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## Comparative Test of Physicochemical Parameters and Microbiological Quality of Different Brands of Paracetamol Tablets Sold in Nigeria

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### ABSTRACT

Paracetamol also known as acetaminophen is a widely used antipyretic and analgesic agent. The therapeutic efficacy of pharmaceutical products depends on both microbial and physicochemical qualities of the products, hence, the need to routinely assess the pharmaceutical quality of the available brands of the tablets to ensure they conform to standard specifications. This study was done to evaluate the microbial and physicochemical qualities of 10 brands of paracetamol tablets sold in Nigeria. The purchased drug samples were evaluated for their uniformity of weight, crushing strength, friability, disintegration time, total viable aerobic count and content of active ingredient. These tests were performed by standard methods and techniques following official pharmacopoeia protocols. The investigated 10 brands of paracetamol tablets passed the standards of the British Pharmacopoeia (BP) regarding microbial specifications. The tablets were uniform in weight with crushing strength 5 KgF - 12 KgF except a brand with crushing strength ranging between 15 KgF – 18 KgF and another brand which has no crushing strength. The disintegration times were within 15 minutes except a brand with a disintegration time of 27 minutes 44 seconds. Friability values were less than 1%. The % content of paracetamol as an active ingredient in the tablets ranges from 90-110%. 8 out of 10 brands of the paracetamol tablets assessed met all compendia standards. However, products of good quality can be

guaranteed through quality control and adherence to the provisions of good manufacturing practices. Also, a routine sentinel market surveillance of pharmaceutical products is encouraged.

**Keywords:** British Pharmacopoeia (BP), United States Pharmacopoeia (USP), Pharmaceutical quality, Acetaminophen, UV/Visible Spectrophotometer, Good Manufacturing Practice, Paracetamol

## **1. INTRODUCTION**

Paracetamol also known as acetaminophen is a widely used analgesic and antipyretic. It is commonly used for the relief of fever, headaches, and other minor aches and pains and is a major ingredient in numerous cold and flu remedies. It is not surprising therefore, that analgesics are among the most widely used categories of drugs. Drugs and pharmaceutical products are manufactured based on stipulated standards. These standards are regulated by the regulatory authorities. The standards are achieved through well-articulated current Good Manufacturing Practices (cGMP). Maintaining cGMP will ensure the formulation of products of acceptable standards in contents of active ingredients, good physical and chemical stability and acceptable microbiological quality. Adulterated and substandard pharmaceutical products pose serious challenge. Microorganisms possess diverse metabolic activities and are likely to present a variety of hazards. The presence of microbial contaminants was not only found to cause physicochemical changes that led to the spoilage of numerous products but was also proved to be a potential health hazard to the consumer. Limits have therefore been set for the presence of microorganisms in medicines by commissions such as BP which vary depending on the products and their intended use. The proliferation of counterfeit and poor quality drugs is a major public health problem, especially in developing countries lacking adequate resources to effectively monitor their prevalence. Reports have been found from various regions across the variations on the physicochemical and pharmaceutical equivalence of the various brands of paracetamol tablets available in the Nigerian market (Oga et al., 2010; Sani et al., 2012; Awemu et al., 2015). Daily healthcare providers are confronted with the problem of generic substitution (Auta et al., 2014) influenced by factors such as cost, efficacy, aesthetic packaging and the assignment of NAFDAC number. This research therefore, evaluates the physical, chemical and microbiological quality of 10 brands of paracetamol tablets sold in Nigeria so as to establish their pharmaceutical quality.

## **2. MATERIALS AND METHOD**

### **2. 1. Drug Sampling**

10 brands of paracetamol tablets (500mg) having different manufacturing dates were purchased from various registered pharmacies within Lagos, Nigeria and labeled with the code A, B, C, D, E, F,G, H, I and J.

### **2. 2. Method**

The following were carried out on the brands of paracetamol tablets:

- a. Physical examination.

- b. Chemical examination.
- c. Microbiological examination.

