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(RESEARCH ARTICLE)

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Assessment of different brands of diclofenac tablets: An evaluation utilizing uv spectroscopy and disintegration test methods

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Abstract

Diclofenac is a non-steroidal anti-inflammatory drug (NSAID), that blocks the cyclooxygenase-1 (COX-1) and COX-2 enzymes to inhibit the prostaglandins production. It is available as a salt in the form of potassium, sodium, or epolamine. They are typically administered orally, intravenously, intramuscularly, transdermally, or rectally. Diclofenac is one of the most widely used NSAIDs in Nigeria, and due to the increase in adulterated and subpar medications in the market, it needs to be properly quantified. In this study, the weight uniformity test, disintegration, and ultraviolet (UV) spectroscopy were used to assess five different brands of diclofenac potassium labeled DIC 1 – DIC 5. Analytical balance was used to measure each weight and conduct the weight uniformity test. Using a disintegration apparatus and 0.1 N hydrochloric acid as the medium, a disintegration test was conducted. The UV spectroscopy includes the use of a UV spectrophotometer and the concentration range of 10 – 50 µg/ml was prepared using pure sample and methanol as solvents and scanned between wavelength 220 – 400 nm. The various brands with concentrations of 20 µg/ml were prepared and scanned. The weight uniformity test was passed by all the brands. One brand failed the disintegration test, but one brand did not disintegrate because it was enteric coated. Three brands passed the test. All brands, except for DIC 2, had percentage purity within the stipulated range for chemical analysis.

Keywords: Diclofenac; NSAID; COX; UV spectroscopy; Disintegration

1. Introduction

Diclofenac is a non-steroidal benzene acetic acid derivative that possesses anti-inflammatory activity [1]. Diclofenac, a non-steroidal anti-inflammatory drug (NSAID), binds and chelates both COX-1 and COX-2, preventing arachidonic acid from being converted into pro-inflammatory prostaglandins [1]. It may also inhibit COX-2-mediated tumor angiogenesis [1]. Compared to several other NSAIDs that contain carboxylic acids, this medication may be more effective against COX-2 [1]. Diclofenac may reduce pain and inflammation when it inhibits COX-2, but when it inhibits COX-1, it may have unfavorable gastrointestinal side effects [1] [2] [3]. The ulcer-causing side effect is caused by COX-1's requirement for maintaining the production of prostanoids, such as prostacyclin (PGI2), which protects gastrointestinal (GI) mucosal tissue and inhibits platelet aggregation [4]. Other common side effects include indigestion, gas, nausea, vomiting, stomach pain, diarrhea, constipation, headache, dizziness, and sleepiness [5]. Ciba-Geigy (Novartis) obtained the patent for diclofenac in 1965. It is chemically known as 2-[(2,6-dichlorophenyl)amino] benzene acetic acid [6], and with chemical structure depicted below. Common brand names include Cambia, Zipsor, Zorvolex, Cataflam, Voltaren, Voltaren-XR, Dyloject [5].

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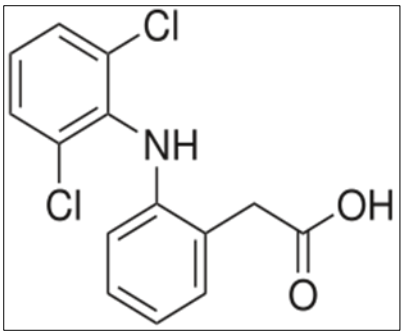


Figure 1 Chemical structure of Diclofenac [1]

