the ultravoilet and visible range of the spectrum. Following are analytical testing method of the famotidine 40 mg tablet by UV-Visible spectrophotometer 1800 UV-VIS (shimadzu).

Diluent Preparation

Methanol : 400 ml
Distilled water : 600 ml
Phosphoric acid : 2 ml
Mixed the above solution and adjusted pH to 5.0 either by NaOH or by Phosphoric acid.

Standard Preparation

Weigh accurately 0.0500 gm of Famotidine standard in 50 ml volumetric flask. Dissolved in diluent and maked up the volume with diluent. Dilute 2 ml of the above solution to 100ml volumetric flask and filled up the volume with diluent and shaked well.

Sample Preparation

Accurately weighed the 20 tablets powder equivalent to Famotidine standard and shift into 50 ml volumetric flask include about 30 ml of diluent and sonicate for about 30 minutes. After 30 minutes maked up the volume with diluent and shaked well. Filtered the above solution through whatman # 1 filter paper. Dilute 2 ml of the above filtrate to 100 ml volumetric flask and filled up the volume with diluent and shaked well .Measured the absorbance of both standard and sample preparation on a suitable spectrophotometer at 265 nm using diluent as blank.

Calculations

Calculate the content of Famotidine per tablet by using following equation.

$$\frac{Asp \times Sw \times 2 \times 50 \times 100 \times P}{Astd \times 50 \times 100 \times Sp.wt. \times 2} = \frac{\% \times Avg.\ wt}{100} = mg/tab.$$

Where,

Asp = Absorbance due to Famotidine in sample preparation.
Astd = Absorbance due to Famotidine in standard preparation.
Sw = Standard weight.
Sp.wt. = Sample weight.
P = Purity of standard.

Dissolution Test. Dissolution tester GDT-7L Galvano scientific used for the comparative study of famotidine 40 mg tablet. Tablet dissolution is a standardized method for measuring the rate of drug release from a dosage form. The principle function of the dissolution test is to optimization of therapeutic effectiveness during product development and stability assessment and routine assessment of production quality to ensure uniformity between products lots.

Dissolution Condition

APPARATUS	USP II (PADDLE)
RPM	50
TIME	30 MINUTES
LIMIT	NLT 75 %

Dissolution Medium

pH 4.5,0.1M potassium phosphate buffer. Prepared by dissolving 13.6 gm of monobasic potassium phosphate (Potassium dihydrogen phosphate) in one liter of water.

Standard Preparation

Weigh accurately 0.0440 g of Famotidine standard in 100 ml of volumetric flask and dissolved in dissolution medium. Pipette 10ml of the above solution into 100 ml volumetric flask and dilute the volume with dissolution medium and shaked well.

Sample Preparation

Place one tablet each in 6 dissolution flask containing 900 ml of dissolution medium, previously adjusted to 37ºC ± 0.5ºC. Immediately operate the apparatus. At the specified time, withdraw the sample from a zone midway after min,30 min between the surface of medium and top of the rotating blade not less than 1 cm from vessel wall. Filtered the sample, evaluated the absorbance of standard and sample preparation on a appropriate spectrophotometer at the wavelength of 265 nm using dissolution medium as a blank.

Calculated the amount of Famotidine dissolved in specified time by using following equation.

$$\frac{Asp \times Sw \times 10 \times 900 \times P}{Astd \times 100 \times 100 \times Sp} = \% \text{ dissolved.}$$

Where,

Asp = Absorbance of sample due to famotidine.
Astd = Absorbance of standard due to famotidine.
Sw = Standard weight.
Sp = Tablet sample.
P = Purity of standard.

RESULTS:

The comparative study of Famotidine 40 mg Tablet showed all the results within the limits and following USP. Physicochemical analysis of three different brands of Famotidine 40 mg tablet followed the weight variation test, disintegration test ,thickness ,diameter, dissolution on single point and assay. Results of weight variation/average weight for Fam-01 was 234.2 mg with (260.127 – 208.272 mg) upper and lower limits,for Fam -2 average weight was 309.5 mg with (356.9 – 262.09 mg) upper and lower limits,for Fam -3 average weight was 201.7 mg with(231.077-172.323mg) upper and lower limits shown in table 02.The results of thickness variation(mm) of Fam- 01 was 4.17 mm with(4.3 – 3.9mm) upper and lower limits, Fam-02 was 4.7 mm with (4.8 – 4.5 mm) upper and lower limits, Fam – 03 was 4.25 mm with (4.85 – 4.01 mm) upper and lower limits shown in table 03. The results of diameter variation of Fam – 01 was 8.83 mm with (9.0 – 8.58 mm) upper and lower limits, Fam – 02 was 9.35 mm with (9.9 – 8.7 mm) upper and lower limits, Fam – 03 was 8.7 mm with (8.89 – 8.50 mm) upper and lower limits shown in table 04.The disintegration test showing results for Fam – 01 was 3 minutes, Fam-02 is 5 minutes,Fam – 03 was 5 minutes with the BP/USP limit(NMT 30 minutes) shown in table 05, The Dissolution test showing the results within the limits. Results for Fam – 01 was 98 %, Fam – 02 was 104.5 %, Fam – 03 is 99.23 % with USP limit NLT 75 % shown in table 6, The results for Assay percent test for Fam -01 is 99.41 % ,Fam-02 was 99.42 % and Fam -03 was 98.08 % with USP limit (90 – 110 %) shown in table 7..

