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# Comparative Quality Assurance Assessment of some Commercially Available Brands of Paracetamol tablets in Benin City Metropolis, Edo State, Nigeria.

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***Abstract:*** *Paracetamol (acetaminophen) is a drug used to temporarily relieve mild to moderate pain associated with headaches, menstrual periods, toothaches, backaches, osteoarthritis, or cold/flu aches and to reduce fever. It is one of the most found over the counter (OTC) drugs in many households and also the most perceived frequently faked product worldwide. This study was carried out to comparatively assess the quality of paracetamol tablet brands sold in the different pharmacies, dispensaries in Benin City metropolis with reference to Pharmacopoeia standards.*

***Materials and method****: A total of 11 brands of paracetamol conventional tablets(500mg) were purchased from different locations in Benin City. Quality control parameters like organoleptic, weight variation, hardness, friability, tensile strength, disintegration time, moisture absorption tendency and dissolution rate were performed as per the pharmacopoeia standards.*

***Results:*** *The results showed that the 11 samples of different brands passed the weight variation test, friability test (0.0 – 0.5%), hardness test (7.25 – 14.65 kg) and disintegration time test (1.07 – 4.65 min). The various brands satisfied the BP, USP requirements for dissolution test as the percentage drug dissolved were≥ 70% within 40 min, except Pcm 9 (≤ 62.0%) within 40 min. The moisture absorption tendencies of the brands were within the pharmacopoeia standard limits, hence with appropriate packaging and storage, the drugs stability would be maintained throughout the shelf lives of the products. From this study and the various results obtained, it can be established that majority of the available brands of paracetamol 500 mg tablets dispensed in Benin City environs are up to pharmaceutical standard of quality for use by consumers.*

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## I. Introduction

Paracetamol (acetaminophen) is used widely as OTC analgesic/antipyretic drug and has been one of the most widely used classes of medication in children and adults[1]. It is a non-opioid analgesic recommended for the first line management of fever, mild to moderate headache, pains, and cold/flu in infants, children and adults[2,3].Sometimes acetaminophen can be used in the management of severe pains associated with cancer alone or in combination with other drugs[4]. It belongs to the class of aniline analgesics. There has been a reported increase in the circulation of counterfeit drugs worldwide which has been attributed to the lack of effective monitoring of the quality of drug products sold in the market places[5,6]. Paracetamol is generally safe and well tolerated for human use at recommended doses. But acute over dosage can cause severe hepatic damage[7]. However, the safety and efficacy of a pharmaceutical dosage form can only be guaranteed when its quality is reliable.This also depends on their formulation and manufacturing process variables adopted by the different manufacturing companies. Hence the possibility of differences in the quality of some dosage forms with reference to the pharmacopoeia standard of quality. Paracetamol is generally considered to be a weak inhibitor of the synthesis of prostaglandins. However, its in-vivo effects are similar to those of the selective cyclooxygenase-2 (COX-2) inhibitor. Paracetamol also decreases prostaglandins concentration in- vivo, but unlike the selective COX-2 inhibitor does not suppress the inflammation of rheumatoid arthritis[8]. There is considerable evidence that the analgesic property of paracetamol is central and is due to the activation of descending serotonergic pathways, although its primary site of action may still be the inhibition of prostagladinssynthesis[9].This study therefore is to compare the physicochemical properties of different brandsof Pcm 500 mg tablets with that of May&Baker (M&B)paracetamol500 mg tablets as reference standard. It is also

to evaluate the bioequivalence of the different brands which will serve as a basis to accessing the quality and the bioavailability of the products upon administration.

## II. Materials and method

**Materials**: Different brands (11) of paracetamol 500 mg tablets were purchased from pharmacy outlets in Benin City metropolis. Benin is a city that comprises in part, four local governments with last known population (2015) of 1,495,800 people – approximately 0.821% of total Nigeria population. Paracetamol powder BP was obtained from Sigma – Aldrich Chemie GmbH, Germany.

