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In vitro Comparative Quality Evaluation of Different Brands of Marketed Paracetamol Tablets Available 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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ABSTRACT

Aim: This study was performed to evaluate the quality of five brands of Paracetamol 500mg tablets from different manufacturers.
Methods: The general quality parameters of these tablets like weight variation, hardness, thickness, diameter, friability, disintegration time and also dissolution time were evaluated according to the established protocols. For measuring weight variation, an electric analytical balance was used. The hardness, thickness and diameter were determined by an automated hardness tester. Friability was measured by a friabilator. Disintegration time and dissolution time were analyzed by disintegration apparatus and dissolution tester respectively.
Results: In this study, all the five brands of the tablets passed the BP or USP standards for *in vitro* evaluation tests with a very slight deviation. All brands complied with the standards for weight variation (550.1±5.88 mg to 631.1±4.71 mg), hardness (121.60±6.6 N to 220.20±7.6), disintegration time (3 minutes 15 seconds to 5 minutes 30 seconds). However, in case of friability, although brand A showed slight deviation, the remaining had shown the satisfactory results with the standard. In addition, the drug release rate of different brands of paracetamol was satisfactory within 30 minutes and ranged from 90.88% to 103.75%.

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Conclusion: It can be concluded that almost all the tablets of paracetamol purchased from retail outlets in Bangladesh are manufactured and marketed according to GMP. Further work is recommended on bioequivalence of these tablets.

Keywords: Paracetamol 500mg; In-vitro quality parameters; dug release rate; friability; hardness.

1. INTRODUCTION

Paracetamol or acetaminophen (4-hydroxy acetanilide) is a widely used non-opioid analgesic and non-steroidal anti-inflammatory drug (NSAID) [1,2]. Over 30 years, paracetamol has been treated as an analgesic for domestic medication and it is also well established as a very effective treatment for the relief of fever and pain in adults and children. It has become the most extensively accepted antipyretic and analgesic all over the world due to being relatively safe in recommended doses [3]. But, overdoses of paracetamol and prolonged duration of taking this drug can cause potentially fatal liver damage [4]. Hepatotoxicity due to paracetamol overdose leads to liver injury which is a common cause of poisoning worldwide as well as toxicity in kidney [5]. Furthermore, DNA synthesis is also hindered by paracetamol that leads to promote genotoxicity and carcinogenicity [6].

It is clearly recognized that paracetamol acts by the same mechanism (inhibition of prostaglandin synthesis by inhibiting cyclooxygenase) like aspirin and other NSAIDs, all show different levels of analgesic, anti-inflammatory, and antipyretic as well as anti-platelet actions [7,8]. It is better tolerated than aspirin in patients whom excessive gastric acid secretion or prolongation of bleeding time may be a concern. It is an over-the-counter (OTC) drug and has become a very common household drug nowadays [9].

Paracetamol is rapidly absorbed and peak serum levels usually occur 30 minutes to 2 hours after ingestion. Elimination from the body is also quick having half-life of about two hours[10]. Paracetamol is soluble in water, alcohol, acetone, glycerol, chloroformand in solutions of alkali hydroxides. It is stable in a saturated aqueous solution having a pH of about 6 but stability decreases in acid or alkaline conditions, the paracetamol being slowly broken down into acetic acid and p-aminophenol [10].

