Journal of Agriculture and Biomedical Sciences – JABS 2025

RESEARCH ARTICLE

A Comparative Study of Pharmaceutical and Bio-Equivalence Characteristics of Different Brands of Extended-Release Diclofenac Sodium Marketed in Zambia Using the Mongoloid Dog Model

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OPEN ACCESS

How to Cite: Musonda S, Muungo T. A Comparative Study of Pharmaceutical and Bio-Equivalence Characteristics of Different Brands of Extended-Release Diclofenac Sodium Marketed in Zambia Using the Mongoloid Dog Model. Journal of Agricultural and Biomedical Sciences;9(1). https://doi.org/10.53974/unza.jabs.9.1.1348

Published: 4th June 2025

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Abstract

This study evaluated the pharmaceutical quality and bioequivalence of three generic brands of 100 mg extended-release diclofenac sodium tablets marketed in Zambia. Comprehensive physicochemical assessments—including weight variation, hardness, friability, disintegration, dissolution, and active content—were conducted alongside in-vivo pharmacokinetic testing using a randomized three-way crossover design in fasted Mongoloid female dogs. All brands complied with most pharmacopeial specifications; however, notable differences were observed in hardness and friability, suggesting variations in manufacturing processes. Dissolution testing showed that only two brands achieved the ≥70% drug release requirement at 45 minutes, although all released more than 80% within 60 minutes. Bioanalytical validation demonstrated high linearity (r=0.998), precision, and accuracy using a UV-spectrophotometric method. Pharmacokinetic analysis showed that all brands were absorbed within 30 minutes and maintained measurable plasma concentrations up to 10 hours. Brands B and C met the FDA's 80–125% bioequivalence criteria for Cmax and AUC, indicating interchangeability. Brand A, however, demonstrated a significantly lower AUC, suggesting reduced systemic exposure despite acceptable physicochemical properties. Overall, while all brands met most quality standards, only two were bioequivalent, underscoring the need for continued regulatory screening of generic extended-release formulations.

Keywords: *Diclofenac sodium, Extended Release, Pharmaceutical equivalence, Bioequivalence.*

1.0 Introduction

Diclofenac sodium extended release is an NSAID used to treat pain and inflammation, especially in arthritis and musculoskeletal conditions. Unlike immediate-release versions, it uses specialized excipients and polymers to ensure a slow, sustained release for prolonged therapeutic effects. The extended-release formulation was developed to address diclofenac's short half-life, first-pass metabolism, and common gastrointestinal side effects, helping maintain consistent drug levels while reducing dosing frequency and adverse effects.

Diclofenac sodium extended-release is a medication used to relieve pain, inflammation, and swelling caused by conditions such as arthritis. It belongs to the class of drugs known as nonsteroidal anti-inflammatory drugs (NSAIDs). It works by reducing the production of certain substances in the body that cause pain and inflammation(Altman et al., 2015).

Diclofenac sodium extended-release is designed with specific excipients and polymers that aid in controlling the discharge of the medication. These excipients manage the dissolution and absorption rates of the medicine, resulting in a gradual and sustained release of the active component, which facilitates a slow and continuous release of the medication within the body over an extended period. Consequently, this protracts the drug's impact, offering prolonged relief from pain and decreased inflammation compared to medications with immediate-release formulations. It is commonly prescribed for ailments that necessitate long-term pain management, such as osteoarthritis or chronic musculoskeletal pain.

While diclofenac sodium is widely used, it has a short half-life and is quickly and almost completely absorbed. About 40% of the drug undergoes first-pass metabolism, resulting in fluctuations in bioavailability (Brunton, P. et al., 2008). Additionally, diclofenac sodium has common side effects that limit its use, including gastric irritation, gastritis, peptic ulcers, and bleeding (Becker & Rachel, 2016). This has led to the development of an extended-release (ER) formulation that aims to maintain therapeutic levels, reduce the frequency of drug administration, and minimize side effects. Since its introduction in 1973, various diclofenac-containing products have been created to improve effectiveness, tolerability, and patient convenience (Altman et al., 2015). Over the years, many different brands of diclofenac products have become available, which are typically cheaper than the original brands, providing more affordable options for consumers cheaper alternatives to the original diclofenac products have become available, giving prescribers and users more options.

