



## COMPARATIVE ASSESSMENT OF THE QUALITY MEASUREMENT OF SOME COMMERCIALY AVAILABLE PARACETAMOL TABLETS

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### ABSTRACT

The study assessment the quality of different brands of paracetamol tablets sourced from medical representatives from different pharmaceutical manufactures in India by evaluating their pharmaceutical and chemical equivalence in order to determine their interchangeability. The physiochemical parameters and assay of the four brands of paracetamol tablets were assessed through the evaluations of uniformity of tablet weight, friability, hardness, disintegration, and assay of active ingredients according to established methods. The results were also subjected to statistical analysis. All the evaluated brands of the paracetamol tablets complied with the established method for uniformity of weight, friability, disintegration, and dissolution time and assay of tablets. The paracetamol tablet, inhibited highest dissolution efficiency up to 20 minutes ( $52.62 \pm 1.76$ ) and lowest  $t_{50\%}$  ( $8.416 \pm 0.744$ ) compared to another tablets. Moreover, this branded tablet showed highest percent of drug content ( $98.95 \pm 0.15$ ) compared to another tablets.

**Keywords:** Paracetamol, statistical analysis, disintegration time, dissolution test.

### INTRODUCTION

Paracetamol is one of the most popular and widely used drugs for the treatment of pain and fever<sup>1</sup>. It has a very similar structure of aspirin and because of this they are recognized by the same enzyme<sup>2</sup>. The enzyme is responsible for biosynthesis of prostaglandins which are involved in the dilation of blood vessels that cause the pain experienced in a headache. Reduction of the amount of prostaglandin, therefore helps prevent headache and other pain like migraine headache, muscular aches, neuralgia, backache, joint pain, rheumatic pain, general pain, toothache, period pain and also used for the reduction of fever of bacterial or viral origin. It is suitable for most people, including elderly and young children, because it has very few side effects<sup>3</sup>. Paracetamol is chemically N-(4-hydroxyphenol) acetamide (figure 1).

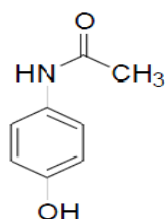


Figure 1: Structure of paracetamol

Paracetamol is classified as biopharmaceutics classification system (BCS) class I drug.<sup>4</sup> It is weak acid with a pKa of 9.0.<sup>5</sup> Paracetamol, like many other analgesics, has a short half life around 2-3 hours which necessitates frequent dosing.<sup>6</sup> In UK the recommended regimen is 500-1000 mg every 4-6 hours. Paracetamol is well absorbed from the proximal small bowel and is not subject to significant first pass metabolism in the liver, with oral bioavailability estimated at between 63-89% in adults.<sup>7,8</sup> Paracetamol is not significantly bound to plasma

proteins, and has a volume of distribution of 0.7-1 L/Kg. Maximal analgesic and antipyretic activity occurs 1-2 hour after peak plasma levels<sup>7,9</sup>, and the time to achieve this varies with the route of administration. Metabolism of paracetamol occurs primarily in the liver, while estimation occurs a most entirely through the kidney following absorption of therapeutic doses, approximately 90% is metabolized by glucuronidation and sulphonation to form non toxic metabolites, which are excreted in the urine.

Quality control procedures, which are useful tools for batch-to-batch consistency in manufacturing, should be performed for every drug product. Drugs having more than three generic products require analysis for their biopharmaceutical and chemical equivalency. These methods ensure that any of the generic products can be used interchangeably. These observation is that most of the generics have much raises the issue of the likelihood of unequal product performance. Pharmaceutical test used in assessing the equivalence includes weight uniformity, crushing strength, friability test, disintegration time, dissolution rate and chemical assay. The aim of the work as a surveillance study is to assess the product quality of different generics of paracetamol tablets, sourced from different pharmaceutical manufacturer's representatives in India by evaluating their pharmaceutical and chemical equivalence in order to determine the appropriateness of their interchangeability.

### MATERIALS AND METHODS

Paracetamol brand having label strength of 500mg (table 1) were purchased from a retail pharmacy. All tests were performed with in a retail pharmacy. All tests were performed within product expiration dates. The reagents



sodium hydroxide, potassium dihydrogen phosphate, hydrochloric acid were obtained commercially and used as received.

