

# Quality Assessment of Brands of Prednisolone (5 Mg) Tablets Marketed in Abuja Metropolis of Nigeria

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## ABSTRACT

This study aims to evaluate the quality of brands of prednisolone tablets marketed in Nigeria. Quality control parameters such as weight variation, hardness, friability, disintegration, assay, and dissolution were assessed. Ten of 11 brands tested met the United States Pharmacopeia (USP) specifications for dissolution of immediate-release dosage forms at stage S1 or S2, but one brand failed to meet the requirement even at stage S3. Using a validated method, all brands except one contained the labelled drug amount per USP specifications ( $100 \pm 10\%$ ). Seven brands failed the hardness test, but there were no issues with other parameters like friability, weight variation, and disintegration. This study demonstrates that most generics of prednisolone tablets currently circulating in Abuja, Nigeria are of good quality.

**KEYWORDS:** Dissolution, disintegration, friability, hardness, assay, weight variation

## INTRODUCTION

The quality of pharmaceutical products remains the focal point in drug production. Quality involves safety and efficacy and its ability to produce the indicated pharmacological effects when taken. The availability of multiple brands of the same drug product in the market has necessitated the routine quality control tests of these products to ensure they are as safe and effective as pharmaceuticals. To improve the overall healthcare delivery system by reducing healthcare costs, the World Health Organization (WHO) recommends that generic drugs are prescribed, which places the healthcare practitioners in a challenging situation over the choice of an ideal brand (1). The rapid importation of less expensive generic drugs from different countries into the Nigerian market is rising; hence the need to carry out routine quality control assessment cannot be over emphasized (2–5).

Chemically equivalent drugs are those drug products that are identical in their active ingredient, strength, concentration, and dosage form (6). A drug product

must deliver an optimal concentration of its active pharmaceutical ingredient (API) at the site of action to attain the desired pharmacological effect. Treatment failures have been observed with some batches of drug products due to variations in the API, manufacturing processes, transportation, distribution, and storage conditions (7). Drug quality implies that the drug product contains the amount of API written on its label within the stated limits of specifications, API content is uniform within dosage units, is free from contaminations, maintains its efficacy, is available therapeutically until use, and when administered, it should release its API for biological availability (8).

Monitoring drug quality is usually challenging in developing countries like Nigeria because of inadequate facilities and trained personnel, poor regulatory mechanisms, and criminal laws not adequately enforced (5). Variable clinical responses to medicines and batch-to-batch inconsistencies have been reported with generics (9, 10). Biopharmaceutical and chemical equivalence analyses should be performed for drugs with more than three generic versions on the market. The generic

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products must be comparable in strength, quality, and purity to ensure that any of the generic products can be used interchangeably (1). The safety and efficacy of medicines can be guaranteed when their quality is reliable and reproducible from batch-to-batch. A thorough analysis includes weight uniformity, friability, hardness, thickness and diameter, assay, disintegration, and dissolution tests (11).

Prednisolone is a glucocorticoid, a derivative of cortisol, and an active metabolite of prednisone that is readily absorbed from the gastrointestinal tract (12). It is a whitish crystalline powder and soluble in water, slightly soluble in alcohol, and very slightly soluble in acetone and dioxane. Its IUPAC name is disodium [2-(8S, 9S, 10R, 11S, 13S, 14S, 17R)-11,17-dihydroxy-10, 13-dimethyl-3-oxo-7, 8, 9, 11, 12, 14, 15, 16-octahydro-6H-cyclopenta[ $\alpha$ ]phenanthren-17-yl]-2-oxoethyl phosphate, with  $C_{21}H_{28}O_5$  as its molecular formula, while its molecular weight is 360.45. The therapeutic indications for prednisolone include endocrine, rheumatic, dermatologic, ophthalmic, respiratory, hematologic, neoplastic, gastrointestinal, and nervous system disorders, allergic conditions, edematous states, tuberculous meningitis, trichinosis, and as a substance of abuse for weight gain due to fluid retention side effects (13–27).

Therefore, the aim of this study is to evaluate the quality of eleven (11) brands of prednisolone tablets marketed in the Abuja metropolis of Nigeria under different names from different companies.

## MATERIALS AND METHODS

### Collection of samples

Different brands of 5-mg prednisolone tablets were sourced from major retail pharmacy outlets and general

outpatient departments of hospital pharmacies within Abuja City of Nigeria according to WHO survey guidelines for quality of medicines (9). The study was performed with unexpired samples. The various brands were coded, and their batch and NAFDAC numbers, country of origin, and dates of manufacture and expiration were recorded (Table 1). All reagents used were of analytical grade.