**Table 1.Information on the various brands of Paracetamol 500 mg tablets**

| *CODE* | *BRAND* | *COUNTRY OF ORIGIN* | *NAME OF MANUFACTURER* | *BATCH/ LOT NO.* | *MANUFACTURED DATE* | *EXPIRING DATE* | *NAFDAC REGISTRATION NO.* |
|---|---|---|---|---|---|---|---|
| PCM1 | EASADOL | NIGERIA | MAY AND BAKER NIG PLC | RI51470 | 09/2015 | 08/2020 | 04-8592 |
| PCM2 | EMZOR | NIGERIA | EMZOR PHARMACENTICAL INDUSDRIES LTD | 58914 | 12/2015 | 12/20 | 04-0411 |
| PCM3 | PARATEX | NIGERIA | PHARMATEX INDUSTRIES LTD (PIL) | T4057 | 12/2014 | 11/2019 | B4-1593 |
| PCM4 | PANDA | NIGERIA | AFRAB CHEM LTD | 15351 | 11/2015 | 11/2020 | 04-2019 |
| PCM5 | PANADOL | NIGERIA | GLAXO SMITKLINE CONSUMER NIG .PLC | 030W | 10/2015 | 10/2019 | 04-0205 |
| PCM6 | TUMOL | NIGERIA | TUYIL PHARM.IND. LIMITED | P22 | 01/2016 | 12/2021 | 04-18353 |
| PCM7 | ARCHY | NIGREIA | ARCHY PHARMACEUTICAL LTD | PT14057 | 10/2014 | 11/2018 | 04-5269 |
| PCM8 | EMCAP® EXTRA | NIGERIA | EMZOR PHARMACENTICAL INDUSTRIES LTD | 5142U | 10/2015 | 10/2019 | 04-1451 |
| PCM9 | DRUGAMOL | NIGERIA | DMG FLEID PHAMACENTICAL LTD | 770405 | 04/2015 | 11/2019 | 04-3649 |
| PCM10 | M&B | NIGERIA | MAY& BAKER NIGERIA PLC | A160134 | 02/2015 | 01/2021 | 04-0633 |
| PCM11 | BENTOS | NIGERIA | BENTOS PHARAMACENTICAL PRODUCTS LTD | A6032A | 02/2016 | 01/2021 | 04-0667 |

**Equipments:**
Digital vernier caliper (Mitutoyo, 530 Series – Standard model).
Monsanto hardness tester (Model: MHT – 20) – Campbell Electronics.
Electronic balance (Ohaus Scout Pro Portable Toploading balance).
Erwekafriabilator (TAR – ERWEKA GmbH)
Manesty disintegration tester (TD71T170 /Labequip Canada)
Rotating paddle dissolution apparatus (USP type 11)
UV-Visible Spectrophotometer (v-750 uv-visible/NIR)
The information on the various brands of paracetamol 500mg tablets is shown on Table 1 with Pcm 10 (M&B) taken as the standard.

**Methods**: Parameters evaluated were dependent on the standards of tablet properties as published in the different international pharmacopoeias and formularies (BP[10], USP[11]).Organoleptic properties which include inscription on the tablet surface, color, finishing (dull/glossy) and coating types were examined. All the samples and their differences in observations were objectively handled.

**Thickness and diameter**: The dimensions of the tablets were measured using vernier caliper instrument. The tablets were randomly selected from each sample brand and measured. The mean of triplicate readings for each was recorded (mm).

**Weight uniformity**: Twenty tablets (20) from each brand were randomly selected and weighed individually and collectively using the digital weighing balance (Ohous-Scout PRO) and values (gm) recorded.

**Hardness test**: The tablet hardness was measured with a Monsanto hardness tester. The force to break the tablet was diametrically applied, by placing the tablet between the anvil and spindle of the tester, and the knurled knob turned until the tablet fits into space and adjusted to zero. The pressure was applied by turning the knurled knob until the tablet breaks; the force (kg) was read and the mean of triplicate determinations of each brand was recorded.

**Tensile strength**: The mean of dimension values of tablet thickness, diameter and hardness of each sample brand was used to calculate the tensile strength of the tablets using the formula:

Tensile strength = $2F/\pi DH$ …….. 1

Where

F = breaking force (kg)
D = tablet diameter (mm)
H = tablet thickness (mm)
$\pi$ = 3.143

**Friability test**: Ten tablets were selected randomly from each brand, weighed together and recorded ($w_1$). The tablets were then placed in the Friabilator and rotated at a set speed of 25rpm, and after 100 revolutions (4min), the machine was stopped and the tablets were dusted and re-weighed ($w_2$). Friability (%) was calculated using the formula:

Friability (%) $= (w_1 - w_2) / w_1 \times 100$……..2

The mean of duplicate determinations was recorded.