### Uniformity of weight

All tablets were evaluated for weight variation test as per USP XXIV monograph. Twenty tablets of each brand were used to evaluate weight variation among tablets and mean and standard deviation were calculated<sup>10</sup>.

### Thickness

The thickness of the tablets was determined using vernier caliper and the results were expressed as mean values of 20 determinations, with standard deviations<sup>11-13</sup>.

### Hardness

The crushing strength was determined with a Monsanto tablet hardness tester. Four tablets were randomly selected from each brand and the pressure at which each tablet crushed was recorded. The test was carried out in triplicate for all brands as per USP XXIV monograph<sup>10,14</sup>.

### Friability

Tablet of all brands were used to evaluate friability as per USP XXIX monograph. Friability testing was done by Roche Friabilator with readings in triplicate<sup>10,14</sup>. The percent friability was determined by using following formula:

$$\% F = \frac{W_1 - W_2}{W_1} * 100$$

Where

$W_1$  = initial weight

$W_2$  = final weight

### Disintegration time

Disintegration time of sin tablets per brands was determined in distilled water maintained at  $37 \pm 0.5^\circ\text{C}$  using tablet disintegration apparatus (Lab Hosp tablet disintegration testing apparatus, India). The disintegration time was taken to be the time no practical remained on the basket of the system.

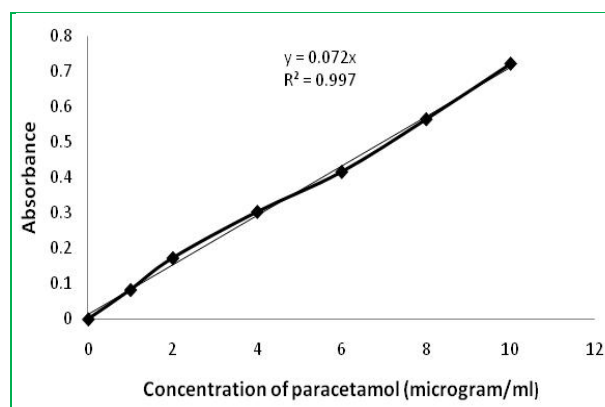
### Dissolution test

Dissolution profiles of the paracetamol tablets were determined in USP phosphate buffer solution (900ml, Ph 7.4,  $37 \pm 0.5^\circ\text{C}$ ) using USP II dissolution test apparatus (UV-1800 Shimadzu). At appropriate time intervals, 5ml sample were withdrawn and was replenished with the same volume of fresh medium. The aliquot following

suitable dilution, were analyzed spectrophotometrically at 247nm. Each test was performed in triplicate.

### Drug content

The tablets were powdered, and 100mg equivalent weight of paracetamol in tablet powder was accurately weighed and transferred into a 100ml volumetric flask. Initially, 10 ml of phosphate buffer (pH 7.4) was added and shaken for 10minutes. Then after the volume was made up to 100ml with buffer. Subsequently, the solution in volumetric flask was filtered, and 1ml of the filtrate was diluted and analyzed (figure 2) at 247nm using UV visible spectrophotometer. The drug content of the each sample was estimated from their previously prepared standard curve<sup>15,16</sup>.



**Figure 2:** Calibration curve of paracetamol in phosphate buffer USP. pH 7.4

### Statistical analysis

By one-way analysis of variance the difference in physicochemical properties was evaluated using Graph Pad Install software. When  $P$  is  $< 0.05$  the difference were considered significant.

## RESULTS AND DISCUSSION

Four brands of paracetamol tablets having 500 mg potency were purchased from local retail pharmacy. All the brands of Paracetamol tablets used were within their self life during the study period. Weight variation, drug content, disintegration time and dissolution are compendia standards. Hardness and friability are referred to as non compendia standards. However, friability is now included in the United States Pharmacopeia (USP, 1995). Tablets were subject to weight variation study (table 2) for uniformity of weight. All brands showed different mean weight which indicates the use of different excipients in the different brands.