The increase in the number of generic drug products from multiple sources has placed people involved in the delivery of health care to select one from among several seemingly equivalent products. For instance, in 1975 approximately 9% of all prescription drugs dispensed in the United States were generic versions [11]. This amount increased from 20% in 1984 to 40% in 1991. Over 80% of the approximately 10,000 prescription drugs available in 1990 were obtained from more than one source and variable clinical responses to these dosage forms supplied by two or more drug manufacturers is documented [12,13]. These variable responses may be due to formulation ingredients employed, methods of handling, packaging and storage and even the rigors of in-process quality control. Many renowned pharmaceutical industries do not maintain guidelines approved by WHO during manufacturing. But people blindly buy these products due to their popularity. So, there is need to determine their pharmaceutical and therapeutic equivalence in order to ensure interchangeability. Generic drug products must satisfy the same standards of quality, efficacy and safety as those applicable to the innovator products. Though, many developing countries do not have an effective way of monitoring the quality of generic drug products available in the market. Post market monitoring functions as a trustworthy role to evaluate the quality, therapeutic efficacy and safety of commercially available pharmaceutical products [14]. Information achieved from such post market monitoring can speed up the improvement process of existing product development [15]. In this study, physical parameters of commercially available paracetamol tablets were evaluated. The aim of the study was to investigate the *in vitro* quality of paracetamol tablets marketed in Bangladesh. The study also provides information about trend and characteristics of paracetamol tablet from different manufacturers, pointing out the relative variation of marketed paracetamol tablet in comparison with standard set by British Pharmacopeia (BP) and United States Pharmacopeia (USP). Moreover, this kind of study will create consciousness among the general consumers and this will lead them to choose the quality product among thousands of existing products available in the market.

2. MATERIALS AND METHODS

2.1 Materials

Legally registered five brands of marketed Paracetamol tablets obtained from local medicine shop sampled as A, B, C, D, and E were used during this study. All others research grade chemical reagents and logistical supports were provided by Pharmaceutical Technology Lab of the Dept. of Pharmacy, Comilla University, Cumilla-3506, Bangladesh. Working standard, United State Pharmacopeia & British Pharmacopoeia were used as a reference for the experiment.

2.2 Methods

2.2.1 Weight variation

In general, weight variation test is used to identify uniformity of dose among tablets. Twenty tablets of each brand were selected randomly and weighed individually with the help of an analytical balance (Boico, Germany).The average weight and deviation was calculated. According to USP, for tablet weighing greater than 325mg there should not be more than two tablets deviating from the average by no more than 5% and none deviated by more than twice of 5 % (10 %) [16].

2.2.2 Hardness, diameter and thickness tests

The crushing strength (N) was determined with a tablet hardness tester (ERWEKA, Germany). Ten tablets were randomly selected from each brand and the pressure or force at which each tablet crushed was recorded. 10 tablets from each brands were taken and both the thickness and Diameter of the tablets were measured with the same machine used for the determination of hardness.

2.2.3 Friability test

Ten tablets from each brand were weighed and subjected to abrasion by using a Friabilator (ERWEKA, Germany) which was operated 100 times at 25 RPM. After 100 revolutions the tablets were again weighed. The loss in weight indicated the friability. Weight loss indicates as the percent friability and the loss of weight should not be more than 1% [17]. The friability was calculated by measuring the difference in weight according to the following equation [18]:

% Friability (f) = (Initial Weight – Final Weight)/ Initial weight × 100

2.2.4 Disintegration time

This test is used to determine the time required for tablet to disintegrate. A 900 ml beaker was filled with water at 37±0.2^{o}C and then six tablets were placed in to the basket rack assembly and connected to the disintegration apparatus (ERWEKA, Germany). The time required for the tablet to disintegrate was recorded.

2.2.5 Dissolution test

Usually dissolution test is carried out to determine drug release pattern during a specific period of time [19].Dissolution test for each of the tablet brands was performed using USP paddle method (Apparatus II) at speed of 100 rpm.About 900 ml of phosphate buffer, pH 7.4 was filled into 1000ml beaker of dissolution apparatus. The dissolution medium was heated up to 37.0± 0.5 ºC by an auto heater. 900 ml of phosphate buffer, pH 7.4 was used as dissolution medium [19]. One paracetamol tablet was placed into each beaker. Aliquots (5ml) of the dissolution medium were withdrawn from beaker at interval of 0, 5, 10, 15, 30 minutes which was replaced with another 5ml of freshly prepared dissolution medium (phosphate buffer, pH 7.4). & then withdrawn solution was filtered through filter paper. Then, the withdrawn solution of the sample was diluted with the dissolution medium and analyzed using UV Spectrophotometer (UV-1800, Shimadzu, Japan) at 257nm for paracetamol. By measuring the absorbance, the percentage (%) of drug release was calculated [19].

