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In-vitro Fundamental Assessment of Disintegration and Dissolution Profile of Enteric Coated Rabeprazole Tablet Commercially Accessible in Bangladesh

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Short Research Article

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ABSTRACT

Objective: An assortment of commercially accessible enteric coated rabeprazole tablets were evaluated comparatively *in vitro* disintegration and dissolution profile in association with its' drug content.
Methods: *In-vitro* disintegration and dissolution profiling of our selected all enteric coated rabeprazole brands in Bangladesh were carried out using a dissolution apparatus USP at a paddle speed of 100 rpm and UV-VIS spectrophotometer. BP method was used to determine the time required for tablet to disintegrate in acid stage, pH 1.2 and buffer stage, pH 6.8.
Results: The *in vitro* disintegration and dissolution time were found to be varying for each tablet, but within the B.P. prescribed limit. Brand10 showed the fastest disintegration. All the brands showed no disintegration, cracks or swelling in 0.1 N HCl, except brand 4 and 10, which showed

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cracks, leakage, and blackspot after 120 min. However, the disintegration of all the products in phosphate buffer meets B.P requirements. Dissolution of tablets in 0.1 N HCl showed less than 10% drug release after 120 minutes. Moreover, the comparison of percentage drug release on the basis of dissolution study demonstrated that Brand 1, 2, 4, 5, 6, 7, 8, 9, and 10 (80% drug release) complied best whereas Brand 3 (78.16% drug release) does not fulfill with pharmacopoeial specification.

Conclusion: All the brands (10) of rabeprazole tablets tested *in vitro* assessment of disintegration and dissolution were showed pharmacopoeial specification except brand 3, 4 & 10. So, this study helps to make pharmacopoeial specified rabeprazole tablets.

Keywords: Rabeprazole; phosphate buffer; dissolution; percentiles.

1. INTRODUCTION

Rabeprazole sodium comes under the class of proton pump inhibitor. The main purpose of an oral tablet is to deliver a certain and defined amount of drug to the human body through GI system. Studies on bioavailability of drugs from a given study showed that in many situations tablets with same drug and drug content did not give the same therapeutic response [1]. Rabeprazole sodium is a substituted benzimidazole. Benzimidazoles are anti-ulcerant compounds known for decreasing gastric acid secretion. These compounds, also known as Proton Pump Inhibitors (PPI) are commonly indicated for the treatment of Gastric ulcer, Peptic ulcer, Duodenal Ulcers, Erosive or Ulcerative GERD (Gastro Esophageal reflux Disease), Symptomatic GERD [2]. Formulation additives in the tablet, physical form of the drug used in the tablet and manufacturing process vary from manufacturer to manufacturer, which is responsible for variation in the observed dissolution profile and therapeutic effect [3]. Enteric coating tablets are composed of three layers, a drug containing core tablet (rapid release function), the press coated swellable hydrophobic polymer layer (Hydroxy propyl cellulose layer (HPC), time release function) and an enteric coating layer (acid resistance function) [4]. The tablet does not release the drug in the stomach due to the acid resistance of the outer enteric coating layer. The enteric coating layer rapidly dissolves after gastric emptying and the intestinal fluid begins to slowly erode the press coated polymer (HPC) layer. Rapid drug release occurs when the erosion front reaches the core tablet since the erosion process takes a long time as there is no drug release period (lag phase) after gastric emptying [5,6]. Rabeprazole tablets are available as enteric coated tablets. Enteric coatings are those which remain intact in the stomach but will dissolve and release the contents once it reaches the small intestine. Their prime intension is to delay the release of drugs which are inactivated by the stomach contents or may cause nausea or bleeding by irritation in gastric mucosa. Now a day, many pharmaceutical companies are manufacturing the drugs for their commercial purpose with insufficient active ingredient in the dosage form as they claimed on the strip [7]. Finally enteric coating was given to bypass the stomach. The enteric coating was carried out by using enteric polymer Methacrylic acid copolymer Eudragit L 30D-55 [8]. Previous work, validated stability indicating assay method was developed for determination of rabeprazole sodium in presence of its degradation products. The developed HPLC method is simple, rapid, precise and accurate and hence can be used in the routine analysis of the Rabeprazole sodium in the laboratory [9]. Studies from P. Suresh Kumar et al clearly reflect that the prepared formulation offers effective resistance in acidic environment and starts its release in the alkaline environment of small intestine. Thus, Instacoat EN-HPMCP A34G00031 Yellow can be successfully employed to retard the release pattern of rabeprazole sodium thereby enhancing the therapeutic efficacy [10]. The comparison of dissolution study demonstrates that RPZ-3 (90% drug release) complied best while RPZ-4 (74.58% drug release) does not comply with USP specification. Almost all the brands except one have passed all the official tests prescribed by USP. The variation in that dissolution study may be due to different formulation additives, physical form of the drug in the tablet and varying of manufacturing processes from manufacturer to manufacturer [11].

