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Comparative Quality Evaluation of Different Brands of Esomeprazole Tablets Available In pharmaceutical market of Bangladesh

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Abstract

Esomeprazole is the S-isomer of omeprazole, used to treat gastro esophageal reflux disease (GERD). It is widely produced and marketed drug by many pharmaceutical companies in Bangladesh. The aim of the study is to compare the different physical parameters including hardness, friability, diameter, thickness, disintegration time, dissolution test and assay for quality evaluation and characterization of tablets of five different brands of Bangladeshi pharmaceutical company. The specified compendial method is followed for their evaluation test. Esomeprazole Mg tablets are enteric coated tablet, there is no disintegration for any brand occurred in 0.1N HCl after 2 hours and all tablets are disintegrated within 30 minutes in phosphate buffer (pH 6.8). Hardness ranges from 5.32 to 7.12 kg/cm2. Drug release after 2 hours in 0.1N HCl were varied from 2.55% to 4.47% which is less than 10% and in phosphate buffer (pH 6.8) the percentage of drug release are between 100.9% and 102.4% after 60 minutes. In case of assay the results of all brands are between 95.28% and 99.40%. The obtained results of all parameters are complied with pharmacopoeial limit. So from this study we can conclude that products of esomeprazole available in Bangladeshi pharmaceutical market meet the quality parameter to satisfy therapeutic efficacy.

Keywords: Esomeprazole, GERD, Proton pump inhibitor, Disintegration, Assay.

Introduction

Esomeprazole is a proton pump inhibitor for the treatment of acid-related diseases such as dyspepsia, peptic ulcer disease, gastroesophageal reflux disease, and Zollinger-Ellison syndrome mainly work by preventing the formation of stomach acid through inhibition of the H+/K+ -ATPase in the parietal cells of the stomach [1, 2] For the wellbeing of the patients, quality of medicine is an absolute necessity. World Health Organization claimed that the manufacturers must undertake responsibility for the quality of the drugs that they produced. [3] Pharmaceutical industry of Bangladesh is now technologically sound with advanced manufacturing facilities. It has grown in the last two decades. After the dissemination of Drug Control Ordinance - 1982, the development of this sector was accelerated. For these developments, the key factors are the skills and knowledge of the professionals and innovative ideas of the people involved in this industry.

About 300 pharmaceutical companies are operating at the moment. Only 3% of the drugs are imported, the remaining 97% come from local companies. [4] Bangladeshi drugs are exporting worldwide including the United States because of its positive developments in the pharmaceutical sector. This sector can develop more and can be an effective exporting sector of Bangladesh if these sectors overcome the underlying obstacles like API importation. [4, 5] The principal criteria for a quality drug product are safety, potency, efficacy, and stability. [6] The major objective of this work is to find out the current status of the quality of the marketed Esomeprazole preparations available in Bangladesh. This work will increase awareness among the health practitioners and drug control authority so that, pharmaceutical manufacturers are forced to produce quality medicine. This study will also provide a comprehensive knowledge about the weight variation, hardness, disintegration, dissolution, percentage of potency of Esomeprazole Mg tablets available in the market and compares these values with the official specifications.

Materials and Methods

Five brands of Esomeprazole tablets, manufactured by five different manufacturers of Bangladesh with labelled contents of 20 mg were obtained from local market. All tablets were of same manufacturing year

Instruments

Dissolution Test Apparatus USP (Minhua, RC-8), UV Visible Spectrophotometer (T60U PG Instruments, England).Electronic Balance (Ohaus CP213 China), Hardness Tester (Monsanto), Friability tester, Disintegration Test Apparatus (Aesico, CAT NO 20066B).

Reagents

Sodium hydroxide (Merck, Germany), and 0.1N HCl, potassium dihydrogen phosphate (Scharlu, Spain) and dipotassium hydrogen phosphate (Scharlu, Spain), distilled water. All the reagents are analytical grade.

