Full Length Research paper

Quality of Diclofenac sodium tablet marketed in Abuja pharmacy

*Waribi Benard, Ogunse Femi and D. E Victor

Department of Pharmacology and Toxicology, National Institute for Pharmaceutical Research and Development, Abuja, Nigeria.

Diclofenac is one of the most commonly used non-steroidal anti-inflammatory drugs for the treatment of pain, rheumatism and other inflammatory conditions. The drug has analgesic, anti -pyritic and anti-inflammatory effects. Rapid and sensitive-reversed phase high performance liquid chromatography (HPLC) method was used to analyze the amount of Diclofenac in the samples. The calibration curve was linear with correlation coefficient (r^2) of 0.9999 at concentration range of 10 to 80 µg/ml and coefficient of variance (CV %) of less than 5%. Percentage content of Diclofenac from the different pharmaceutical preparations was within 97.5 to 115.5%, but 42.86% failed with over range, while 57.14% passed the British Pharmacopoeia (BP) specification range of 95 to 105.0% of the prescribed content. The drug release profiles were evaluated *in vitro* using a dissolution test apparatus. The USP paddle method was used to perform the dissolution profiles of Diclofenac Sodium. From the result, there is still need for the policy markers in the country to checkmate the imports of different brands of pharmaceutical products into the Nigerian market, since almost 50% of the drug analyzed is above the stated amount claimed by the manufacturers.

Key words: Diclofenac, reversed phase- high performance liquid chromatography (HPLC), ultraviolet (UV)-spectrophotometer, percentage content, Nigerian market.

INRODUCTION

Diclofenac sodium is 2-[{2, 6-dichlorophenyl} amino] benzene acetic acid or 2-(2, 6 -dichloroanilino) phenyl acetic acid (Figure 1), is a non-steroidal anti-inflammatory drug (NSAID) used for the treatment of different diseases such as rheumatoid arthritis, ankylosis spondylitis, osteoarthritis and sport injuries. Non steroidal anti-

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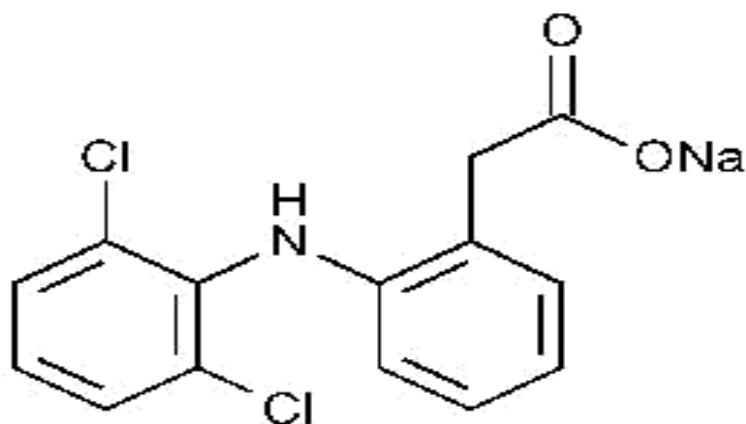*Corresponding author. Email: Bernard.waribi@gmail.com

Figure 1. Structure of diclofenac.

inflammatory drugs (NSAIDs) are among the most frequently prescribed drugs worldwide and are used for relief of inflammatory, chronic (e.g., rheumatoid arthritis, osteoarthritis, and gout), and acute (e.g., headache, postoperative pain, and orthopedic fractures) pain conditions (McCarberg and Gibofsky, 2012). The growing demand for NSAIDs stimulates higher level of quality control of these therapeutic substances and preparations.

Diclofenac is mostly available in tablets and injection as potassium or sodium salt with the later being common in Nigeria and are readily available as over-the counter pharmaceutical preparations.