**Disintegration test**: The USP disintegration apparatus was used. It consists of 6 glass tubes of 3 inches length open at the top, and held against a 10-mesh screen at the bottom end of the basket rack assembly. A tablet was placed in each tube and the basket rack positioned in distilled water that was maintained at a temperature of 37± $0.5^0$C. This was done such that the tablet remained 3.5cm below the surface of the liquid on their upward movement and descent not closer than 2.5cm from the bottom of the beaker. Perforated plastic disc was placed on the top of the tablets to impart an abrasive action to the tablets and also to prevent the tablets floating to the top. The apparatus was operated and the time it took for all the particles to pass through the 10-mesh screen was recorded. The mean of the time for the six tablets of each brand to disintegrate was recorded. For uncoated tablets the USP and BP specifies disintegration time of 15min[12,13].

**Preparation of standard drug solution**: Pure Paracetamol powder BP (10mg) was dissolved in 50 ml of 0.1N HCl, stirred for 5min and the volume made up to 100 ml to obtain a stock solution containing 100µg/ml. Serial dilution was done to obtain concentrations of 2, 4, 6, 8 and 10µg/ml respectively. Absorbance of these solutions was determined using UV Spectrophotometer at maximum wavelength of 242nm and plotted against concentration.

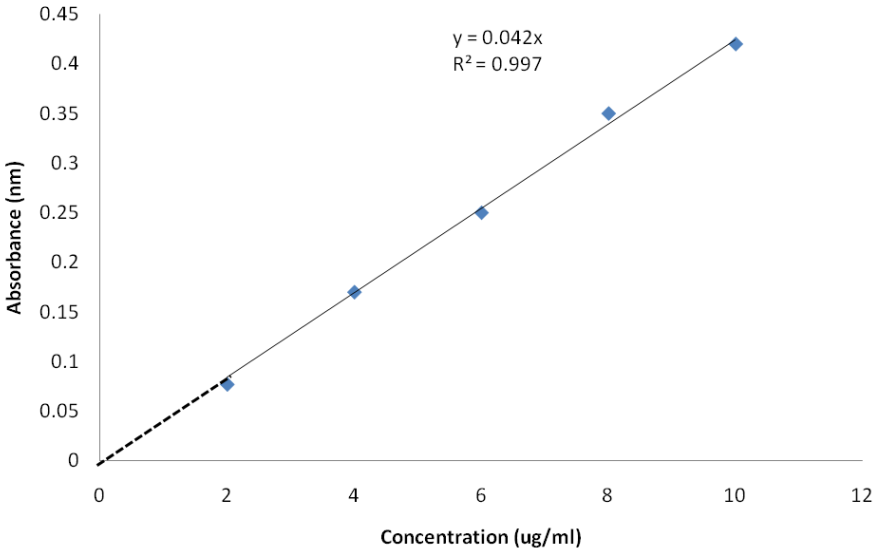


**Fig 1: Standard Curve for Pure Paracetamol powder BP at wavelength 242nm**

**Determination of dissolution rate**: The dissolution medium (900 ml of 0.1N HCl) was maintained at 37 ± $0.5^0$C. The USP dissolution apparatus Paddle method was employed[13]. A tablet was placed at the bottom of the dissolution flask and the paddle rotated at 50 rpm. Aliquot samples (5ml) were withdrawn from the flask at 5, 10, 15, 20, 45 and 60min interval into appropriately labeled test tubes. A 5ml fresh dissolution medium at same temperature was used to replace the 5ml aliquots withdrawn each time to maintain sink condition. All samples withdrawn were filtered using Whatman filter paper No. 1. The filtrate was further diluted to 10 ml with 0.1N HCl and their absorbance measured using UV Spectrophotometer at maximum wavelength of 242nm. The amount of the drug dissolved at each interval was calculated using the standard calibration plot. The procedure was repeated for the different brands and the percentage drug dissolved at the different time intervals was calculated and recorded using the formula:

$$\%drug\ dissovled = \frac{\text{Conc.} \times \text{dilution factor} \times \text{vol. of dissolution medium}}{\text{Actual content of active ingredient}} \times \frac{100}{1}$$