Collection of Samples

There are many brands of Esomeprazole tablets in Bangladesh. Samples were collected from retail medicine shop of different areas of Dhaka city and collected samples covered top, middle and lower companies ranked by Bangladesh Pharmaceutical Index, 3Q'2011. The samples were properly checked for their physical appearance, the name of the manufacturer, batch number, manufacturing data, expiration date, manufacturing license number, drug administration registration number, and the maximum retail price at the time of purchase. The samples were then properly coded for analysis (E01, E02, E03, E04, and E05).

Collection of Standard

The reference standard of Esomeprazole was obtained from Incepta Pharmaceutical Ltd. as gift sample for research. The purity of the reference standard was 92.11%.

Weight Variation Determination

20 tablets from each brand products were weighed individually in a weighing balance .The average weight of the tablet, as well as their percentage deviation, were calculated (Table 1). [7]

$$\% \text{ of weight variation} = \frac{\text{Individual weight} - \text{average weight}}{\text{Average weight}} \times 100$$

Hardness Test

Hardness indicates the capability of a tablet to withstand mechanical shocks during handling in manufacturing, packaging, and shipping. [8] The hardness of five brands of Esomeprazole was determined and the observed results are shown in the table-2.

Disintegration Test

6 tablets from each brand were used for the disintegration test in 0.1N HCl at 37 ± 2 ℃ for 2 hours and then in phosphate buffer (pH 6.8) using a disintegration apparatus. The disintegration time was taken to be the time when no particle remained on the basket (Table 3). [9]

Assay

Preparation of Standard Curve: 10 mg of Esomeprazole Mg was measured by the electronic balance and placed in a 100ml volumetric flask and dissolved phosphate buffer (pH 6.8).The concentration of the solution was attained 100µg/ml by adding phosphate buffer (pH 6.8) up to 100 ml.1ml of a solution was taken from the 100 ml of volumetric flask and phosphate buffer was added up to 10 ml and the concentration was 10µg/ml. A series of the standard solution of Esomeprazole e.g. 2, 4, 8, 10, 12, 16 µg/ml, were taken to measure absorbance at 300 nm against a blank for each solution by UV-spectrophotometer .The measured absorbance's were plotted against the respective concentration of the standard solutions which give a straight line (Figure 3).

Preparation of standard solution: To prepare a standard solution, 20 mg of Esomeprazole was measured by the electronic balance and placed in 100 ml volumetric flask and dissolved in methanol. Then the concentration of the solution was attained 200µg/ml by adding phosphate buffer (pH 6.8) up to 100 ml. Then 1 ml of solution was taken and diluted to 10 ml with phosphate buffer and absorbance was measured. To get more precise absorbance it was done at least two times.

Preparation of assay solution: 10 tablets of each brand of Esomeprazole was weighed and powdered. 20 mg of Esomeprazole magnesium equivalent to Esomeprazole was weighed and dissolved in methanol and added phosphate buffer up to about 70 ml. Then the solution was sonicated about 15 minutes in the sonicator. After cooling the solution, phosphate buffer was added into the volumetric flask up to 100 ml and the solution was filtered. 1 ml of sample was taken in a test tube and made the volume 10 ml with phosphate buffer. Absorbance was measured at 300 nm using UV spectrophotometer. This was done at least 3 times for each brand of Esomeprazole.

Calculation: Finally the assay was calculated by using the following equation.

$$\text{Assay of sample} = \frac{\text{Absorbance of sample} \times \text{Weight of standard}}{\text{Absorbance of standard} \times \text{Weight of sample}} \times DF \times \text{Potency} \times \frac{\text{Wt. Av}}{\text{Wt. Avg}}$$

Where,

DF = Dilution Factor

Wt. Avg = Average Weight of sample.