**a) Physical Examination**

The physical examination being carried out the brand paracetamol was sub divided into the following;

**i) Uniformity of weight test**

Twenty tablets were randomly selected from each brand and weighed individually using the analytical weighing balance (Shimadzu ATX224). The weight of 20 tablets altogether was also weighed and the mean weight was calculated. The weight variation was calculated as mean  $\pm 5\%$  of the mean. If two tablets out of 20 are outside the range, the tablets are considered to have failed the test. (BP 2012).

**ii) Hardness test**

The crushing strength of 5 tablets from each brand were determined with a tablet hardness tester and the average were calculated. If the tablets are outside the range of 4 Kgf – 12 Kgf, they are considered to have failed the test

**iii) Friability test**

The weight of twenty tablets from each brand were determined with an electronic weighing balance and were put in the friability test apparatus which consists of a plastic chamber that revolves at 25 rpm, dropping the tablets through a distance of six inches in the apparatus which is then operated for 100 revolutions. The apparatus is set to four minutes after which the tablets are reweighed. The weight loss was obtained from the difference between the initial and the final weight. The friability was calculated as the percentage weight loss. The tablets pass the test if they have a friability of  $\leq 1\%$ . (BP 2012).

**iv) Disintegration time test**

The disintegration time of 6 tablets per brand was determined with a disintegration test apparatus (Erweka ZT4, Germany). 1 tablet is placed in each tube and the basket rack is positioned in a 1-Litre beaker of water at a temperature of 37 degree such that the tablet remain 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement. The time taken for all six tablets to disintegrate completely was taken as the disintegration time. The tablets pass the test if they have a disintegration time of  $\leq 15$  mintes (BP 2012).

**b) Chemical Examination**

The chemical examination was carried out using UV/Visible spectrophotometer which was used to determine the percentage content of paracetamol. 10 tablets were weighed and crushed into powder, a quantity of powder approximately 0.05g was weighed into a 200 ml volumetric flask, 20 ml of 1M NaOH was added and made up to mark with distilled water. 5 ml of the solution was taken using a bulb pipette into another 100 ml flask, 9.5 ml of 1M NaOH was added and made up to mark with distilled water. The absorbance of the final solution was

measured at 257 nm with an UV/Visible spectrometer (Cecil) using a blank solution prepared by diluting 10 ml of 1M NaOH to 100 ml of distilled water. The tablets pass the test if the percentage of acetaminophen in the tablet is within 90-110% (USP 2011). The percentage content of acetaminophen is determined using eq. (1)

$$(\text{Absorbance} \times \text{Average weight} \times \text{Factor}(11.188))/\text{weight taken} \dots\dots \text{eq. 1}$$

**c) Microbiological Examination**

1 tablet approximately equal to 1g (which is determined from the average weight per tablet) is dissolved in 9 ml TSB which contains polysorbate 80. 1 ml of the mixture was then transferred aseptically into 2 plates each labeled TSA and SDA respectively and 2 ml into 10ml of MCB culture tube which contains an inverted durham tube for gas collection. TSA and SDA were poured into the plates appropriately. The TSA and MCB were incubated at 37 degree celsius for 72 hrs and 48 hrs respectively while the SDA plate was incubated at 25 degree celsius for 72hrs and observed daily. The tablets pass the test if the total viable bacterial and fungal count is  $\leq 100$  cfu/ml and no coliform is present. (BP 2012).

**3. RESULT**

**3. 1. Physical examination result**

Tables 1-3 and Figures 1-3 shows the physical parameters of the various brands of paracetamol tablets. The hardness test on the tablets shows that only 2 tablets are outside the range of 4KgF - 12KgF (BP 2012). All the tablets have a friability of  $\leq 1\%$  which also conforms to BP 2012. Table 1 also shows that the uniformity of weight test on the tablets indicated no significant variations in the weights of tablets within the different brands but there were significant weight variations among tablet of the same brands. Hence, all the brands conformed to the British pharmacopoeia specification which recommends that not more than 2 of the individual tablet weight should deviate from the average weight by more than  $\pm 5\%$  and none should deviate by more than  $\pm 10\%$ . The disintegration times of all the tablets are also within 15 minutes (BP 2012) except brand E with disintegration time of 27 minutes 44 seconds