However, owing to the importance of Diclofenac salts in pharmaceuticals and its widespread use, efforts have been made towards the development of simple and reliable analytical methods. Spectrophotometric methods have also been described for the determination of Diclofenac in pharmaceuticals (Sena et al., 2004; Khaskheli et al., 2009), showing reasonable sensitivity with significant economic advantages over other methods including HPLC (Hanysova et al., 2005; Choudhary et al., 2009), liquid chromatography (Senthie et al., 2006), capillary electrophoresis, LC- APCI-MS, differential scanning calorimetric and nuclear magnetic resonance, that are time consuming or require expensive and sophisticated instruments, and for this reason they are not suitable for routine analysis. HPLC method has been highly used for quality control of drug due to its sensitivity and high precision. UV method is very simple, rapid, and economical allows the determination of pharmaceuticals with enough reliability.

Conventional tablets and hard gelatin capsule dosage forms possess high disintegration time so patients obtain pharmacological effect after 30 to 45 min of dosage form administration that may result in high incidence of non-compliance and variable bioavailability (Seager, 1998). This can be achieved by addition of various super dis-integrants like croscarmellose sodium, crospovidone, and sodium starch glycolate, alone or in various combinations.

Due to the fast disintegration of dosage form, patients obtain quick pharmacological effect of active pharmaceutical ingredient (Chang et al., 2000; Dobetti, 2000; Kuchekar and Arumugam, 2001).

Diclofenac is well absorbed orally, 99% protein binding, metabolized and excreted both in urine and bile. The plasma half- life is 1 to 2 h. However, it has good tissue penetrability and concentration in the synovial fluid is maintained about three times more than in the plasma, thereby extending the therapeutic effects within the joints (Clarke, 1986).

Some patients experienced no relief from musculo-skeletal disorder and other pains after using various brands of Diclofenac sodium tablets. These prompted us to investigate the quality of the Diclofenac sodium tablet marketed in Abuja pharmacy stores, using high performance liquid chromatography and ultra-violet spectrophotometer.

MATERIALS AND METHODS

All reagents and solvents used in this study were of analaR and HPLC grade. The Diclofenac reference standard was also from Sigma. An Agilent 1100 series High Performance Liquid Chromatography System, with a C18 (25 cm length × 4.5 mm diameter and 5 μm particle size) column was used for the determination of Diclofenac content in the tablets.

Sample collection

The literature search and market survey indicate that in the Nigerian markets, there are nine brands of Diclofenac tablets. Seven brands were gotten of which five were normal and two were slow release. The different brands of the Diclofenac tablets were randomly purchased from reputable pharmacy stores within Abuja and subjected to the following assay procedures.

Weight variation

Twenty tablets were selected at random and average weight was
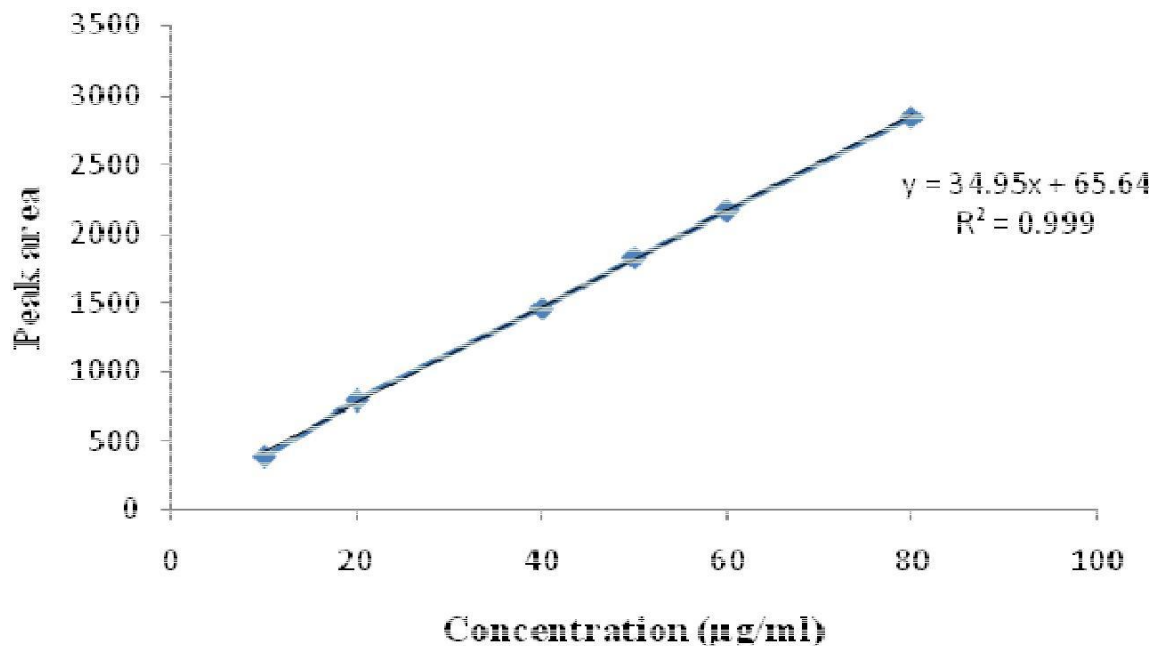
Figure 2. Calibration curve for Diclofenac.