### Weight Variation Determination

Using the USP method, 20 tablets were randomly selected and were weighed individually using an analytical balance (Type AB54, Mettler Toledo, Switzerland). The average weight ( $AV$ ) and percent deviation ( $D\%$ ) of the tablets were calculated with the following equation, where  $D$  is the difference between the tablet weight and the average weight:  $D\% = (D / AV) \times 100$ .

### Hardness Test

Six tablets were randomly selected from each brand for the hardness test using a hardness tester (D-6072, Erweka). Each tablet was held between a fixed jaw and moving jaw of the tester. The pressure applied to the edge of the tablet increased gradually by moving the screw knob until the tablet broke. The pressure required to break the tablet was noted from the scale. The average and standard deviation were calculated for each brand.

### Friability Test

Based on the USP method, the initial weight ( $W1$ ) of 10 tablets selected randomly from each brand was determined and placed in a friabilator tester (Type TA, Erweka, Germany), set at 25 rpm for 4 min, after which the tablets were dusted and weighed ( $W2$ ). The percent friability ( $F$ ) was calculated using the equation:  $F = [(W1 - W2) / (W1 \times W2)] \times 100$ .

Table 1. Prednisolone Tablets Used in This Study

| Brand Code | Country  | Batch No. | NAFDAC No. | Manf. Date | Expiry Date |
|------------|----------|-----------|------------|------------|-------------|
| P1         | Nigeria  | Kp22      | 04-8680    | 08/16      | 08/20       |
| P2         | India    | 16pd18    | 04-7051    | 08/16      | 05/19       |
| P3         | Nigeria  | 0902      | A4-8538    | 09/17      | 08/20       |
| P4         | Malaysia | Bh12404   | 04-2403    | 12/17      | 12/20       |
| P5         | China    | 160501    | 04-9973    | 05/16      | 05/19       |
| P6         | Nigeria  | Kp17108   | A4-7721    | 09/17      | 08/20       |
| P7         | India    | Ttf86     | B4-1625    | 06/18      | 05/21       |
| P8         | UK       | HS10090   | -          | 06/17      | 05/20       |
| P9         | Nigeria  | 018093402 | B4-1084    | 09/18      | 08/21       |
| P10        | India    | 170513    | A4-8907    | 12/17      | 11/20       |
| P11        | India    | R61701    | 04-8733    | 06/17      | 05/20       |

NAFDAC – National Agency for Food and Drug Administration and Control; Manf – manufacture.

### Disintegration Test

The disintegration test was performed according to USP (28). A disintegration apparatus was used (Type ZT4, Erweka) with 600 mL distilled water maintained at  $37 \pm 2$  °C as the medium. Tablets from each batch (a total of 6) were taken randomly for the test. The disintegration time was recorded as how long it took for the tablet to break into pieces small enough to pass through the basket mesh into the medium.

### Assay Test

A validated method was used to assess linearity and range (12). A calibration plot over a concentration range of 2–12 µg/mL was calculated. The recovery test was carried out by adding a known amount of the reference sample of the drug to pre-analyzed tablet solutions. The resulting solutions were then reanalyzed by proposed methods (12). The limit of detection and quantitation were evaluated using the slope and standard deviation values from the calibration curve.

### Preparation of Standard Stock Solution

Prednisolone (10 mg) reference powder was weighed accurately using an analytical balance and dissolved in 80 mL of distilled water in a 250-mL conical flask. A 2 mL aliquot of methanol was used to bring the sample into solution. The content in the flask was stirred using a magnetic stirrer for 10 min and transferred to a 100-mL volumetric flask. The conical flask was rinsed with 20 mL of distilled water and used to reach 100 mL in the volumetric flask to have a concentration of 100 µg/mL.

### Preparation of Working Solution

A working solution was prepared by further diluting the standard stock solution. Six aliquots (0.2, 0.4, 0.6, 0.8, 1.0, and 1.2 mL) of stock solution were pipetted out and increased to 10 mL to reach concentrations of 2, 4, 6, 8, 10, and 12 µg/mL using distilled water as blank. Absorbance was estimated at 246 nm with a UV/VIS spectrophotometer (Cary 60, Agilent Technologies).

Approximately 10 prednisolone tablets (5 mg) were weighed and ground into powder using pestle and mortar. An equivalent quantity (50 mg) was transferred into a 50-mL flask and dissolved with distilled water using a magnetic stirrer for 30 min. From the solution, 1 mL was pipetted out and increased to 100 mL to reach a concentration of 10 µg/mL using distilled water as blank. Absorbance of the working solution was estimated using a UV spectrophotometer by comparing to the standard stock solution.

