



POST MARKET EVALUATION OF DIFFERENT BRANDS OF PARACETAMOL (500 MG) TABLET AVAILABLE IN RURAL AREA OF NAGPUR

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ABSTRACT

Paracetamol tablets are popular over the counter (OTC) products among the patients as a good analgesics and the objective of this study was to compare the quality of the Paracetamol tablet formulations those are locally available in rural market of Nagpur. The four popular brands (A, B, C, D) of Paracetamol conventional tablet of 500 mg strength were chosen. The quality of tablet formulations of different brands for various official parameters like friability, weight variation, disintegration time, dissolution and drug assay tests were performed as per the pharmacopeia. The result of all these parameters of different brands was in the pharmacopoeial limits so it could be concluded that marketed pharmaceutical tablets of Paracetamol of these brands are safe, effective and efficacious as well as satisfy quality control limits of pharmacopeia. The objective of the study was to determine the biopharmaceutical and chemical equivalence of four brands of Paracetamol tablets marketed in rural area of Nagpur region. using in vitro tests. The physicochemical equivalence were assessed through the evaluation of both official and non-official standards such as uniformity of weight, friability, hardness, disintegration, assay and dissolution rate. All the brands complied with the official specifications for uniformity of weight, disintegration and dissolution tests.

KEYWORDS: Paracetamol, Dissolution, Post market.

INTRODUCTION

The quality of pharmaceuticals is a global concern, counterfeit medicines are increasingly detected worldwide. Constant screening of marketed drugs by the drug regulatory authority or a consumer organization, using pharmacopoeias method enables consumer to be aware of the quality of drug. In order to ensure the requisite quality, drug manufacturers test their products during and after manufacturing and at various intervals during the shelf life of the product. When there is shortage in market of the multinational brand and some life saving drugs, the patients are always reluctant to take the alternate local brands of same generic. If the patient does so, he would not psychologically satisfy & ultimately results in poor patient compliance. Some multinational brands are out of reach from buying due to high prices and comparatively local brands of same generic are available at much lower prices.^[1]

Post market qualitative studies and evaluations include activities performed to get more precise information of a product being get marketing authorization and availability for community use.

The data (qualitative and quantitative) obtained as a result of such post market evaluation could be used for product development and improvements in product quality as per standards. As it is known that the market authorization of a product for community use is granted by regulatory authorities on behalf of limited data obtained by clinical trials and scientific literature, so the post market evaluations and as a result obtained data could be extensively used to judge the approved products for their quality, efficacy and safety for general end consumers. So post market qualitative evaluation should be a continuous activity throughout the product life cycle Post market evaluation of a product has been identified to include: evaluation and investigation of reported product complaints and procedure for production and review of label claim; general public access to data taken and reported to drug regulatory authorities, and in vitro testing of product for complaints to official specifications.^[2]

Paracetamol or acetaminophen are active metabolites of phenacetin It is a widely used over-the-counter analgesic and antipyretic. Chemically, it

is 4-hydroxy acetanilide (acetaminophen). It is classified as a non-steroidal anti-inflammatory drug (NSAID) by some sources, and not as a NSAID by others, while most sources implicitly distinguish them, for example by mentioning both NSAIDs and Paracetamol in the same sentence. Paracetamol has few anti-inflammatory effects in comparison to NSAIDs.^[3]

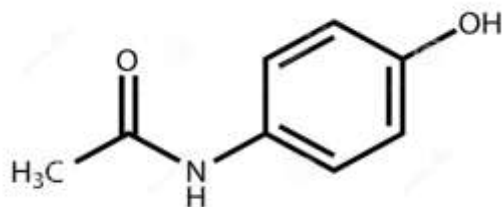


Figure 1: Molecular Structure of Paracetamol.