**Table 1:** Paracetamol brands used in the study

Code	Brand name	Batch no.	Date of manufacture	Expiry date	Labeled strength	Manufacturer
A (F1)	Paracip	GS1406	06/2011	05/2014	500 mg	HSN international (Haridwar)
B (F2)	Crocic	R1118	03/2011	02/2014	500mg	Remidex Pharma Pvt Ltd. (Bangalore)
C (F3)	Calpol	RF461	04/2011	03/2014	500mg	GlaxoSmithKline Pharmaceuticals Limited (Mumbai)
D (F4)	Pyrigesic	0021	05/2010	04/2013	500mg	East India pharmaceutical works limited.



**Table 2:** Weight variation, thickness and diameter of paracetamol tablets

Code	Weight (mg) (mean±SD, n=20)	Thickness (mm) (mean±SD, n=20)	Diameter (mm) (mean±SD, n=20)
A	583.5±0.009	4.182±0.04	12.6±0.16
B	594.0±0.005	4.287±0.05	12.6±0.15
C	628.2±0.009	4.306±0.07	12.6±0.19
D	570.3±0.005	4.946±0.05	13.1±0.05

**Table 3:** Drug content, hardness friability and disintegration time of paracetamol tablets

Code	Drug content (%) (Mean±SD, n=3)	Hardness (%) (Mean±SD, n=3)	Friability (%) (Mean±SD, n=3)	Disintegration time (min) (Mean±SD, n=6)
A	98.95±0.15	5.3±0.28	0.008±0.0041	1.32±0.025
B	97.68±0.10	3.5±0.50	0.010±0.0008	1.54±0.017
C	96.78±0.44	3.3±0.28	0.035±0.050	2.56±0.11
D	96.81±0.301	4.8±0.28	0.015±0.013	4.76±0.23

**Table 4:** Characteristics of paracetamol tablets

Code	A	B	C	D
t <sub>50%</sub> (minutes)	8.416(0.744)	11.012(0.782)	17.2(7.43)	10.54(0.385)
DE <sub>20</sub> (minutes)	52.62(1.76)	43.93(7.04)	39.189(1.41)	47.31(0.804)

Figures in parentheses indicate ± SD, n=3 for t<sub>50%</sub> and DE<sub>20</sub> minutes

It is evident that the deviations from the average weight are within limits in all brands since all brands having uniform weight. Crown thickness and diameter uniformity of tablets are necessary not only for consumer requirements but also for packaging. ± 5% variation is permissible. The thickness and diameter values of the branded tablets (table 2) were within limit.

The weight variation test is clearly not sufficient to assure uniform potency of tablets. The potency of tablets is expressed in terms of grams, milligrams, or micrograms of drug per tablet and is given as the label strength of the product. The BP specification is that the content of drug should not be less than 95% and not more than 105%. The potency of the tablets was found to be 96.78-98.95% (table 3). The result ascertains the presence and compendia quantity of paracetamol in all the brands and so could not be judged as counterfeits without active pharmaceutical ingredients. However, statistically significant difference ( $P < 0.0001$ ) of drug content was observed in different tablet brands. The hardness of the tablets is an essential criterion in the determination of the ability of the tablets to resist chipping, abrasion or breakage under conditions of storage, transportation and handling. The hardness of the tablet was found to be 3.3-5.3 kg/cm<sup>2</sup> (table 3). Brand C required the least pressure before fracture while brand A required highest pressure. The results of the analysis of variance revealed no significant difference ( $P = 0.003$ ) in hardness of all the four brands at 95% confidence interval. Tablet hardness is not an absolute indicator of strength since some formulations, when compressed into very hard tablets, tend to cap on attrition, losing their, crown portions. Therefore, another measure of tablets strength, its friability, is often measured. Conventional compressed tablets that lose less than 0.5% of their weight are generally considered acceptable. The friability of the