**Table 1.** Average Hardness Result

Brand code	Average Hardness (KgF)
A	6.6
B	6.0
C	11
D	8.6
E	0.0
F	16.2
G	6.8

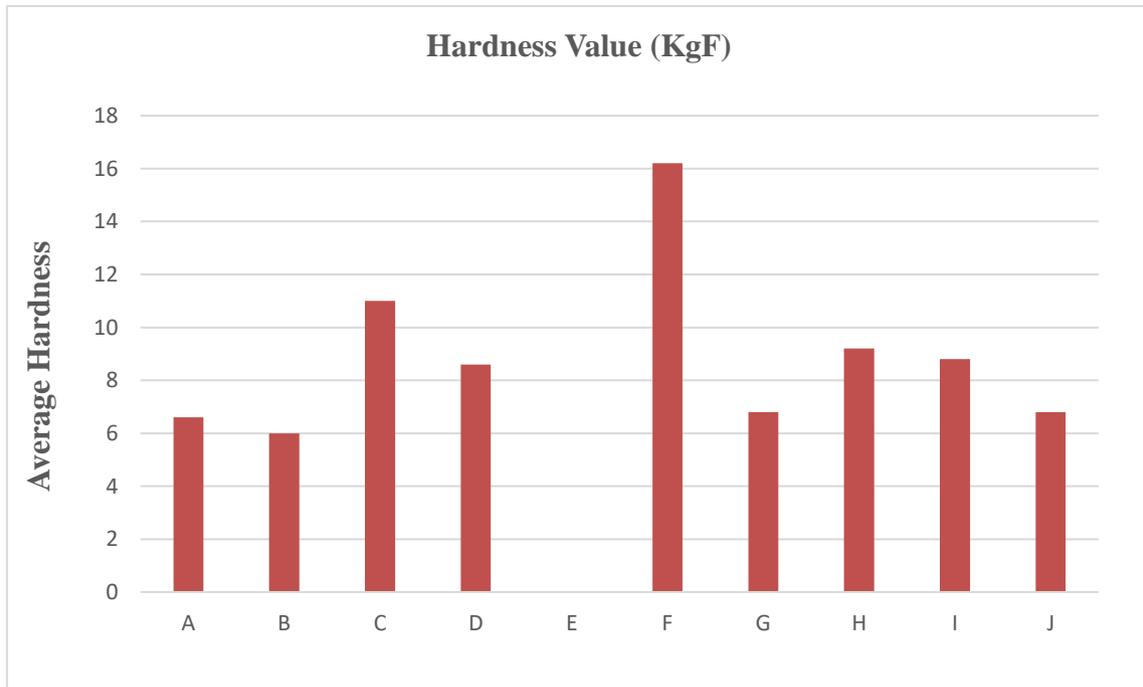
H	9.2
I	8.8
J	6.8

**Table 2.** Disintegration Time and Friability

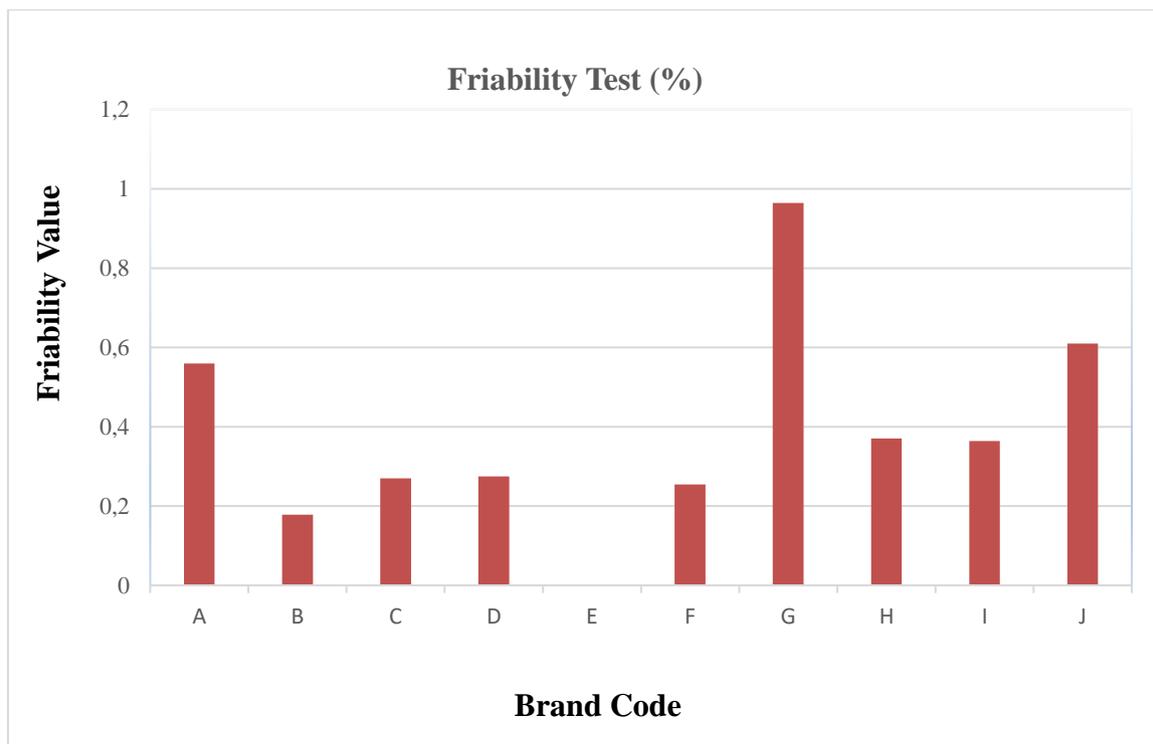
<b>Brand code</b>	<b>Disintegration time (minutes)</b>	<b>Friability (%)</b>
A	3.55	0.5597
B	1.43	0.1784
C	1.31	0.2697
D	6.34	0.2745