determined. Then individual tablet was weighed and the weight was compared with the average weight (Chang et al., 2000).

Mobile phase

The column was equilibrated with a mobile phase composition of acetonitrile/water (60/40%) v/v filtered through 0.45 µm membrane, sonicated for 30 min and run at a flow rate 1 ml/min with run time of 5 min and UV detection at 278 nm.

Samples

Seven different commercial brands of Diclofenac sodium/Potassium tablets were purchased (5 fast released and 2 sustained released) from registered pharmacy shops in Abuja. The tablets samples contained 50 mg Diclofenac per tablet and 100 mg slow release tablets. Before purchase all tablets were checked for manufacturing license number, batch number and date of manufacture and expiring dates. These tablets were randomly coded (A, B, C, D, E, F, G).

Calibration curve

Standard solution of 1 mg/ml of the reference standard was prepared in a 50% methanol, from which different concentrations from 10 to 80 µg/ml were prepared in 50% methanol and 20 µl introduced into the column in triplicates.

Assay of pharmaceutical preparations

Twenty tablets of each brand were weighed individually and the average weighed calculated after which was finely powdered using glass mortar and pestle. An equivalent weight containing 50 mg of the powdered Diclofenac were accurately weighed and dissolved in a volume of 50% methanol. The solutions each were ultra sonicated

for 15 min and then made up to mark in 50 ml volumetric flask with mobile phase. The solution was centrifuged for 10 min at 4500 rpm, the resulting supernatants were then filtered with 0.45 µm membrane filter paper and 20 µl of filtrate aliquot was introduced unto the column at 1 ml/min flow rate.

In vitro drug dissolution studies

Dissolution test was performed on the tablets using an Erweka dissolution tester apparatus. The medium used was 900 ml 0.1 N HCl, and phosphate buffer (USP, 2003) thermostatically maintained at 37 ± 0.5°C at a paddle rotational speed of 50 rpm. 5 ml aliquot of dissolution medium was withdrawn at 5 min intervals using a syringe and needle and this was replaced with fresh 5 ml of the phosphate buffer medium after each withdrawal. The withdrawn samples were filtered and analyzed for Diclofenac using a Shimadzu UV spectrophotometer (Shimadzu Japan) at a pre-determined wavelength of 276 nm.

RESULTS AND DISCUSSION

The HPLC method was simple, selective and repro-ducible. The calibration curve reflects the linearity in the concentration range of 10 to 80µg/ml with a correlation coefficient (r) of 0.999 (Figure 2) and a coefficient of variance (CV %) for both inter-day and intraday assay were less than 5%. The quantification of Diclofenac was based on the calibrated curve constructed. The method of linear regression was used for the calculation and the linear regression equation was:
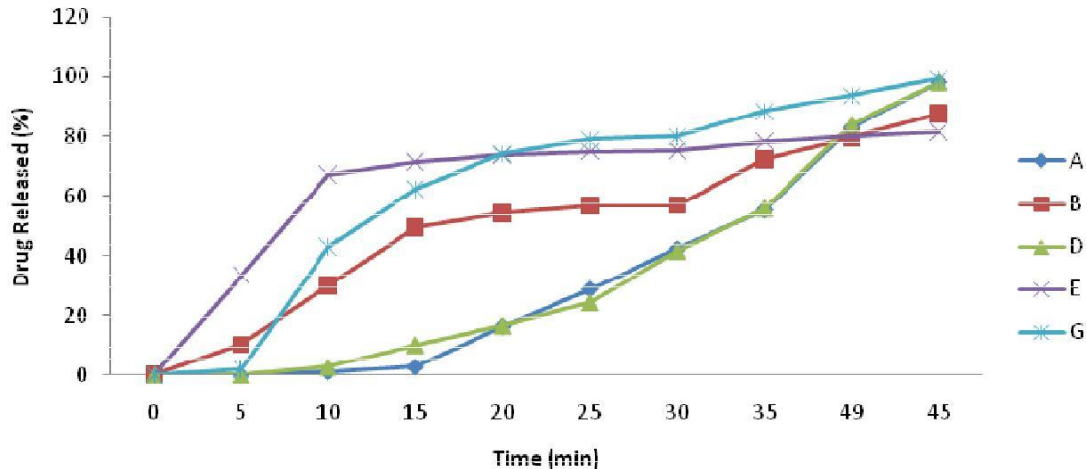
$y = 34.95x + 65.64$.