**…….3**

**Humidity sorption of paracetamol tablets**

The method adopted byShende*et al*., (2009), for a solid dosage formulation was employed[14]. The tablets were stored for 10 days in a controlled environment of 75% relative humidity and temperature of $25^0$C. Saturated solution of Sodium chloride was used to obtain the above conditions using laboratory desiccators. The Petri dish containing the tablets was then placed in the 75% relative humidity chamber to observe the moisture uptake. The weight increase due to moisture absorption was measured by taking weight at different time intervals of 24 hr and 48 hr, followed by consecutive weighing at every 72 hr for a period of 10 days.

## III. Results and Discussion

**Organoleptic properties**: Table 2 shows the organoleptic properties of the various brands of paracetamol tablets. The different brands had suitable appearances. They were evenlycoloured, smooth with clear inscription markings. The appearance of a tablet is important as it allows for good consumer acceptability and hence adequate compliance to the dosage regimen by the patients.

**Table 2: Result on organoleptic parameters of brands of paracetamol tablets**

| CODE NO | BRAND NAME | CLOLOUR | COATING TYPE | INSCRIPTION | FINISHING |
|---|---|---|---|---|---|
| **PCM 1** | EASADOL | WHITE | FILM COATING | EASADOL 500 | SMOOTH |
| **PCM 2** | EMZOR | WHITE | FILM COATING | EMZOR 500 | SMOOTH |
| **PCM 3** | PARATEX | WHITE | FILM COATING | NONE | SMOOTH |
| **PCM 4** | PANDA | WHITE | FILM COATING | NONE | SMOOTH |
| **PCM 5** | PANADOL | WHITE | FILM COATING | PANADOL® | SMOOTH |
| **PCM 6** | TUMOL | WHITE | FILM COATING | TUMOL 500 | SMOOTH |
| **PCM 7** | ARCHY | WHITE | FILM COATING | NONE | SMOOTH |
| **PCM 8** | EMCAP | WHITE | FILM COATING | EMCAP 500 | SMOOTH |
| **PCM 9** | DRUGAMOL | WHITE | FILM COATING | NONE | SMOOTH |
| **PCM 10** | M&B | WHITE | FILM COATING | M&B 500 | SMOOTH |
| **PCM 11** | BENTOS | WHITE | FILM COATING | NONE | SMOOTH |

**Table 3: Results on the various parameters carried out on the tablet brands**

| CODE NO | Mean weight(g) | Mean diameter (mm) | Mean thickness (mm) | Mean hardness (kg) | % friability | disintegration time (min) | Moisture absorbance (%) | Tensile Strength (kg) |
|---|---|---|---|---|---|---|---|---|
| Pcm1 | 0.63 | 17.75 | 5.23 | 12.05 | 0.2 | 1.07 | 0 | 0.81 |
| Pcm2 | 0.51 | 12.50 | 4.75 | 11.10 | 0 | 4.23 | 0 | 1.17 |
| Pcm3 | 0.57 | 12.10 | 4.40 | 13.20 | 0.4 | 2.58 | 0.2 | 1.55 |
| Pcm4 | 0.66 | 13.40 | 4.45 | 12.50 | 0.5 | 1.32 | 0 | 1.26 |
| Pcm5 | 0.77 | 17.65 | 5.21 | 13.10 | 0.2 | 3.68 | 0.1 | 0.89 |
| Pcm6 | 0.65 | 18.38 | 5.60 | 11.40 | 0.1 | 2.46 | 0.13 | 0.62 |
| Pcm7 | 0.58 | 12.28 | 4.35 | 10.25 | 0.2 | 2.42 | 0.06 | 1.20 |
| Pcm8 | 0.51 | 15.30 | 5.19 | 7.25 | 0.3 | 4.65 | 0.07 | 0.57 |
| Pcm9 | 0.83 | 12.17 | 4.27 | 14.65 | 0.2 | 1.82 | 0.10 | 1.76 |
| Pcm10 | 0.89 | 12.45 | 4.40 | 12.35 | 0.4 | 1.08 | 0.01 | 1.41 |
| Pcm11 | 0.63 | 10.26 | 4.30 | 12.15 | 0.2 | 1.95 | 0.21 | 1.70 |