E	27.44	0.0000
F	9.53	0.2548
G	4.23	0.9641
H	7.42	0.3703
I	5.16	0.3639
J	5.8	0.6097

**Table 3.** Uniformity of weight.

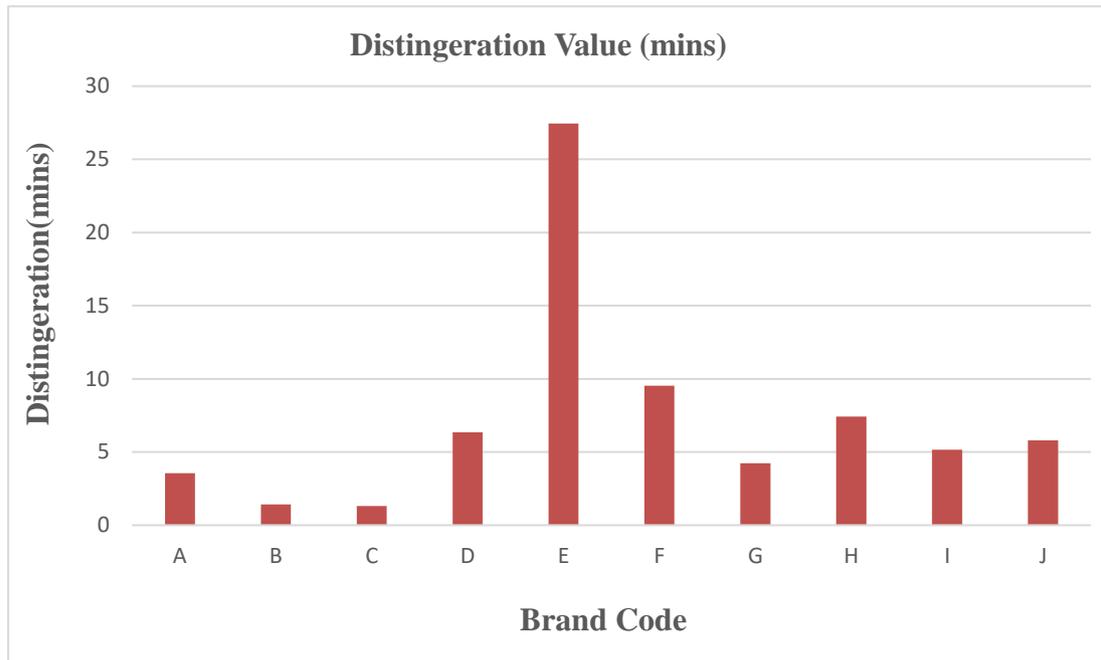
<b>Brand code</b>	<b>Uniformity of weight (g)</b>
A	0.5597±0.0280(0)
B	0.5609±0.0280(0)
C	0.5575±0.0278(0)
D	0.5466±0.0273(1)
E	0.5804±0.0290(0)
F	0.5890±0.0295(1)
G	0.5701±0.0285(0)
H	0.5366±0.0268(0)
I	0.5510±0.0276(0)
J	0.5736±0.0287(0)



