COMPARATIVE IN VITRO DISSOLUTION STUDY OF COMMERCIAL AVAILABLE PARACETAMOL TABLET.

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Abstract
Paracetamol is a widely used medication to treat pain and fever. It is typically used for mild to moderate pain. Paracetamol is generally safe at recommended doses and many commercial brands of this drug are available in the pharmaceutical market. In this report we seek to compare the % of drug release by using in vitro dissolution test method for Paracetamol tablets of different batches of two different brands. The purpose of this study was to evaluate the pharmaceutical quality of the Paracetamol tablets dispensed in Bangladesh by determining the dissolution rate and to find out whether different batches of the same brand tablets comply with the BP specification or not. We will also get to know whether there exists consistency among different batches of a same brand. Two different commercially available brands of Paracetamol (500mg) were evaluated in this study. 10 batches of Paracetamol tablets of each brand were collected from pharmacy shops of Dhanmondi area, Dhaka, Bangladesh. Tablets of each batch belonged to Brand 1 showed % of drug release above 80% after 45 minute and for Brand 2, % of drug release after 45 minutes was 78%-81%. For brand 1, the in vitro dissolution profile was found to be varying for each tablets but most of them were within the prescribed limit provided in the BP specification 2009. For brand 2, tablets of five batches among the 10 collected batches failed to meet the specification. By using the data from the study, manufacturer will be more cautious in manufacturing quality drugs. General people can be aware regarding the medicines they take. The present study was performed in a limited scale, yet on the data reported in this study can help the drug control Authority to get an idea about the quality status of the marketed Paracetamol in Bangladesh. But to get overall picture further large scale of study is needed.

Keywords: Dissolution, Paracetamol Tablet, Pharmaceutical market, Vitro dissolution Test.

INTRODUCTION
Paracetamol, also known as acetaminophen, is a medication used to treat pain and fever. It is typically used for the relief of mild to moderate pain. Paracetamol is generally safe at recommended doses for human use. But, overdoses of Paracetamol can cause potentially fatal liver damage and in a rare individual, a normal dose can do the same. Serious skin rashes may rarely occur. It appears to be safe during pregnancy and when breastfeeding.

Paracetamol was discovered in 1877. It is the most commonly used medication for pain and fever in both the United States and Europe. It is on the WHO Model List of Essential Medicines, the most important medications needed in a basic health system.

The safety and efficacy of a pharmaceutical dosage form can be guaranteed when its quality is reliable. The efficacy of pharmaceutical dosage forms generally depends on their formulation properties, and manufacturing methods, hence it is likely that the quality of dosage form may vary. Dissolution test is one of the in vitro tests usually employed to assess the quality of oral pharmaceutical solid dosage forms such as tablets and capsules. In vitro dissolution test can be used to guide formulation developments, identify critical manufacturing variables, and monitor formulation quality from batch to batch. Therefore it was decided to carry out the comparative evaluation of in vitro dissolution qualities of various commercially available Paracetamol tablet samples. Paracetamol tablet of 500 mg were chosen for the study.

METHODS AND MATERIALS
Sample collection and Coding: Two different commercially available brands of Paracetamol tablet (500 mg) were evaluated in this study. 10 batches of each brand of Paracetamol tablets were collected from pharmacy shop of Dhanmondi area, Dhaka. And they were coded as given in the table 1.

Table(1) Coding of the collected samples of two different brands

<table>
<thead>
<tr>
<th>Brand 1 Batch No</th>
<th>Brand 2 Batch No</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTT1 5045</td>
<td>PTF1 T1195082</td>
</tr>
<tr>
<td>PTT2 5047</td>
<td>PTF2 T1195042</td>
</tr>
<tr>
<td>PTT3 5052</td>
<td>PTF3 T1194002</td>
</tr>
<tr>
<td>PTT4 5058</td>
<td>PTF4 T1194066</td>
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<td>PTT5 5057</td>
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<td>PTT6 5010</td>
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<td>PTT7 5044</td>
<td>PTF7 T1194040</td>
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<tr>
<td>PTT8 5046</td>
<td>PTF8 T1195085</td>
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<tr>
<td>PTT9 5048</td>
<td>PTF9 T1195099</td>
</tr>
<tr>
<td>PTT10 5056</td>
<td>PTF10 T1195088</td>
</tr>
</tbody>
</table>