### Dissolution Test

The dissolution test was performed according to USP

(28). A tablet was placed in a single-station dissolution apparatus (Type DT, Erweka) with 900 mL of distilled water maintained at  $37 \pm 0.5$  °C and rotated at 50 rpm. After 30 min, a 10-mL sample was withdrawn, filtered, and analyzed using the UV/VIS spectrophotometer at 246 nm. Readings were taken in triplicate.

## RESULTS AND DISCUSSION

A linear relationship was evaluated across a range of analytical concentration of the drug substance by diluting a standard stock solution and taking the absorbance reading at 246 nm. The results obeyed the Beer-Lambert law in the concentration range of 2–12 µg/mL, having a linear equation of  $y = 0.0412x - 0.00119$  with a correlation coefficient value ( $R^2$ ) of 0.9957. The limit of detection and quantitation values were 0.3137 and 0.9506. The mean percent recovery was within the range of 97.90% to 104.58%, showing that the method was accurate and indicating non-interference with the excipients of the formulation.

A summary of the properties of the various brands whose quality was assessed is shown in Table 2. The weight variation is a valuable in-process control measurement of tablets, and it ensures consistency of the dosage unit during compression. Some variation in weight cannot be avoided and is allowed within the limits of deviation specified in the compendia. This test is done to determine dose variation of individual tablets; however, it does not guarantee that the API is uniform across tablets, especially in formulations with low dose concentrations. Variations in tablet weights within a single batch may cause variations in disintegration and dissolution characteristics. Hence, strict adherence to good manufacturing practice (GMP) during granulation and compression ensures tablets are uniform in weight (28). The compendial specification for uniformity of weight states that for tablets weighing 130–324 mg, weights of not more than two tablets should deviate from the average weight by more than 7.5%, whereas tablets weighing less than 130 mg should not deviate by more than 10% (27). Variation in average weights across different brands may exist due to excipients and powder properties (29–31). All 11 brands of prednisolone tablets passed the weight variation test according to USP specification.

The hardness test is the direct application of a compressional force to a tablet until it fractures (32). This test demonstrates how tablets could withstand pressure or stress in the process of handling, manufacturing, packaging, and transportation. Though not an official pharmacopeia quality control test, hardness tests

Table 2. Disintegration Time, Hardness, Weight Variation, Friability, and Assay Results of Prednisolone Tablets

| Brand Code | Weight Variation (g) | Hardness (KgF) | Friability (%) | Disintegration Time (min) | Assay (%)    |
|------------|----------------------|----------------|----------------|---------------------------|--------------|
| P1         | 0.14 ± 0.4           | 3.70* ± 0.7    | 0.00           | 3.37 ± 0.9                | 105.25 ± 0.7 |
| P2         | 0.15 ± 0.2           | 6.00 ± 0.5     | 0.10           | 6.83 ± 0.7                | 102.74 ± 1.0 |
| P3         | 0.13 ± 0.2           | 2.80* ± 0.6    | 0.13           | 5.88 ± 0.6                | 102.98 ± 0.8 |
| P4         | 0.15 ± 0.1           | 3.90* ± 0.5    | 0.12           | 0.54 ± 0.1                | 98.02 ± 0.7  |
| P5         | 0.13 ± 0.5           | 4.20 ± 0.6     | 0.01           | 0.38 ± 0.1                | 97.75 ± 0.6  |
| P6         | 0.16 ± 0.3           | 2.20* ± 0.1    | 0.23           | 0.25 ± 0.8                | 103.3 ± 0.9  |
| P7         | 0.15 ± 0.3           | 1.90* ± 0.4    | 0.19           | 0.36 ± 1.3                | 98.41 ± 1.1  |
| P8         | 0.10 ± 0.3           | 2.60* ± 0.3    | 0.15           | 1.59 ± 1.4                | 67.25* ± 1.8 |
| P9         | 0.15 ± 0.1           | 4.00 ± 0.6     | 0.02           | 18.00* ± 0.4              | 107.00 ± 1.3 |
| P10        | 0.14 ± 0.4           | 1.90* ± 0.1    | 0.35           | 0.84 ± 1.0                | 100.92 ± 0.4 |
| P11        | 0.16 ± 0.2           | 5.70 ± 0.1     | 0.00           | 0.69 ± 1.1                | 99.92 ± 0.4  |

\*Did not meet criteria for United States Pharmacopeia.

may account for the weight, nature, and quantities of excipients used during the formulation process (1). The hardness test assesses the tablet's resistance to permanent deformation, which is affected by its density and porosity and affects disintegration, friability, and dissolution, thus affecting bioavailability. Tablets must be stable enough to withstand the physical factors to which they are subjected. When a tablet is too hard, it may not disintegrate in the required time, and when it is too soft, it will not withstand handling. Several factors have been found to affect the hardness of tablets; these include lubricant type and concentration, particle size and density, tableting speed, compression force, storage conditions, binder type, and drug concentration (29–31, 33–38). An increase in binder concentration increases the mechanical strength of tablets. The ideal mechanical strength of a conventional tablet is between 4 and 10 kg (39). As shown in Table 2, only samples 2, 5, 9, and 11 passed the hardness test, and the rest failed to comply with the specification.