**Figure 1.** Hardness value for different brand code of paracetamol



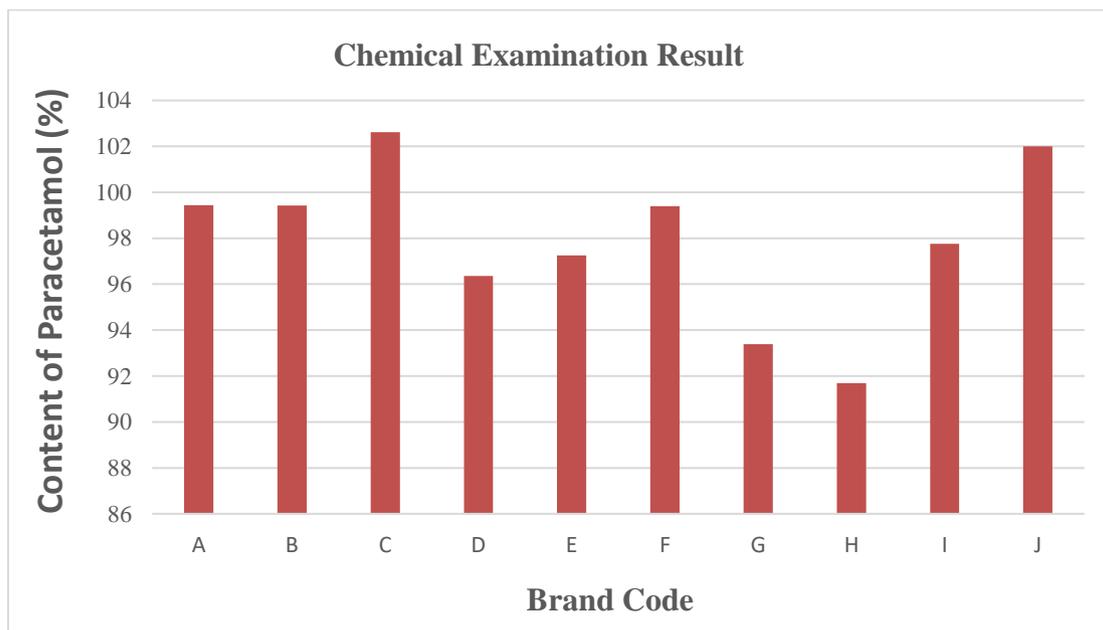
**Figure 2.** Friability value for different brand code of paracetamol



**Figure 3.** Disintegration value for different brand code of paracetamol

### 3. 2. Chemical examination result

Table 4 and Figure 4 shows that the % content of paracetamol in all the brands of paracetamol tablets analyzed ranges from 91.69-102.62%. The result conforms to USP 2011 which recommends that the active component should range from 90-110%.