So, the study was undertaken with the objective of evaluating different brands of commercially available rabeprazole enteric coated tablets to get awareness about the pharmaceutical company that gives appropriate active ingredient present in dosage forms released into the

market. In the present study we are comparing enteric coated rabeprazole tablets of different brands available in Bangladeshi market.

2. MATERIALS AND METHODS

2.1 Sample Collection and Identification

All Rabeprazole sodium brands in Bangladesh having label strength of 20 mg were purchased from retail pharmacy. All tests were performed within expiratory date.

2.2 *In Vitro* Disintegration Test

The disintegration test was performed according to British Pharmacopoeia (B.P.) procedure. At random six (6) tablets from each brand were selected and placed one in each of the tube of the basket-rack assembly of disintegration apparatus (APP double unit, Scientica). The assembly was inserted in the simulated gastric fluid, 0.1 N HCl at 37±2°C for 2 hours. At the end of 2 hrs, tablets were observed for any sign of disintegration, cracking or softening. Then, immediately tablets were taken outside and immersion fluid was replaced with simulated intestinal fluid, 0.05 M, phosphate buffer, pH 6.8 and apparatus was operated on same condition until all the tablets were changed into granules. The specification for disintegration of enteric coated tablets in intestinal fluid is 45 minutes according to B.P.

2.3 *In Vitro* Dissolution Test

In vitro drug release was carried out for all brands of tablets according to B.P dissolution procedure for enteric coated tablets. The dissolution of six randomly selected enteric coated rabeprazole was monitored using an automated dissolution tester (VDA-6 DR, USP Standard). The USP 27, apparatus 2 paddle method was used at 100 rpm for 2 hours in 1000 ml simulated gastric fluid, 0.1N HCl, pH 1.2 at 37±0.5°C. After 2 hours, 20 ml of the sample was taken out and released drug content was assessed using UV spectrophotometer (UV-1650 pc, UV-VIS Spectrophotometer, SHIMADZU) at 284 nm. After completing the taking UV absorbance for 20 tablets in acidic medium, tablets were withdrawn from apparatus vessels and 1000 ml of intestinal fluid, 0.05 M, phosphate buffer pH 6.8 was taken and maintained at 37±0.5°C for 45 minutes and 100 rpm. After 45 minutes about 20 ml of sample was withdrawn from each vessel and the filtered samples were analyzed using UV spectrophotometer at 284 nm for rabeprazole. By measuring the absorbance of all brands tablets, the percentage (%) of drug release was calculated.

3. RESULTS AND DISCUSSION

All selected brands of rabeprazole tablets were showed no evidence of disintegration, cracks or swelling in simulated gastric fluid consisted of 0.1N HCl, pH 1.2 excepting brand 4 and brand 10 tablets, which showed leakage and cracking after 120 minutes while disintegration of all brands of rabeprazole in simulated phosphate buffer, pH 6.8, met BP specification. Physical changes in disintegration of rabeprazole enteric coated tablets in simulated gastric fluids are shown in Fig. 1.

The overall disintegration time for rabeprazole sodium tablets brands was ranged from 12 minutes to 35 minutes, shown in Fig. 2. The mean disintegration time was 17.5±6.73 (95 % CI: 12.68-22.31) minutes, and encountered B.P. specifications. The highest disintegration time was recorded in brand 5 (35 minute) whereas lowest disintegration time was in brand 4 (13 minute).

Dissolution of rabeprazole is noted the percentage average drug releases was assessed in simulated gastric fluid, pH 1.2 and intestinal fluids, pH 6.8. In Fig. 1 showed % drug releases of all brands rabeprazole tablets in simulated gastric fluid, brand 5 showed lowest values, 0.21% and highest, 9.11% for brand 4 of rabeprazole tablet. The dissolution of selected rabeprazole brands in simulated gastric fluid was carried out for 120 minutes in accordance with BP specifications. In simulated intestinal fluids generated with 0.05 M phosphate buffer, % average drug releases are shown in Fig. 2 and 98.03% for brand 5 is documented as the highest released drug while 78.16% is recorded as lowest released drug value at the end of 45 minutes of dissolution profiling of enteric coated rabeprazole sodium tablets. The dissolution of enteric coated rabeprazole sodium tablets is shown in Figs. 3 and 4.