Diclofenac occurs as a salt either as sodium, potassium, or epolamine salt [6] [7] [8]. Diclofenac sodium can be given via oral ingestion as a tablet or suspension, intramuscular injection, intravenous injection, transdermal application, or suppository via the rectal route [7] [8] [9]. For oral administration, diclofenac potassium is available as a tablet or suspension. A transdermal patch for diclofenac epolamine is readily available [7]. Various methods have been used for the quantification of diclofenac in pharmaceutical formulations. These include titration via non-aqueous medium [10], potentiometric titration [11] [12] [13] [14], Ultra Violet (UV) spectroscopy [10] [15], Capillary zone electrophoresis [16] [17] [18], High Pressure Liquid Chromatography (HPLC) [19] [20], High Pressure Liquid Chromatography - Mass Spectroscopy (HPLC-MS) [21], Spectro fluorometry [22], Thin Layer Chromatography (TLC) [23] [24], Gas Chromatography (GC) [25], Voltammetry [25] [26] [27] and Polarographic analysis [28]. Drug adulteration is constantly changing, with an overall trend toward a decline in the purity of most drugs over the years [29]. Different kinds of adulterants comprise of chemical contaminant, microbiological contaminant, and Substitutes [29]. To increase bulk, improve or mimic a pharmacological effect, or speed up the delivery of a drug, adulterants are purposefully added. Those present unintentionally are because of poor manufacturing techniques [30] [31]. Counterfeiting in pharmaceuticals is becoming an increasing global dilemma with a serious impact on lower-income countries (LIC) and lower-middle-income countries (LMIC) [32] [33]. Diclofenac is among the top three NSAIDs been utilized in Nigeria for the management of pain [34] [35].

2. Methods

2.1. Weight Uniformity Tests

Twenty tablets of the different drug samples were randomly selected and weighed individually, and their respective weights were recorded. Their respective mean and standard deviation were then calculated [36] [37] [38].

2.2. Disintegration Test

Each brand was placed in each of the six tubes of disintegration apparatus after which the assembly was suspended in the beaker containing 0.1 N HCl. The time taken for all the tablets to disintegrate was noted.

2.3. Assay of diclofenac tablets

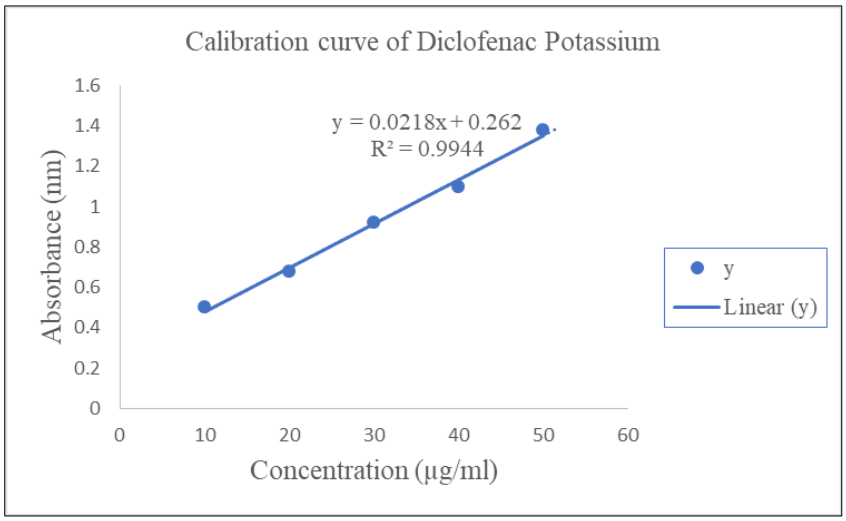
The standard solution with various concentration of 10 µg/ml, 20 µg/ml, 30 µg/ml, 40 µg/ml, 50 µg/ml, and 60 µg/ml were prepared using methanol. They were all scanned through wavelengths of 220 - 400 nm. Twenty tablets of drug sample (DIC 1) were triturated and dissolved in methanol, shaken for 30 minutes, filtered and concentration of 20µg/ml was prepared using methanol and scanned through a wavelength of 220 - 400 nm. The same procedure was carried out for the remaining brands. The amounts of drug present in the samples were deducted from the calibration curve.