The friability test is another mechanical characteristic of a tablet with the compendial specification of not more than 1% (27). The hardness test is a bulk deformation of the tablet, but friability is a surface deformation that may be enhanced by the morphology of the tablet (35). Tablets must withstand attrition in a pack, owing to partial powdering, chipping, or fragmentation of the tablets during handling and transportation. Cotton or other cellulose materials are commonly placed in containers of tablets to keep them closely packed to decrease rilling and fractional contact on transportation or handling and agitation. The rougher the tablet's surface, the more friable it will be, although moisture content of tablet granulation has a profound effect on tablet friability (36).

Other factors that may affect friability include binder type and concentration and excipients used in the formulation (30, 34, 37). All samples met USP specifications for friability, indicating mechanical stability.

The disintegration test measures the time required for the breakdown of a tablet or capsule into fragments or granules small enough to pass through the disintegration basket mesh when it comes in contact with gastrointestinal fluids. Disintegration is the first step towards dissolution; it is used as a control for orally administered tablets and immediate-release dosage forms. In formulation development, disintegration characteristics can act as an in-process control test to ensure lot-to-lot uniformity. The rate of disintegration is directly related to the rate of dissolution. However, a disintegration test may act as a surrogate to dissolution testing if the dosage form does not modify the release characteristics, if the drug has a dose/solubility ratio of  $\geq 250$  mL over a pH range of 1.2–6.8, if more than 80% of the dose dissolves within 15 min at pH values of 1.2, 4.0, and 6.8, and if a relationship has been established between dissolution and disintegration. Drug absorption and efficacy relies on disintegration time. The type and quantity of excipient used, storage conditions, and processes involved in manufacturing affect the disintegration of a tablet (34, 36). Disintegration time is affected by the extent of fluid influx into the tablets, which also depends on porosity (28). Ideally, a conventional tablet should disintegrate within 15 min. (27). The results showed that all brands met this requirement except sample 9, which disintegrated in 18 minutes. Longer disintegration time for sample 9 might be due to excessive binder, the type and concentration of disintegrant, humidity, or the compression force (29, 35, 39, 40).

According to the USP, prednisolone tablets should contain 90–110% of the label amount. All the brands met the specification, except sample 8, which had an assay value of 67%. The failure of sample 8 may be due to errors during tableting, weighing, or mixing.

The dissolution test measures the proportion of drugs dissolving in a prescribed time under standardized in vitro conditions. To predict in vivo bioavailability of most oral drugs, in vitro dissolution studies is necessary. Ideally, it should differentiate bad products from good ones. The rate of dissolution determines the rate and extent of absorption and subsequent therapeutic outcome of a drug. For this purpose, dissolution of solid oral drug products has emerged as a very important quality control test for assuring uniformity of product and batch-to-batch equivalence. The factors that affect dissolution include type and concentration of binder, hardness, surface area, the distance of diffusion, solubility of the drug, manufacturing process, and diluents (30, 34, 41–44). The dissolution may be performed by collecting one aliquot from the bath after 30 min. Since the USP acceptance criteria for stage S1 for immediate-release solid dosage form states that each unit should not be less than  $Q + 5\%$  after six tests, where  $Q$  is the amount of dissolved active ingredient specified in the monograph ( $Q = 70\%$  for prednisolone tablet). Samples P3 and P9 did not meet S1 criteria as shown in Figure 1; hence further testing was required. At the end of stage S2, which requires 12 tests, the average of the 12 units should be greater than or equal to  $Q$  and no unit should be less than  $Q - 15\%$ . Sample P3 was 69% (Fig. 2), and P9 was 72% (Fig. 3), but some of the units tested were less than  $Q - 15\%$ . Thus, further testing was required as they did not pass stage S2 criteria. Stage S3 criteria state that the average of 24 units should be greater than  $Q$ , no more than two units are less than  $Q - 15\%$ , and no unit is less than  $Q - 25\%$ . Sample P9 met all these requirements (Fig. 4), but sample P3 still failed with a value of 60% (Fig. 5).