The rest of released drug content was more than 80% and acknowledged levels were 96.76%, 92.01%, 88.78%, 90.72%, 88.10%, 92.30%, 84.12%, and 89.71% respectively for rabeprazole brands of 1, 2, 4, 6, 7, 8, 9, and 10 in simulated intestinal fluids but in simulated gastric fluids, in

Fig. 1, brand 1(2.25%), brand 5(0.21%), brand 6(4.64%), brand 8(1.38%), brand 10(4.01%) were showed respectively less than 5% average drug released in the period of 120 minutes while brand 2(6.72%, brand 3(8.74%), brand 4(9.11%), brand 7(8.97%), and brand 9(6.32%) were possessed more than 5% of average drug released but not conquered the 10% of average drug released of all brands rabeprazole tablets.

The percentiles of % drug released in simulated gastric and intestinal fluids are shown in Fig. 5. The correlation of % drug released between simulated gastric and intestinal fluid was positive correlation ($R^2 = 0.811$).

Disintegration and dissolution time is delivered to fix whether tablets or capsules disintegrate within the recommended time when positioned in a liquid medium at the experimental conditions. The results of this study are indicated that the % drug released of rabeprazole tested excepting brand 3 fulfilled all the B.P. specifications.

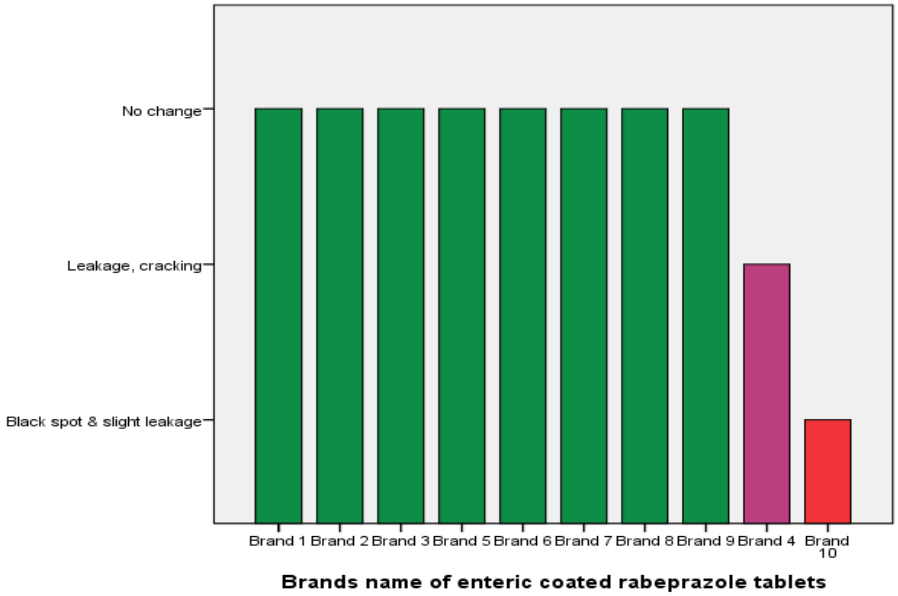

Fig. 1. Physical changes in disintegration of rabeprazole enteric coated tablets in simulated gastric fluids comprising of 0.01N HCl, pH 1.2

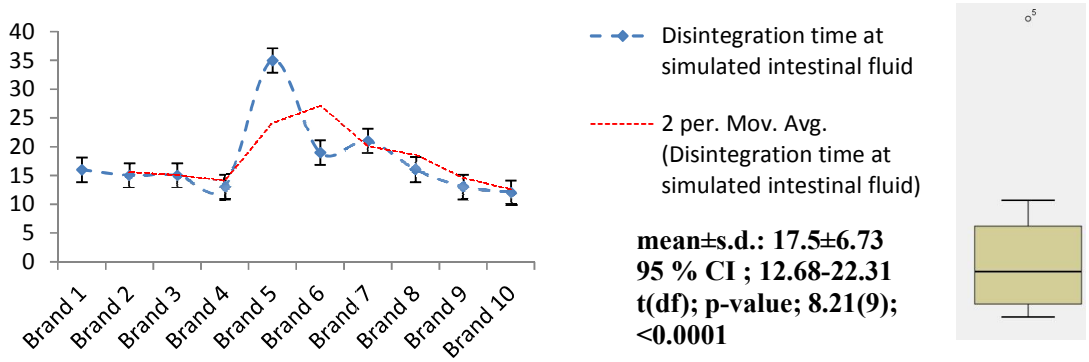

Fig. 2. Disintegration time at simulated intestinal fluid 0.05 M, Phosphate buffer, pH 6.8, after 45 minutes. Boxplot of disintegration time shows outlier of brand 5