2.3 Statistical Analysis

All statistical analysis was performed by MS Office Excel 2010 and Graph Pad Prism software version 7. Results generated were presented as Mean ± Standard Deviation.

3. RESULTS AND DISCUSSION

In this study all paracetamol brands were subjected to different quality control tests like weight variation, hardness, thickness, diameter, friability disintegration, and dissolution test. To conduct each test during this research standard books BP [20] and USP [21] were widely used.

3.1 Weight Variation

Weight variation functions as a pointer for good manufacturing practices (GMP) that is maintained by the manufacturers as well as amount of active pharmaceutical ingredient (API) contained in the formulation [22]. The limit of deviation is ±10% for tablets weighing 130 mg or less, ±7.5% for tablet weighing more than 130 mg to 324 mg and±5% for tablet weighing more than 324 mg. According to USP not more than two tablets should cross the single limit and none of them should cross the double of the limit. The weight variation for all the tablets used in this study showed compliance with the official specifications of USP. As depicted in Table 1, brand A showed the highest deviation, no tablet crossed the limit and brand C showed least deviation among all the five brands [23].

3.2 Hardness, Thickness and Diameter Tests

Hardness has impact on disintegration. Therefore, adequate tablet hardness and resistance to powdering are essential requisites for quality products [24]. This test measures the ability of tablets to withstand pressure or stress during handling, packaging, and transportation [25]. The results of the hardness test are displayed in Table 1. All brands represented hardness value of >50 N; thus, all products conformed to fulfill the requirement for hardness test. However, the average hardness of the products is different from each other, and it is observed that tablet hardness ranged from 121 N for brand A to 220 N for brand E. The reason for this variability between brands may have been related to pharmaceutical manufacturer's formulation conditions such as alteration in machine speed, granulation techniques, and amount of lubricants added during manufacturing processes [26].

By monitoring the thickness and diameter of the tablets at regular intervals, potential problems relating to tablet weight and hence content uniformity can be detected at an early stage [27]. As shown in Table 1,the average thickness of Brand A, B, C, D, E were found 3.74, 4.75, 5.97, 4.77 and 5.75 mm respectively. In consideration of average thickness, the variation of thickness was satisfactory for all brands.

Among the five marketed brand paracetamol 500mg tablets of this study, brand-Chad highest average diameter (16.04mm) whereas brand-A had lowest average diameter (12.99 mm) (Table 1).

3.3 Friability Test

Friability reveals good mechanical strength of the tablets [28]. The result of friability test as shown in Fig. 1, four brands (B, C, D and E) had percent friability below 1% which indicates tablets from other brand (A) may face difficulty during storage or transportation. Among five brands, brand-A showed maximum friability (1.13%), whereas brand-B showed minimum friability (0.24%).This result of friability ensures that all the tablets of each brand were mechanically stable [18].

Table 1. Average weight, diameter, thickness, and hardness of five brands of paracetamol 500mg tablet

Brand	Average weight (mg)	Diameter(mm)	Thickness(mm)	Hardness(N)
A	570.29±7.46	12.99±0.01	3.74±0.05	121.60±6.6
B	630.12±5.35	13.07±0.05	4.75±0.06	183.80±8.5
C	631.1±4.71	16.04±0.02	5.97±0.01	171.00±8.9
D	550.1±5.88	15.00±0.03	4.77±0.06	132.00±8.3
E	570.16±6.65	14.52±0.02	5.75±0.04	220.20±7.6