**Figure 4.** Percentage content of paracetamol of the different brands of paracetamol tablet

**Table 4.** Percentage content of paracetamol in the different brands of the tested paracetamol tablet

BRAND CODE	CONTENT OF PARACETAMOL (%)
A	99.44
B	99.42
C	102.62
D	96.36
E	97.25
F	99.40
G	93.39
H	91.69
I	97.76
J	102

### 3. 3. Microbiological examination result

Table 5 shows the total viable aerobic count of microorganisms present in the analyzed paracetamol samples and they all conform to BP 2012 (Total bacteria should be  $\leq 1000$  cfu/ml and total fungi should be  $\leq 100$  cfu/ml).

**Table 5.** Total viable aerobic count in the different brands of the tested paracetamol tablet

Brand code	Total bacteria (cfu/ml)	Total fungi (cfu/ml)	Coliform
A	<10	<10	NIL
B	<10	<10	NIL
C	$5 \times 10$	<10	NIL
D	<10	$6 \times 10$	NIL
E	$1 \times 10$	<10	NIL
F	<10	<10	NIL
G	<10	<10	NIL
H	$1 \times 10$	<10	NIL
I	<10	<10	NIL
J	<10	<10	NIL

#### **4. DISCUSSION**

The investigation shows that 8 out of the 10 brands of paracetamol tablets analyzed passed the physical test. Tablet is defined as a compressed dosage form containing medicaments with or without excipients. According to the Indian Pharmacopoeia, pharmaceutical tablets are solid, flat or biconvex dishes, unit dosage form, prepared by compressing a drug or a mixture of drugs, with or without diluents. They vary in shape and differ greatly in size and weight, depending on amount of medicinal substances and the intended mode of administration. Tablet hardness test measures the crushing strength of a tablet. The crushing strengths shown by the tablet will ensure resistance to damage during handling, packaging and transportation. Although only 8 brands passed the hardness test, this could be as a result of moisture gain and subsequent loss on storage under varying humidity conditions. A high crushing strength in turn could lead to a high disintegration time which lead to brand E having a high disintegration time.

Friability is the tendency for a tablet to chip, crumble or break following compression. This tendency is normally confined to uncoated tablets and surfaces during handling or subsequent storage. It can be caused by a number of factors including poor tablet design (too sharp edges), low moisture content, insufficient binder, etc.

For obvious reasons, tablets need to be hard enough such that they do not break up in the bottle but friable enough that they disintegrate in the gastrointestinal tract. All the tablets passed friability test according to BP 2012. The uniformity of weight of the tablets is a measure of drug content and release of the tablets. However, variation among the brands of tablets is as a result of different excipients used by the companies.

From the findings made in this study, it could be inferred that very small level of microbial contamination of the tablets in this investigation were observed. Tablets are compact drug delivery systems with low water content which usually afford them good protection against microbial contamination. Spoilage and clinical infections resulting from microbial contamination of tablets under hot and humid conditions of the tropics have been reported. Tablets also undergo deleterious changes as discoloration, weakening of tablets matrixes and decreases in the potency of active ingredients when improperly stored. Potential contamination of tablets may arise from heavy microbiological burden in raw materials, though this is usually drastically reduced by lethal drying stage of wet granulation. However, the decreasing use of direct compression in manufacturing of tablets in pharmaceutical industries implies that some contaminants may survive up to the compression stage.

The assay result shows that the percentage content of acetaminophen as an active ingredient in the paracetamol tablets met compedial requirement which means that the drug is in the right prescription.

#### **5. CONCLUSIONS**

All the brands of paracetamol tablets analyzed passed the official requirements for microbiological quality (BP 2012). The assay result also shows that the percentage content of paracetamol in all the brands analyzed ranges from 90.0-110% as per USP 2007 specifications. 8 out of 10 brands passed the physical parameters tests according to the BP 2012 except 2 brands. It is therefore suggested that for better patient acceptability, the quality of product as well as Good Manufacturing Practice should be enforced and maintained so as to prevent

antibiotic resistivity and access to safe and quality drugs. Also, a routine market surveillance of pharmaceutical product is encouraged so as to discourage marketing of poor quality products.

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