Figure 3. Percentage cumulative drug release against time.

Table 1. Percentage content and weight variation for the different tablets using HPLC method.

Sample code	Weight variation (g) ± SD	Nominal concentration (µg/ml)	Calculated Concentration (µg/ml)	Percentage content (%)	Remarks (BP, 2004)
A	0.2278±0.007	20	20.704	105.17	Passed
B	0.1852±0.003	20	22.394	111.98	Failed
C	0.2184±0.002	20	22.680	113.40	Failed
D	0.3195±0.006	20	23.101	115.50	Failed
E	0.2545±0.004	20	20.330	101.65	Passed
F	0.3083±0.004	20	19.500	97.51	Passed
G	0.2123±0.005	20	19.520	97.60	Passed

Result for percentage content shows that samples B, C and D failed out of the seven different brands with over range percentage drug content (Table 1). Percentage content of Diclofenac from the different pharmaceutical preparations were within 98 to 115.5%, where 42.86% failed with higher percentage content, while 57.14% passed the BP stipulated range (95 to 105.0% of the prescribed content) (BP, 2004a).

Dissolution test

Dissolution test is an important parameter for assessing drug release from pharmaceutical dosage forms. It is used as an indirect method of measuring drug availability (Mbah et al., 2012). A fast-dissolving tablet gets dispersed quickly and releases the drug easily. Figure 3 shows the cumulative percentage of Diclofenac released from the different samples. Samples E and G, show fast dissolution by releasing more than 50% of the drug content in 15 min, while samples A and E follow the same dissolution pattern. The samples were found to follow the following dissolution order E>G>B>D>A. The study

shows the different dissolution profile of these different brands of Diclofenac sodium tablet retailed in pharmacy stores in Abuja.

The dissolution profile (Table 2) shows that formulations A, B, D, E and G released at least 80% of Diclofenac in 45 min, this conforms with the BP requirement that at 45 min, not less than 70% of the prescribed or slated amount of active ingredient should have been released at completion of test (BP, 2004b). The dissolution profile of brands C and F which are sustained release was not assessed.

Conclusion

All the brands of the samples passed the *in vitro* drug release analyses, but there was a 45% failure in drug content. This study confirms the need for constant surveillance on marketed drugs products within the country to ensure that commercially available drugs in markets confirmed with the Pharmacopeia standards, so as to meet up with national health delivery policy in Nigeria.

Table 2. Illustrate the cumulative percentage of drug release.

Time (min)	Cumulative drug release (%)				
	A	B	D	E	G
0	0	0	0	0	0
5	0	10.4	0	33.6	2.14
10	1.1	30.0	2.7	67.3	43.93
15	2.7	49.6	10.2	71.3	62.50
20	16.4	54.5	16.6	73.8	74.29
25	28.8	56.7	24.3	75.0	78.93
30	42.3	57.0	41.6	75.2	80.0
35	55.4	72.5	56.0	78.3	88.50
40	83.0	79.5	84.0	79.9	93.80
45	98.2	87.8	98.2	81.5	99.40

Conflict of interest

Authors declare that they have no conflicts of interest

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