In-vitro Dissolution Studies

In-vitro dissolution studies were carried out using dissolution USP apparatus # II. The dissolution medium was 900 ml of 0.1N HCl and 900ml of phosphate buffer (pH 6.8), which was maintained at 37 ± 0.5 °C and 75 RPM. In all dissolution experiments, 5 ml of dissolution samples were withdrawn and replaced with the equal volume fresh dissolution medium at regular intervals. Collected dissolution samples were used for determination of released Esomeprazole concentrations by using a UV-VIS spectrophotometer against a blank at 300 nm (Table 5).

Results and discussion

All the brand of Esomeprazole tablets used in this investigation was within their shelf life. All tablets obtained from local market were subjected to a number of tests in order to assess quality parameters like assay, weight variation, hardness, and disintegration time. All the tablets of different brand contained Esomeprazole within 100 ±5 % of the labeled claim. The USP [10] and IP [11] specifications for the assay are that the Esomeprazole content should be not less than 95 % and not more than 105 %. Therefore, the assay results ascertain the quality of Esomeprazole in all the products. Weight variation does serve as a pointer to good manufacturing practices (GMP) maintained by the manufacturers as well as the amount of active pharmaceutical ingredient (API) contained in the formulation. The weight variation for all the tablets used in this study showed compliance within the official specifications [7, 12], as none of the products deviated by up to 5 % from their average weight.

Weight Variation Test

The weight variation test is a satisfactory method of determining the drug content uniformity of tablets. When the weight variation is within the specifications the tablets are thought to contain a uniform active ingredient to give desired therapeutic response. But when the weight variation is out of the specification the tablets are thought to contain less or more active ingredient to give an ineffective therapeutic response or toxic effect respectively. It may vary due to result from, poor granulation flow properties, resulting in uneven die fill. The USP 12 specification of weight variation: ±7.5 for 130 to 324mg average weight of tablet & ± 5% for more than 324mg of an average weight of the tablet. Twenty tablets were selected from each of the brands and weighed individually using electronic balance. Their average weights were calculated. For all tablet brands following mathematical equation was used for weight variation.

[13] It was observed that all of the brands meet the USP specification. (Table 1)

Hardness Test

Hardness test of material is indicative of its strength. Most important physical feature for assessing tablet is hardness. [14] In this study, the hardness of different brands of Esomeprazole tablet was measured by hardness tester. The acceptable limit of hardness of a tablet is 4 to 7 kgf (kilogram of force). [15, 16] Besides, a force between 4 – 10 Kg is also considered to be satisfactory. [17] The hardness of five brands of Esomeprazole was determined and the observed results are shown in the table-2.The comparative Hardness of various brands of Esomeprazole tablets is graphically shown in Fig-1.

Disintegration time

Disintegration is the breakdown process of a tablet into smaller particles and is the first step towards dissolution .Enteric coated are to point out no proof of disintegration once one hour in simulated stomach fluid and are to disintegrate in 2 hours and the time per the monograph within the intestinal fluid .To be compliance with USP standards, the tablets should disintegrate, and particle must pass through the three inches long glass tubes and held against a 10-mesh screen within the time given. [18] The onset of action of a dosage form of a drug depends on the time to be taken by the tablets to unharness the active ingredients into the succus. The tablets ought to be disintegrated within the acceptable time, otherwise, the prescribed course is affected and also the drug might not exert its effect properly. The disintegration time of five brands in phosphate buffer (pH 6.8) of Esomeprazole is shown in table-3. Before checking the disintegration in phosphate buffer (pH 6.8) they were treated with 0.1 N HCl for 2 hours but no disintegration occurs because of its enteric coating. The method specified in the USP/BP was used and the specification of disintegration time is 5 to 30 minutes. [10, 12] None of the samples exceeded the specification for disintegration time. Disintegration time of various brands of Esomeprazole tablet is shown in Fig-2.

Assay

The assay results of all brands are between 95.28% and 99.40%. They meet the U.S.P specification for assay (Table 4).