Table 3 shows the means values of the different parameters evaluated for all the brands of paracetamol tablets. Tablet thickness specification is characteristic to each product and values must be within ±5% of specified values.The result showed that the tablets passed the test by not deviating from the mean by more than ±5%. Factors such as the density of the granules, the applied compression pressure can affect the variation of

tablet thickness. None conformity to thickness specification can cause packaging problem and consequently increase cost of transportation[15,16]. The uniformity of tablet diameter depends on the diameter of the punch and die used for the compression process. The standard deviation permitted is ±5% of the mean diameter. The result of the tablet brands evaluated shows that all the brands complied with the test[17]. The different brands were hard enough to withstand packaging and transportation hazards. Their values complied with the BPC specification of ≥ 4kg. Tablet hardness depends on particle size distribution, moisture content of granules, compression pressure and the type and concentration of binders used in the formulation. The weight uniformity test as specified by the USP standard is that not more than 2 of the tablet samples should deviate from the average weight within ±5% for tablets of 324 mg and above[17]. Flow properties and lubrication of the granules are factors that can affect the weight uniformity of tablets within a batch. Tensile strength provides a more fundamental measure of the mechanical strength of the compressed material, and takes into account the geometry of the tablet. From the results of the 11 brands evaluated, all were found to be sufficiently strong; values ranging from 0.57-1.76kg. Thus all the tablet brands were strong enough to withstand the mechanical stress and abrasion as they are packaged and transported from one location to another. The USP specify that the disintegration time of uncoated tablets should not exceed 15 min[17]. Results in Table 3 showed that all the brands passed the disintegration test as specified.

Friability test measures the ability of the tablets to withstand abrasion during handling. It determines the physical strength of compressed and uncoated tablets upon exposure to mechanical shock and attrition. Conventional compressed tablets that lose less than 0.5% to 1% of weight are considered acceptable[18,19]. From the result on Table 3, the 11 brands of paracetamol complied with the requirement for friability since their values fall within 0% - 0.5%.Moisture absorption plays remarkable negative role in pharmaceutical products particularly for solid dosage forms. It is evident from Table 3 that product brands Pcm 1, 2 and 4 did not absorb moisture after 10 days of exposure to the environment. The moisture absorption levels of the other brands (0.01 – 0.21%) were within the acceptable levels for solid dosage forms[14]. Physical and chemical stability of some drugs are affected by moisture as it increases the rate of drug decomposition, causes agglomeration of powders and granules and discoloration. Moisture accelerates the hydrolysis of drug as well as facilitates reaction with other excipients thereby affecting stability and shelf life of the final product[20].

Dissolution profiles: Figures 2a and 2b show the dissolution profiles of the different brands of paracetamol tablets in 0.1N HCl. The results show that all the brands complied with the British Pharmacopoeia 2003 requirements which states that 70% of the drug should dissolve within 40min for conventional solid dosage forms. This requirement was met by all the brands under investigation, with Pcm 10 having the highest dissolution rate. Drugs with poor dissolution profile may not be available at the right amount and early enough in the plasma to elicit therapeutic effect at the target organ or tissue[21]. This is because any factor that affect dissolution rate may also affect the rate and extent of drug absorption[22].