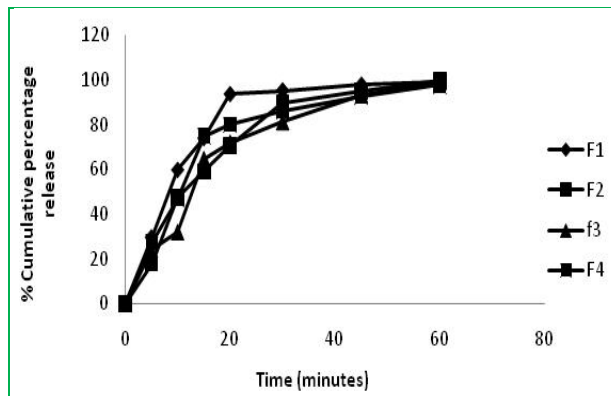
tablets (determined using Friabilator) was found between 0.008 – 0.035% (table 3) that was below 1% indicating sufficient mechanical integrity and strength of the tablets. Analysis of variance revealed no significant difference in friability ( $F_{\text{calculated}} < F_{\text{tabulated}}$  at 95% level) of branded tablets. For most tablets, the first important step toward solution is breakdown or disintegration of the tablets into smaller particles or granules. Various formulations factors are known to affect disintegration time of tablets. Disintegration time is a necessary condition and could be the rate determining step in the process of drug absorption. The type and amount of excipients used in the tablet formulation as well as the manufacturing process are all known to affect the disintegration time of all tablets. The disintegration time of paracetamol 500mg tablets were determined according to the procedure reported in USP (USP 2007). The results of the disintegration test are presented in Table 3. The results showed that all the brands passed the disintegration test. However, analysis of variance revealed significant difference in disintegration time ( $F_{\text{calculated}} > F_{\text{tabulated}}$  at 95% level) of branded tablets.

The drug release study is a measure of the amount of the drug released into the dissolution medium with time. These studies give an idea of amount of drug available for absorption after oral administration. Drugs with poor dissolution profile will not be available in the body system to elicit therapeutic effect. The results of dissolution tests in terms of dissolution efficiency and time to dissolve 50% drug (t<sub>50%</sub>) are collected in table 4, whereas the dissolution curves of paracetamol tablets from different manufactures are shown in figure 3.

The dissolution efficiency (DE) is defined as the area under the dissolution curve up to a certain time, t,



expressed as a percentage of the area of rectangle described by 100% dissolution in the same time.



**Figure 3:** Dissolution profile of four brands of paracetamol tablet

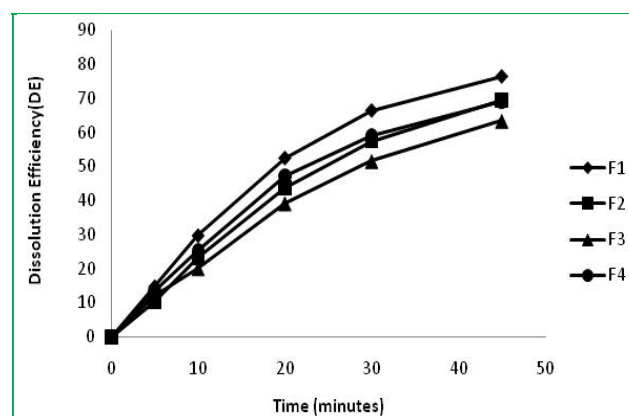
$$DE = \left[ \frac{\int_0^t y \cdot dt}{y_{100} \cdot t} \right] \times 100\%$$

Where  $y$  is the drug percent dissolved in time  $t$ .

DE can have a range of values depending on the interval chosen.

However, while comparing a set of data a constant time interval should be selected. In the present study,  $DE_{20}$  minutes (dissolution efficiency up to 20 minutes) were calculated from dissolution profile of four brands of paracetamol tablets and used for comparison.

The time required for 50% ( $t_{50\%}$ ) of drug to be released from four brands of tablets A, B, C and D were 8.416, 11.012, 17.2 and 10.54 minutes respectively (table 4). Moreover the DE also follows the same trend with brands A, B, C and D having 52.62, 43.93, 39.189 and 47.31% respectively. Dissolution efficiency curves of tablets are presented in Figure 4. From the dissolution efficiency profile, it was observed that the dissolution efficiency increased in the following order  $C \rightarrow B \rightarrow D \rightarrow A$ .



**Figure 4:** Dissolution efficiency of Paracetamol tablets

## CONCLUSION

The present quality control method is useful in monitoring the production consistency of batch-to-batch product release of each brand of paracetamol and in comparing the quality characteristics of different brands marketed. The study attempted to assess the quality of paracetamol tablet and the physicochemical equivalence of the four brands. Drug content, hardness, friability, disintegration time and dissolution profile of all products used in the study were within specified limits. Hence the safety, quality, and efficacy of essential drugs in the region should be continuously monitored through post marketing surveillance practices.

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