All Values are expressed as mean±SD

Table 2. Percentage of friability of five brands of paracetamol 500mg tablet

Brand	Initial average weight of (10) tablets	Final average weight of (10) tablets	% Friability
A	5.713	5.648	1.1377
B	6.321	6.306	0.2373
C	6.309	6.249	0.9510
D	5.515	5.498	0.3082
E	5.712	5.688	0.4201

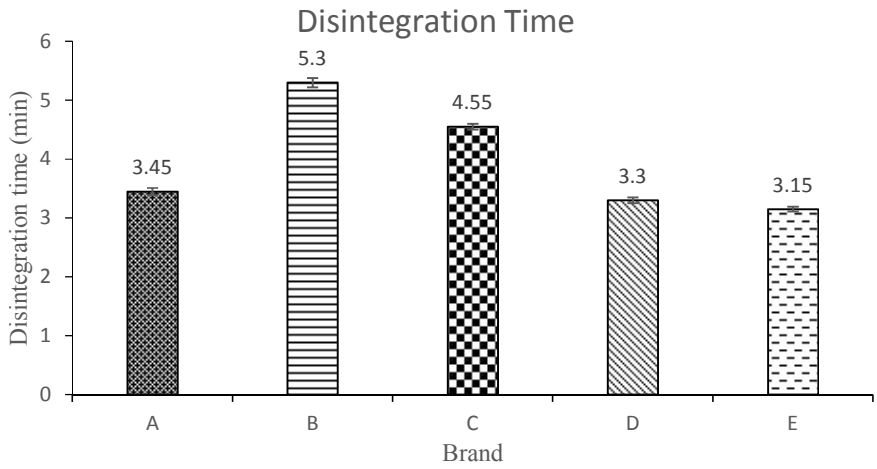

Fig. 1. Disintegration time of five brands of paracetamol 500mg tablet

Table 3. Dissolution profile of five brands of paracetamol 500mg tablets

Brand	% of Drug Release (5 min)	% of Drug Release (10 min)	% of Drug Release (15 min)	% of Drug Release (30 min)
A	30.89± 0.98	42.25±1.46	75.93±1.87	99.51±2.38
B	26.18±0.65	40.81±1.07	71.33±1.59	91.35±2.57
C	39.29±1.68	56.28±4.21	80.54±3.66	101.15±1.44
D	37.26±3.67	52.98±2.55	79.94±4.78	103.75±4.06
E	35.31±2.34	50.78±2.12	78.24±2.36	90.88±3.52

All Values are expressed as mean ± SD

3.4 Disintegration Test

Disintegration plays an essential role in a tablet's dissolution. BP specifies that uncoated tablets should disintegrate within 15 minute which is 30 minute in case of USP [29]. Table 1 shows that all the brands met the requirement of official criteria. Brand B took maximum time of 5.30 minute and brand E took the minimum time of 3.15 minute to disintegrate.

3.5 Dissolution Test

Dissolution is another very important quality control parameters that is directly interconnected to the absorption and bioavailability of drug [30].The present study exposed that at different time intervals drug release rate is better in paracetamol tablet brands comparing with the paracetamol alone. After 10 minutes, the release rate of tablet brands of paracetamol was 40.81% to 56.28%. Finally after 30 minutes, the release rate of tablet all brands of paracetamol also showed more than 90% drug release after 30 minutes.

4. CONCLUSION

In the present manufacturing practice, *in-vitro* quality control parameters test plays an important role to compare with various brand generic molecules and to provide enough therapeutic activity of the dosage form. The quality parameters should be followed by the specification of the standards. From the study, it is evident that all the brands met the quality specifications of BP and USP standards with some exceptions. This study states the necessity for constant surveillance on the marketed drugs by the regulatory bodies to ensure good quality pharmaceutical products circulating in the market originated from different manufacturers although *in vivo* testing is required for final remarks regarding the quality of marketed brands of Paracetamol.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely

no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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