DISCUSSION:

The main objective of this research work was to evaluate and compared the effectiveness of the three different brands of famotidine 40 mg tablet available in local markets of Karachi. According to the BP/USP limits evaluation of physical and chemical test like weight variation test ,thickness, diameter disintegration ,dissolution and assay percent test were showing results within their specified upper and lower limit of 7.5%.There is no official limits of thickness and diameter but all brands of famotidine 40 mg tablet were having similar thickness and diameter within the brands. And disintegration time were also found within the limits of BP/USP , brand Fam-01 were dissolved within 3 minutes as compare to the other brands which were took 5 minutes to dissolved.US Pharmacopeial limits of dissolution test is NLT 75 % in 30 minutes and all brands of famotidine 40 mg tablet dissolved within time but Fam - 02 have shown the excellent results as compared to other brands. assay percent limits of famotidine 40 mg tablet according to the USP have 90 – 110% and all brands were found within the limits.

CONCLUSION:

It was concluded from the results of famotidine 40 mg tablet that all brands showing minor variation in there invitro quality control test but these variation were found under the specified limits of USP/BP, so quality standards of all three brands are same but there is a difference in there packaging and there MRP's.

Table 1 : Specifications of famotidine tablets 40 mg different Brands

NO	Brand Name	Serial number	Code Number	Batch number
1	Nocid	Fam-1	018064	J0022
2	Bessfam	Fam-2	047460	009
3	Famosure	Fam-3	029249	025

Table 2 : Statistical weight Variation test of famotidine tablets 40 mg

No	Serial number	Batch number	Average weight (x)mg U.S.P	Standard deviation (S)	Upper Limit U.S.P (UCL=X+ 7.5 S)	Lower Limit U.S.P (LCL=X+-7.5 S)
1	Fam-1	J0022	234.2	3.457	260.127	208.272
2	Fam-2	009	309.5	6.321	356.9	262.092
3	Fam-3	025	201.7	3.917	231.077	172.323

Table :3 Statistical thickness Variation test of famotidine tablets 40 mg

No	Serial number	Batch number	Average thickness (mm)	Standard deviation (S)	Upper Limit (UCL=X+ 3S)	Lower Limit (LCL=X+- 3 S)
1	Fam-1	J0022	4.17	0.068	4.374	3.966
2	Fam-2	009	4.7	0.048	4.844	4.556
3	Fam-3	025	4.25	0.078	4.484	4.016

Table :4 Statistical diameterVariation test of famotidine tablets 40 mg

No	Serial number	Batch number	Average diameter (mm)	Standard deviation (S)	Upper Limit (UCL=X+ 3S)	Lower Limit (LCL=X+- 3 S)
1	Fam-1	J0022	8.83	0.0823	9.076	8.581
2	Fam-2	009	9.35	0.187	9.911	8.789
3	Fam-3	025	8.7	0.066	8.898	8.502

Table :5 Disintegration test of famotidine tablets 40 mg

Serial number	Code Number	Batch number	Disintegration Time Result (min)	B.P/USP Spec.	Deviation From BP/USP
Fam-1	018064	J0022	3 min	NMT 30 min	Pass
Fam-2	047460	009	5 min	NMT 30 min	Pass
Fam-3	029249	025	5 min	NMT 30 min	Pass

Table :6 Dissolution test of famotidine tablets 40 mg

Serial number	Code Number	Batch number	Dissolution test Result (%)	USP Spec.	Deviation From Official limit
Fam-1	018064	J0022	98.0	NLT 75%	Pass
Fam-2	047460	009	104.5	NLT 75%	Pass
Fam-3	029249	025	99.23	NLT 75%	Pass

Table :7 Assay percent test of famotidine tablets 40 mg

Serial number	Code Number	Batch number	Assay percent test Result (%)	USP Spec.	Deviation From Official limit
Fam-1	018064	J0022	99.41	90 -110%	Pass
Fam-2	047460	009	99.42	90 -110%	Pass
Fam-3	029249	025	98.98	90 -110%	Pass

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