Paracetamol is used for the relief of pains associated with many parts of the body. It has analgesic properties comparable to those of aspirin, while its anti-inflammatory effects are weaker. It is better tolerated than aspirin in patients in whom excessive gastric acid secretion or prolongation of bleeding time may be a concern. Available without a prescription, it has in recent years increasingly become a common household drug.^[4]

However, aspirin, Paracetamol and other NSAIDs all act by the same mechanism (inhibition of prostaglandin synthesis by inhibiting cyclooxygenase (COX) and all show varying levels of analgesic, anti-inflammatory, antipyretic and antiplatelet actions. Regarding comparative efficacy, studies show conflicting results when compared to NSAIDs. A randomized controlled trial of chronic pain from osteoarthritis in adults found similar benefit from Paracetamol and ibuprofen. Paracetamol is generally safe for human use at recommended doses. However, overdoses of Paracetamol can cause potentially fatal liver damage and in rare individuals, a normal dose can do the same. The quality of pharmaceuticals is a global concern; counterfeit medicines are increasingly detected worldwide.^[5]

This study focus on the investigation of the quality of Paracetamol tablet which is registered by drug regulatory body of India, Drug Administrative and Control Authority of (DACA). The aim of the study was to investigate the in-vitro quality of Paracetamol tablet marketed in rural area of Nagpur. The study provides information about trend and characteristics of counterfeit and substandard if any of Paracetamol tablet, point out the relative variation of marketed Paracetamol table in comparison with standard set by British Pharmacopeia (BP), United States Pharmacopeia (USP) and Indian Pharmacopeia (IP) & the degree of adherence of

marketed tablet to the standard set by regulatory body in India.

MATERIAL AND METHOD

Material

Chemicals and reagent

Paracetamol, having a label strength of 500mg of four different brands were purchased from registered pharmacy shop in Savner, Nagpur. The products were coded as A (Calpol, Glaxo Smithkline Pharmaceutical Ltd.); B (Dolo, Microlabs Ltd.); C (P 500, Apex Laboratory Ltd.); D (Paracetamol) and the study were performed within product expiration dates. Methanol (AR Grade) were obtained from Loba Chemie Pvt. Ltd, Mumbai (India) and all other chemicals used were of analytical grade. Freshly prepared distilled water were used throughout the work.

Apparatus and Equipments

Double beam UV-Visible Spectrophotometer (Systronic's Model no: 2201), Analytical balance (Electric precision balance, Model no.:3003), Hardness Tester (Monsanto, Mht-20), Tablet Friability Tester (Roche, FTV-2), Disintegration apparatus (ED-2L), Dissolution apparatus (EDT-08LX) and Ultrasonicator (Toshcon, SW 4).

Method^[6]

Thickness and Diameter

The thickness and diameter of the tablets were determined by using Vernier callipers. Randomly 10 tablets were selected and used for determination of thickness. The result was expressed in Mean and unit in mm.

Weight variation

Sample tablets (20 in number) of each brand were weighed together and average weight was determined. Each tablet was weighed individually on analytical balance. The percentage (%) deviation, and standard deviation was determined.

$$\% \text{ Deviation} = \frac{W_{avg} - Wind}{W_{avg}} * 100$$

Where,

W_{avg}: Average weight of tablets

Wind: Individual weight of tablet

Hardness

Sample tablets (10 in number) of each brand were taken, a tablet was placed vertically on the Monsanto hardness tester. The load was then applied along the radial axis of the tablet. The pressure was then increased as uniformly as possible until the tablet breaks and the pressure required to break the tablet was then read off the machine and recorded.

Friability

5 tablets of individual brand were weighed and placed in Roche friability apparatus. The apparatus was rotated at the speed of 25 rpm for 4 minutes. After 100 revolutions the tablets were weighed and recorded. The % friability of the tablets was then calculated using formula:

$$\% F = \left[1 - \left(\frac{W}{W_0} \right) \right] \times 100$$

Where,

% F = Friability in percentage,

W_0 = Initial weight of tablets,

W = Weight of the tablets after revolution.

Tablet Disintegration

The disintegration time of randomly selected six tablet of individual brands was determined at temperature of $37 \pm 0.2^\circ\text{C}$ containing simulated gastric fluid (0.1N HCl) using a Multi-unit disintegration tester (USP) apparatus. The time taken for tablets to disintegrate was noted down.