Preparation of Dissolution medium: Definite amount of Disodiumhydrogen phosphate and Sodiumhydrogen phosphate were dissolved to prepare the buffer dissolution media and pH was adjusted to 5.8 for the buffer solution. Finally 5M Phosphate Buffer of pH 5.8 was prepared.

Preparation of Stock Solution: Paracetamol standard was weighed and dissolved in 100 ml pH 5.8 Phosphate buffer in a volumetric flask to prepare the stock solution of 1000 µg/ml.

Preparation of standard curve: From the stock solution using serial dilution, six diluted solutions of 2µg/ml, 4µg/ml, 10µg/ml, 14µg/ml, 18µg/ml, 20µg/ml were prepared. Then absorbances were taken at 257 nm. The measured absorbances were plotted against the respective concentration of the standard solution which gives a straight line (Figure 1).
Preparation of sample solution: Collected Paracetamol (500 mg) tablets were placed in 900 ml pH 5.8 phosphate buffers in the vessel of apparatus II, at temperature of 37°C. One tablet was placed in the vessel, and operated at 50 rpm. Each 5 minute, 10 ml specimens were withdrawn for 30 minute. After filtering and proper dilution, the absorbance was taken at 257 nm.

RESULT AND DISCUSSION

The rate of dissolution may be directly related to the efficacy of the tablet product, as well as to bioavailability difference between formulations. Therefore an evaluation as to whether or not a tablet release its drug content when placed in the environment of the gastrointestinal tract is often of fundamental concern to the tablet formulation.

All the samples used for the study were within their shelf life at the time of investigation. Two brands all samples were showed good result in dissolution test.

% of Drug release = (amount of dissolved drug ÷ dose of the drug) × 100%

Amount of dissolved drug = (dissolution factor × dissolution medium × X mg)

To be compliance with BP standard at least 80% of tablets must be released within 45 minutes.

The % of Drug release of 10 batches of the two brands are shown in the Figure 2 and Figure 3 respectively.

For Brand 1 (PTT 1, PTT2, PTT3, PTT4, PTT5, PTT6, PTT7, PTT8, PTT9, PTT10) all samples % of drug release after 45 minutes and therefore, meet the BP specifications.

For Brand 2, five samples (PTF1, PTF2, PTF3, PTF6, and PTF8) met the specification and another samples (PTF4, PTF5, PTF7, PTF9, PTF10) failed to meet the specification.

CONCLUSION

In the pharmaceutical industry, batch-to-batch consistency of solid oral dosage forms can be assessed by the in-vitro dissolution testing. For the drug development it is also an important criterion as it can be used to predict in vivo drug release profiles.

In vitro drug dissolution data from dissolution testing experiments can be useful in the correlation of pharmacokinetic data by means of in vitro-in vivo correlations (IVIVC). If the correlation can be established well, it can be very helpful for drug formulation design and post-approval manufacturing changes. Analytical data from drug dissolution testing are sufficient in many cases to establish safety and efficacy of a drug product.

Two different commercially available brands of Paracetamol (500 mg) were evaluated in this study. 10 batches of Paracetamol tablets of each brand were collected. Tablets of Brand 1 from each of the batch showed % drug release above 80% after the specified time. Tablets belonged to Brand 2, 5 of the 10 batches failed to meet the BP specification after 45 minute. The result showed that the Brand 1 samples comply with the specified dissolution rate.

The project work will help to raise awareness among people, health practitioners and drug control authority so that pharmaceutical manufacturers produce and maintain quality medicine and people may not waste their hard earning money by buying low quality product. The present study was performed in a limited scale, to get overall picture further large scale of study is needed.

Reference