Dissolution test

The dissolution rate of five brands of Esomeprazole tablets was determined. The observed results are shown in table-5.USP specification is not more than 10% in 0.1 N HCl after 2 hours (Table-5.1) and not less than 75% of the labeled amount of Esomeprazole to be dissolved after 45 minutes (Table-5.2). The five brands of Esomeprazole tablets meet the specifications. [19] All the brands meet ***the specification of the U.S.P standard as they did not*** release more than 10% drug in 0.1 N HCL after two hours treatment and release in cases of all brands more than 75% within 45 minutes in phosphate buffer (pH 6.8) Dissolution rate of various brands of Esomeprazole tablet is shown in Fig-3. Esomeprazole tablets have been analysed to find their correct quality status. For this purpose, the marketed sample of five brands of Esomeprazole tablets was analyzed by using established methods and apparatus. The result of weight variation, hardness, disintegration time, dissolution and assay potency tests of all marketed products comply with pharmacopoeial limit. All of the brands have proved that they have the quality which meets the BP and the USP specification. The present study, although performed on a limited scale yet on the basis of professional judgment the data reported in this study can help the Drug Control Authority to get an idea about the quality status of the marketed Esomeprazole preparations in Bangladesh.

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Table 1: Weight Variation Test of Esomeprazole tablet

Sample code	Average weight per tablet (mg)	SD
E01	275.6	0.58
E02	270.7	0.25
E03	165.9	0.79
E04	279.7	1.79
E05	167.3	0.88

Table 2: Hardness of 5 brands of Esomeprazole tablets

Name	Hardness ($kg/cm^{2)}$	SD
E01	5.32	0.35
E02	6.71	0.88
E03	5.76	1.01
E04	6.26	0.21
E05	7.12	0.56

Table 3: Disintegration time of various brands of Esomeprazole tablets.

Sample code	Disintegration time(min)	SD
E01	29.05	1.05
E02	26.83	1.22
E03	19.93	2.15
E04	26.28	0.84
E05	28.18	1.63

Table 4: Potency of Esomeprazole Tablet

Sample code	Potency (%)	SD
E01	95.28	2.14
E02	98.45	1.25
E03	99.4	0.95
E04	98.63	1.44
E05	98.27	0.89

Table 5: Dissolution Rate of Various Brands of Esomeprazole Tablets.

Table 5.1: % of drug release after 2 hours in 0.1 N HCl

Sample code	% of drug release after 2 hours in 0.1 N HCl	SD
E01	2.55	0.56
E02	2.64	0.85
E03	3.88	0.48
E04	4.47	0.25
E05	2.94	0.66

Table 5.2: Dissolution in Phosphate buffer (pH 6.8)

Sample code	% of drug release after					
	10minutes	20 minutes	30 minutes	45 minutes	50 minutes	60 minutes
E01	15.05	30.65	42.85	76.78	95.44	100.86
E02	11.86	14.06	54.09	76.5	95.30	102.37
E03	18.61	43.59	72.28	85.78	97.45	101.20
E04	13.27	17.44	53.86	81.25	94.36	105.89
E05	13.5	16.78	42.7	79.59	93.75	101.99