Pharmacopoeial Assay^[7]

20 tablets from each brand of Paracetamol was weighed using analytical balance and were finely powdered. An accurately weighed portion of powder equivalent to 150mg Paracetamol was transferred to volumetric flask of 200 ml, to it 50 ml of 0.1M sodium hydroxide (NaOH) and 100ml of distilled water was added and sonicated for 15 minutes and diluted up to 200ml and filtered. 10ml of the filtrate was transferred to 100ml volumetric flask and further diluted to 100ml with distilled water. The absorbance of resulting mixture was taken at

257nm. the drug content was calculated by taking A (1%, 1cm) as 715 at the maximum 257 nm.

Tablet Dissolution^[8]

Dissolution test was carried using U.S.P. Type- 1 (Basket) Single flask Dissolution Apparatus. Gastric Fluid was taken as a Dissolution Medium. The tablets were immersed into 900 ml, of dissolution medium. The temperature of the dissolution medium was maintained at $37 \pm 0.2^\circ\text{C}$. The basket was rotated at a speed of 150 rpm. After an interval of every 15 minutes, 2 ml of the medium was pipetted out and replaced with fresh medium (0.1N HCl). The process was continued for 60mins. The pipetted samples were then diluted to 10 ml, with fresh dissolution medium and filtered. The absorbance of the filtered samples was taken using U.V. Spectrophotometer at λ_{max} 257 nm and the % drug release of each brand of Paracetamol tablet was calculated by using standard calibration curve method.

General Appearance

The thickness and diameter of all brands of Paracetamol tablets was measured by using Vernier Calliper. 3 tablets of each brand were used and average values were calculated. The results are shown in Table 1.

Weight Variation

Tablets were taken, weighed and their average weight was calculated. The results are shown in Table 1. The uniformity of weight determination for all the brands of Paracetamol tablets showed values which complied with the USP specifications for weight uniformity as none of the brands deviated by upto $\pm 5\%$ from the mean value.

Table 1: Data for Thickness, Diameter and Weight variation of Paracetamol tablet.

Sr. no.	Sample Code	Thickness (mm \pm SD)	Diameter (mm \pm SD)	Weight Variation (Mean weight \pm SD)
1	A	4.3 \pm 0.27	13.1 \pm 0.24	0.984 \pm 0.012
2	B	4.2 \pm 0.23	13.2 \pm 0.08	0.928 \pm 0.003
3	C	4.4 \pm 0.17	13.17 \pm 0.23	0.950 \pm 0.010
4	D	5.2 \pm 0.21	13.15 \pm 0.19	0.881 \pm 0.025

Hardness

The hardness of individual brand of Paracetamol tablets was measured by using Monsanto hardness tester and the observed results showed that all the brands have acceptable crushing strength of between 4 kg/cm² to 10 kg/cm². Results are showed in Table 2.

Friability

Friability is an important parameter which is related to hardness, disintegration and dissolution. The result of tablet friability test showed that virtually all the brands of Paracetamol tested had impressive

friability values ranging from 0.22 \pm 0.008 % to 0.56 \pm 0.014 % and thus have meet the specification of USP which specifies that the friability study must not lose 1% of their initial weight Table 2.

Disintegration

The observed disintegration times for all the brands of Paracetamol investigated was found within the acceptable range of 23.2 \pm 0.21 to 28.19 \pm 0.22 which is less than 30 min limit prescribed by official compendium Table 2.

Pharmacopoeial Assay

Test for percentage of content is based on the assay of the individual content of active ingredient of a number of single dose units. All brands of tablets contained the Paracetamol ranging from 96.36 ± 0.71

to 99.30 ± 0.05 which is within 90 - 110 % of the labelled claim (Table 2) as per IP, USP and BP specifications. Thus, the assay results ascertain the presence and compendial quality of the drug in all products.

Table 2: Comparative evaluation of different quality control parameters of Paracetamol.