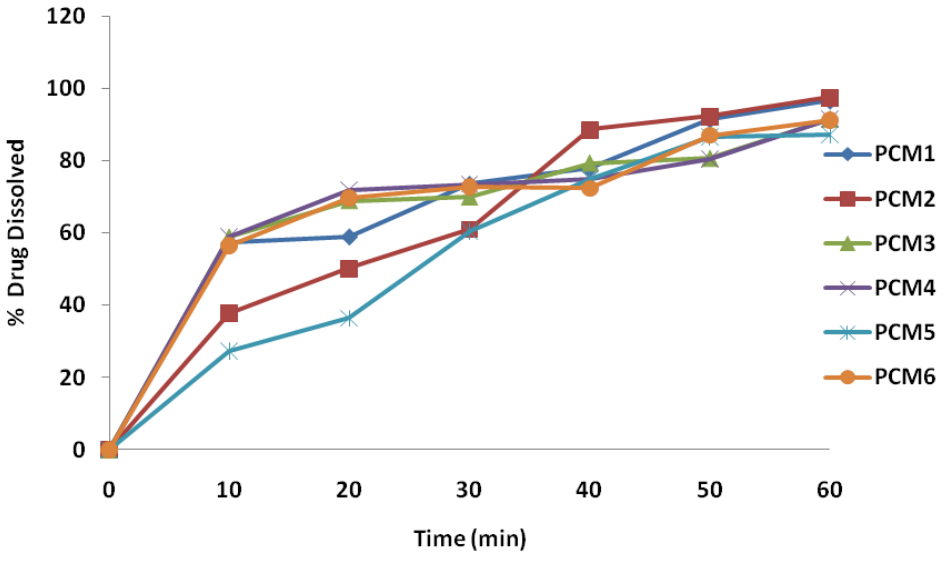


**Fig 2a. Dissolution profiles of 6 brands of paracetamol 500 mg tablets.**

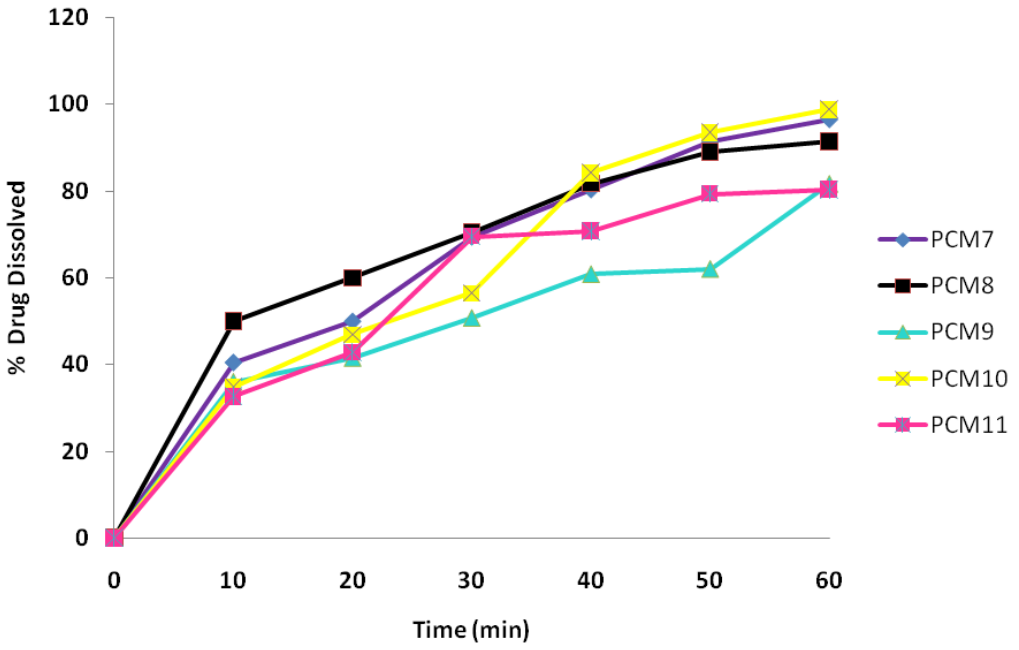


**Fig 2b. Dissolution profiles of 5 brands of paracetamol 500 mg tablets.**

## IV. Conclusion

The results of the evaluation of the organoleptic parameters and the physicochemical properties of the different brands of paracetamol 500 mg tablets, revealed that the 11 brands conform to the pharmacopoeia standards of quality. The 11 brands had suitable appearance to enhance consumer acceptance. The tablets were sufficiently strong enough to withstand possible packaging and transportation hazards. The disintegration time of the various brands was within the 15min specified for uncoated tablets. The USP specified that 70% of the drug must be dissolved within 40min. The result showed that all the brands met this pharmacopoeia standard of quality.From the results of this study, it can be inferred to a very reasonable extent that the majority of the commercially available brands of paracetamol500 mg tablets sold and dispensed for patients use in Benin City metropolis meet the pharmaceutical standard of quality and are safe for use by consumers.

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