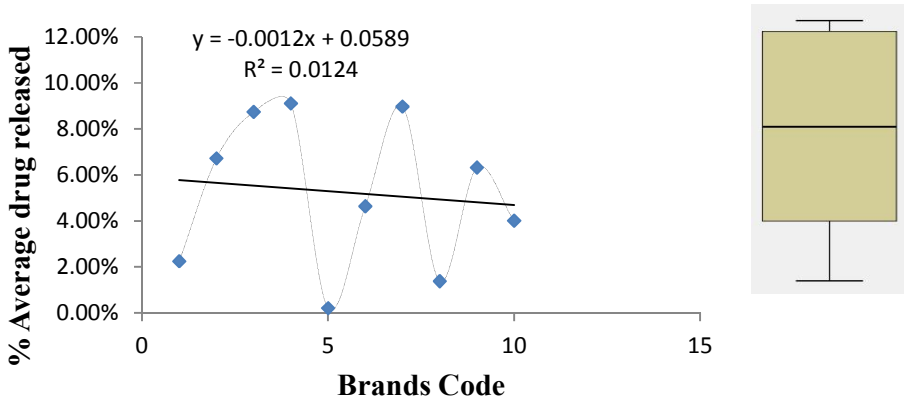

Fig. 3. Dissolution profile of enteric coated rabeprazole tablets in simulated gastric fluid, 0.1N HCl, pH 1.2

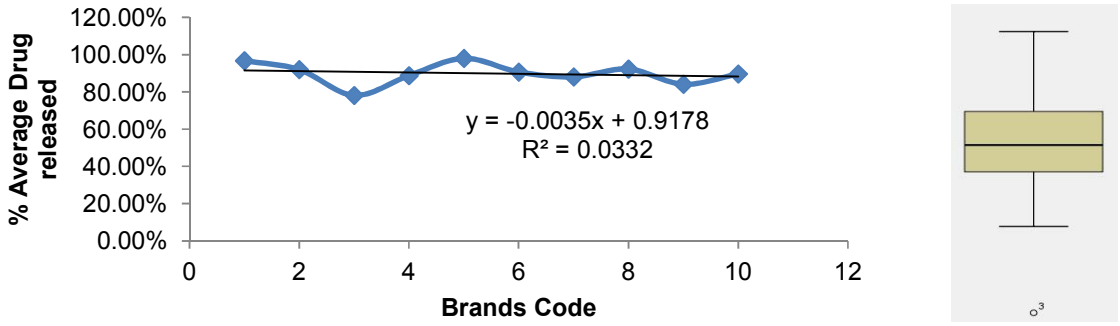

Fig. 4. Dissolution profile of enteric coated rabeprazole tablets in simulated intestinal fluid, 0.05M, Phosphate buffer, pH 6.8

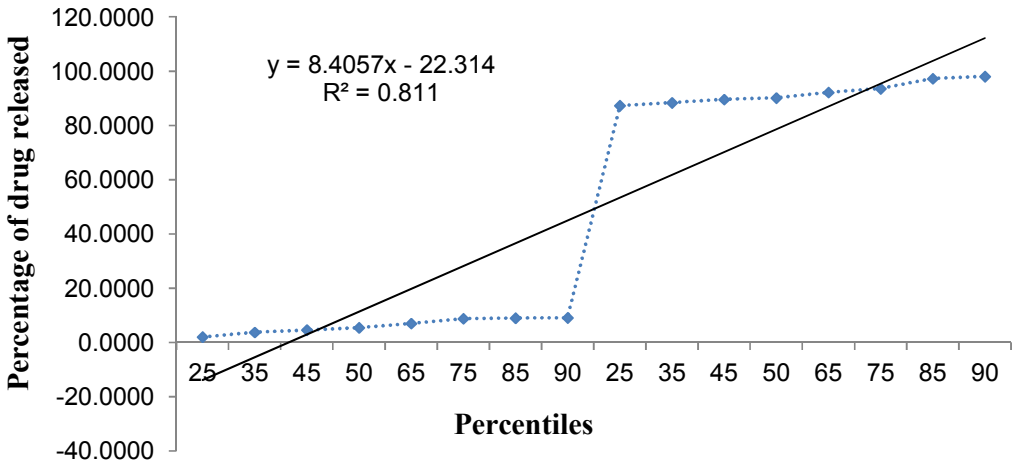

Fig. 5. Comparative percentiles of percentage of drug released in both of simulated gastric fluids, 0.1 HCl, pH 1.2 and simulated intestinal fluids 0.05 M phosphate buffer, pH 6.8

4. CONCLUSION

Our suggested study discusses the comparative dissolutions for multi-sourced rabeprazole tablets available in Bangladesh and the *in vitro* drug release profile of all formulations was evaluated and the release studies demonstrated that the release of selected drugs from all formulations was generally B.P. specified with some anomalies of products 3, 4, and 10. So, this study is recommending the manufacturers to overcome the problem to meet the requirements of the rabeprazole enteric coated tablets.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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