Sr. no.	Sample Code	Hardness (kg/cm ²)	Friability (%)	Disintegration (Min.sec)	% Drug Content
1	A	4.5 ± 0.40	0.56 ± 0.014	23.2 ± 0.21	98.18 ± 0.04
2	B	5.4 ± 0.29	0.35 ± 0.02	28.19 ± 0.22	99.30 ± 0.05
3	C	7.25 ± 0.37	0.22 ± 0.008	25 ± 0.21	96.36 ± 0.71
4	D	4.17 ± 0.17	0.33 ± 0.016	26.25 ± 0.23	98.22 ± 0.14

DISSOLUTION

Dissolution of drug from oral solid dosage forms is an important aspect for drug bioavailability and brand to brand consistency. The in-vitro drug release characteristics of the tablets were studied. The dissolution of all brands showed the highest percent release concentration in Sample B (99.54 %) while the lowest percent release concentration was recorded in sample D (96.66%) (Table 3 & 4 & Figure 2 & 3).

Table 3: Standard calibration curve for Paracetamol.

Sr. No.	Concentration (µg/ml)	Absorbance
1	5	0.229 ± 0.005
2	10	0.358 ± 0.001
3	15	0.567 ± 0.00
4	20	0.723 ± 0.00
5	25	0.883 ± 0.002
6	30	1.032 ± 0.001
Slope		0.032
Intercept		0.057
Correlation Coefficient		0.997

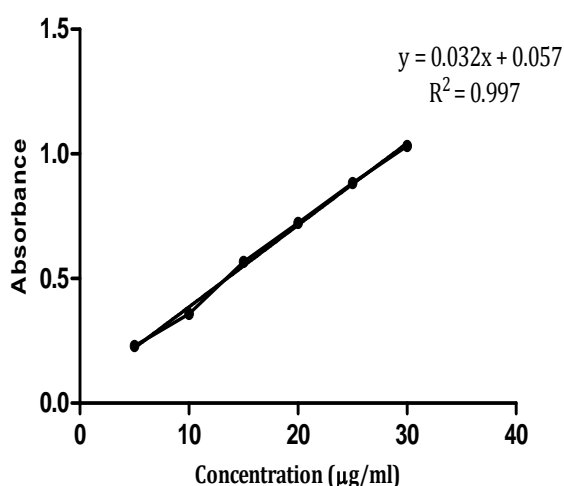


Figure 2: Standard Calibration Curve of Paracetamol at 257 nm.

Table 4: Drug release of four different brands of Paracetamol tablets.

Sr. no.	Time (Min)	% drug release			
		A	B	C	D
1	15	51.64	50.94	54.55	72.9
2	30	75.47	69.66	72.9	85.14
3	45	90.72	82.8	89.46	92.52
4	60	96.84	99.54	97.92	96.66

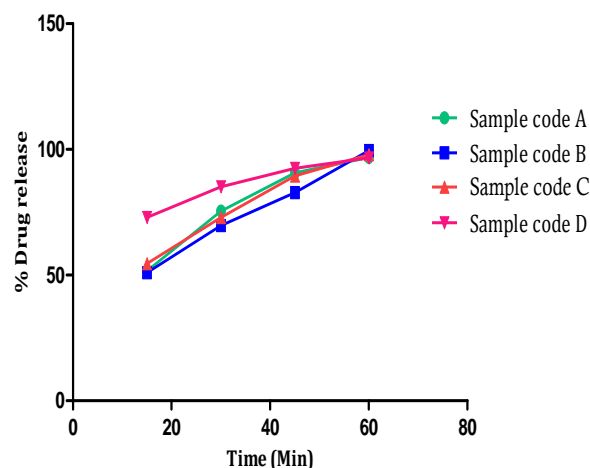


Figure 3: Dissolution profile of tested Paracetamol tablets.

CONCLUSION

Based on the results obtained, it can be concluded that of all the four tested brands of Paracetamol tablets (A, B, C and D) that evaluated in this study; were passed the pharmacopoeial limit tests and their dissolution profiles were found to be similar; thus could be considered biopharmaceutically and chemically equivalent.

These types of studies should be conducted more frequently not only to build public awareness about the quality of marketed pharmaceutical products but also because these type of studies are very helpful for the advancement of our pharmaceutical sector. Sub-standard drugs manufacturing can also be prevented by conducting this study.

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