3. Results

Table 1 The various brands of Diclofenac potassium tablets, their corresponding mean, weight uniformity test, disintegration time and Percentage purity

Sample	Mean weight (g)	Number of tablets deviated	Disintegration time (mins)	Percentage purity (%w/w) ± SD
DIC 1	0.320	Nil	11	96.4 ± 0.003
DIC 2	0.772	Nil	None	106.9 ± 0.005
DIC 3	0.644	Nil	52	104.4 ± 0.001
DIC 4	0.224	Nil	8	102.7 ± 0.002
DIC 5	0.335	Nil	10	97.2 ± 0.002

*SD = Standard Deviation



*R2 = Regression Square

Figure 2 Calibration curve for UV Spectroscopy of Diclofenac Potassium

4. Discussion

According to the data from the weight uniformity test, none of the percentage deviations for the tablets were higher than those listed in the official compendia. Apart from DIC 4, every brand's average weight was greater than 250mg, and no brand's percentage deviation exceeded 10%. The official compendia states that no tablet should have a percentage deviation greater than 15%, and none of the DIC 4 tablets had a percentage deviation that was greater than 15%. The average weight of DIC 4 was less than 250 mg. All brands passed the weight uniformity test because their percentage deviations were less than the stated values. Tablets' active ingredients need to disintegrate into smaller particle that is then dissolved to allow absorption for them to carry out their pharmacological functions. The disintegration test is used to determine how long it takes for no tablet residue to be visible on the disintegration apparatus' screen. Typically, the test lasts an hour. The compendia state that uncoated or film-coated tablets should dissolve within 15 minutes or less, and since DIC 1, DIC 4, and DIC 5 (Table 2) all broke down within that time frame, they passed the test however 52 minutes passed before DIC 3 disintegrated, exceeding the time limit. This will have an impact on the bioavailability of this brand because a prolonged disintegration test means that the active ingredients will take longer to enter the body and begin their pharmacological effects, delaying the onset of action. As was already mentioned, DIC 2 is enteric coated, which means it was designed to withstand the stomach's acidic environment and as a result did not disintegrate in the medium used in the disintegration apparatus. As seen in Figure 2, the drug follows the Beer-Lambert law, the λmax is 280 nm and the calibration curve generated was used to interpolate the corresponding values. The calibration curve's output is a linear graph with the equation y = 0.0218x + 0.262 and a regression square value of 0.994. Apart from DIC 2, whose percentage purity was higher than the permitted range, all

brands in Table 1's comparison of the various brands' percentage purity fell within the official compendia's specified range of 95 to 105 % w/w. The differences may be the result of a small adjustment made to the manufacturing process to consider the degradation of the drugs during storage. Additionally, the high value may be due to the presence of impurities with similar functional groups that were introduced during the synthesis of the active ingredients or degradation products. An R2 value of 0.994392 indicates that the regression model's independent variable(s) account for 99.44 % of the variability in the dependent variable, which is a testament to the method's accuracy and precision [39] [40]. This implies that the model accurately predicts the data [39][40]. The statistical significance of the relationship between the independent and dependent variables is indicated by the low p-value of 0.003591. The variables are significantly correlated because the p-value is less than the significance level of 0.05 [40][41][42]. The regression model has a better fit for the data, as evidenced by the coefficient's standard error of 0.031348 [39][43]. A strong correlation between the independent and dependent variables is indicated by the high R2 value, low p-value, and low standard error [44].

5. Conclusion

All the brands passed the weight uniformity test because none of them had a percentage deviation that was greater than the value stated in the official compendia. The tablets from three brands disintegrated in less than 15 minutes, passing the disintegration test. The remaining brand was enteric coated and did not disintegrate, while one of the brands failed because it took longer than allowed. Four brands passed the UV spectroscopic analysis because their percentage purity was within the acceptable range as specified in the official compendia. Due to changes in the manufacturing process or the presence of impurities with similar functional groups, the remaining brand's purity percentage was higher than the permitted range.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest in this manuscript.

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