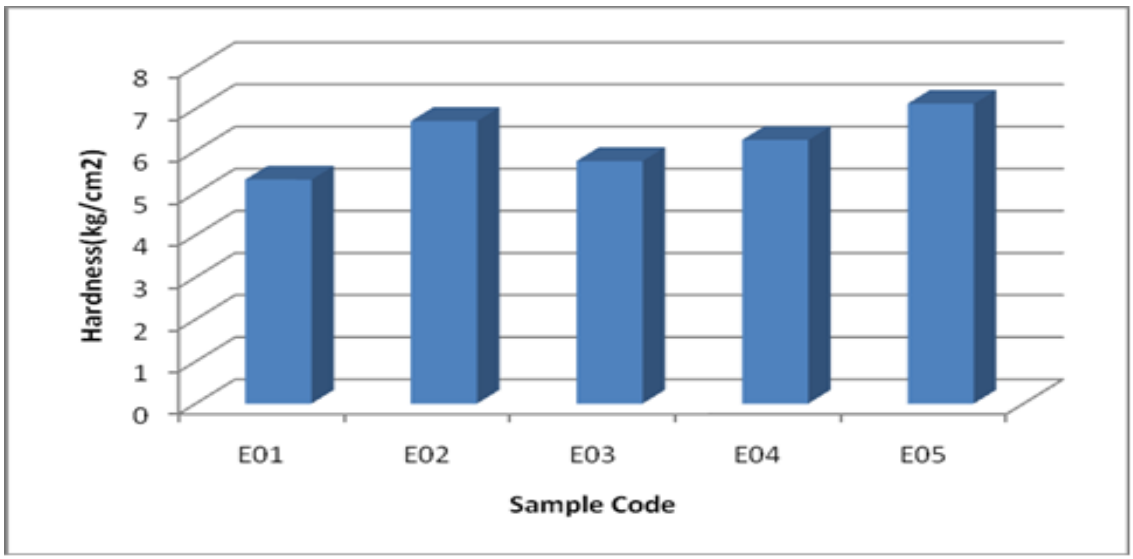

Figure 1: Hardness of various brands of Esomeprazole tablets

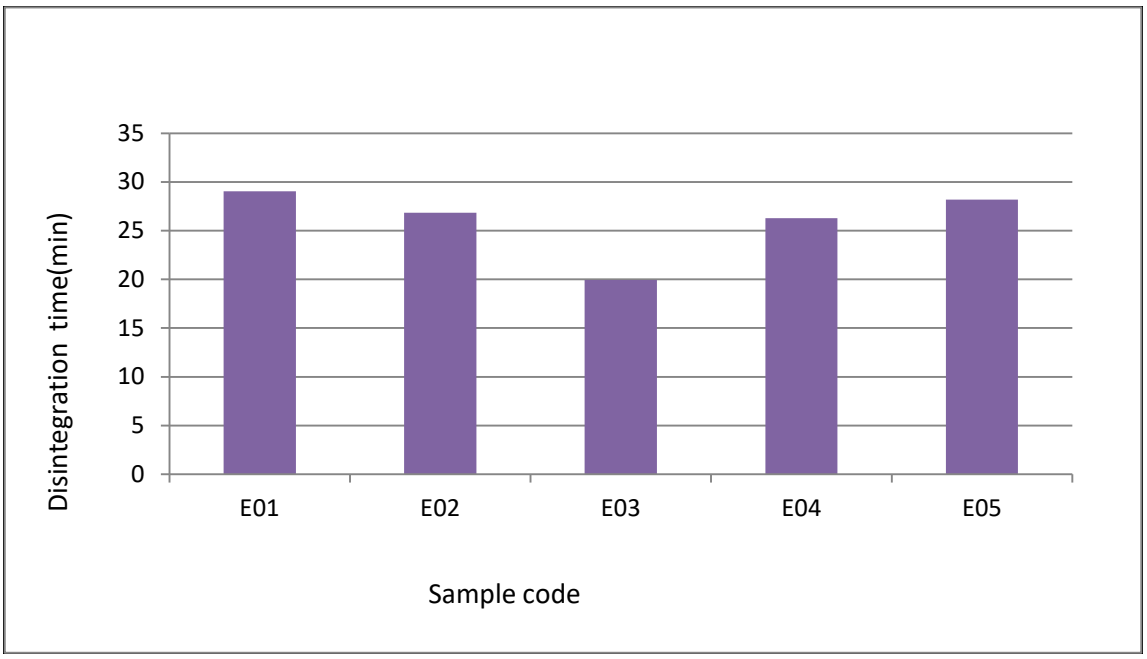

Figure 2: Disintegration time of various brands of Esomeprazole tablet