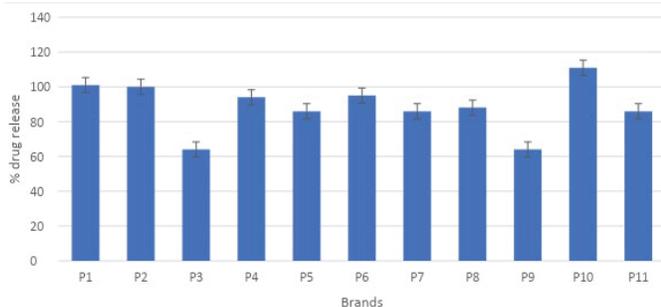


Figure 1. Dissolution test results (mean  $\pm$  SD) for 11 brands of 5-mg prednisolone tablets at stage S1.

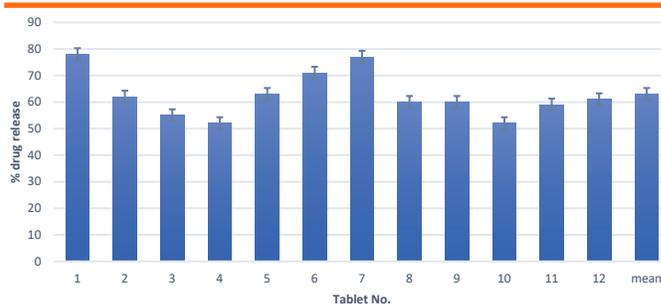


Figure 2. Dissolution test results (mean  $\pm$  SD) for 5-mg prednisolone tablets of sample P3 at stage S2.

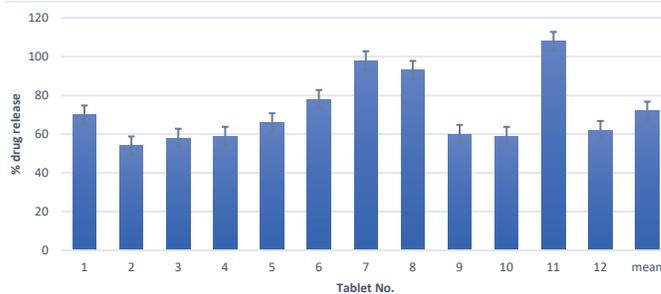


Figure 3. Dissolution test results (mean  $\pm$  SD) for 5-mg prednisolone tablets of sample P9 at stage S2.

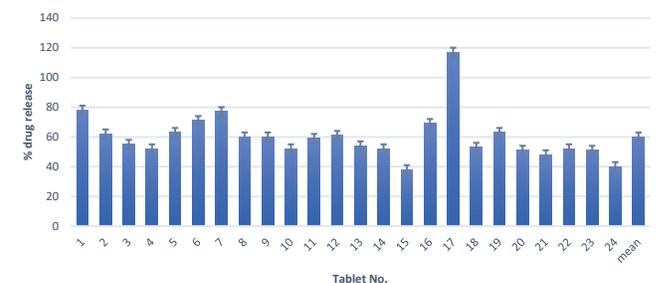


Figure 4. Dissolution test results (mean  $\pm$  SD) for 5-mg prednisolone tablets of sample P3 at stage S3

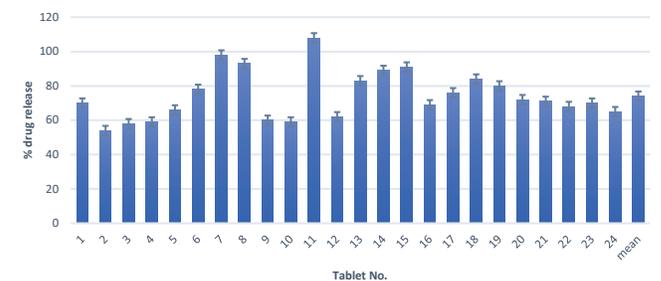


Figure 5. Dissolution test results for 5-mg prednisolone tablets of sample P9 at stage S3.

## CONCLUSION

Manufacturers in the pharmaceutical industry produce various health commodities that save lives, but poor-quality pharmaceutical products might lead to treatment

failures. A quality drug product maximizes therapeutic efficacy, which may increase customer satisfaction and market demand. In the present study, 10 out of 11 brands of prednisolone 5-mg tablets met USP specifications for dissolution. No problems were found in weight variation, friability, and disintegration time. We conclude that most prednisolone tablets marketed in the Abuja metropolis of Nigeria meet all USP specifications.

### CONFLICT OF INTEREST

The authors disclosed no conflicts of interest related to this article.

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