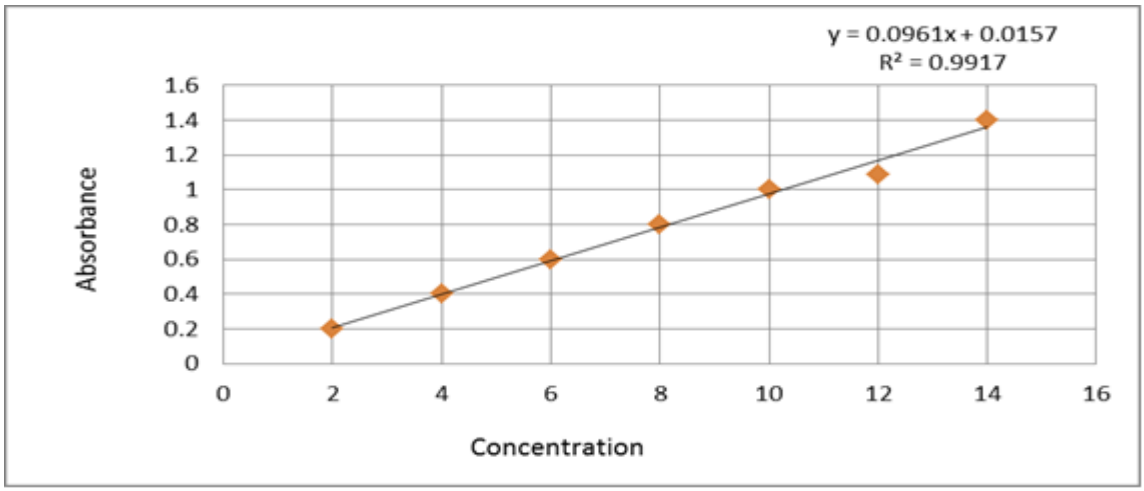

Figure 3: Standard curve of Esomeprazole

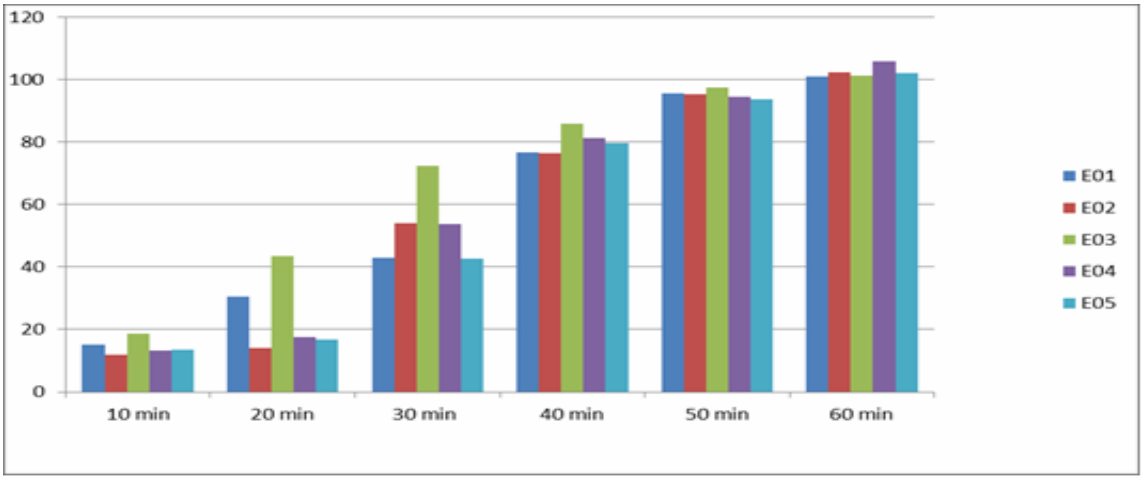

Figure 4: Dissolution rate of various brands of Esomeprazole tablet