However, there have been reports of different clinical responses to these products from different manufacturers. This has led to variations in the pharmaceutical properties and Bioequivalence of different brands of extended-release diclofenac sodium. In order for drug products to be considered pharmaceutically equivalent, they must have the same dosage forms, routes of administration, and contain the same amounts of active ingredients. In contrast, Bioequivalence refers to the similarity in bioavailability of two pharmaceutical products that are equivalent to each other. The intention is to provide the patient with consistent treatment that delivers the active ingredients in a consistent and repeatable way, thereby honestly assessing the effectiveness of the therapy (Ayorinde et al., 2012).

2.0 Materials and Methods

2.1 Study Population

The study population consisted of dogs with an average age of 2 years and weighing around 16 kg (with a range of 14-18 kg). The total number of animals was 9 (3 multiplied by 3), with each group containing 3 animals. By substituting these values into the formula, the sample size for the Study was determined to be six animals. The Study required the dogs to fast before receiving a 100 mg dose of diclofenac sodium tablets orally.

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2.2 Study Site

Samples of selected brands were purchased from selected retail pharmacies in Lusaka Urban District. Physicochemical properties and drug release tests were carried out at the Food and Drugs Control Laboratory based at University Teaching Hospitals. Bioequivalence profile tests were carried out at the same laboratory (Food and Drugs Control Laboratory) in Lusaka. In vivo experiments in dogs were carried out at the School of Veterinary Medicine at the University of Zambia.

2.3 Chemicals and Reagents

Glacial acetic acid (HPMC, Changzhou, China), perchloric acid (Asymchem, Pennsylvania, Lehigh Valley), acetic anhydride (IndiaMART, Mumbai, India), potassium hydrogen phthalate (Sigma, Darmstadt, Germany), sodium hydroxide (Quinmu Chem, Jiahengyuan, China), crystal violet indicator HClO4 Hydrochloric acid (HCl) (Dong Ying Kang Sheng, scoparone, China), ethyl acetate (India MART, Mumbai, India) were all analytical grade purchased from Kasma distributor.

2.3.1 Procurement of Diclofenac Sodium Tablets

Diclofenac sodium was bought directly from Germany. Three brands of diclofenac sodium extended-release tablets (100 mg) made by pharmaceutical companies in Germany and India were acquired from nearby pharmacies. Loperamide hydrochloride was also obtained from pharmacy retail shops. The manufacturing and expiry dates, batch number, lot number, and production license number of all brands were carefully examined and recorded in Table 1. Each brand had a shelf life of three years, and at the time of testing, each brand had at least more than a year remaining before the expiration date.

Table 1: Products Documentation Information of Diclofenac Sodium Three Different Brands

Sample Code	Country of Origin	Date of Manufacture	Expiry Date	Product Registration Number (ZAMRA,2018)
Brand A	German	Oct-18	Sep-21	130/005
Brand B	India	Apr-18	Mar-21	022/011
Brand C	India	Jun-19	May-22	245/005

2.3.2 Preparation of Standard Solution

With precision, 10 mg of diclofenac sodium was measured on a German analytical top balance (FA 2104A) and then placed into a 10 ml volumetric flask. It was dissolved in methanol with a base (methanol: 0.1M NaOH; 7:3 v/v). The volume was adjusted using methanol with a base to reach the mark and create a stock solution with a concentration of 1000 µg/ml. Using this stock solution, aliquots of 0.02, 0.04, 0.06, 0.08, 0.1, 0.12, 0.14, 0.16, 0.18, 0.20, 0.22, and 0.24 ml were taken and transferred into separate 10 ml volumetric flasks. The volume was adjusted to the mark with methanol with a base, resulting in working standard solutions with concentrations of 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24 µg/ml, respectively as shown in Table 2.

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Table 2 Dilutions of Diclofenac Solutions Made

Stock Solutions in ml	Concentrations in µg/ml
0.02	2
0.04	4
0.06	6
0.08	8
0.1	10
0.12	12
0.14	14
0.16	16
0.18	18
0.20	20
0.22	22
0.24	24

2.4 Instruments

A PerkinElmer double-beam UV-Visible spectrophotometer equipped with 10 mm matched quartz cuvettes was used for all analytical measurements. Diclofenac sodium solutions were scanned between 200–400 nm using a spectral bandwidth of 2 nm, with basified methanol as the blank. A 10 µg/mL working solution was used to determine the wavelength of maximum absorbance (λmax). Method validation followed US-FDA guidelines and included assessments of linearity, accuracy, precision (intra-day and inter-day), limit of detection (LOD), and limit of quantification (LOQ). To assess linearity, standard solutions of 2, 6, 10, 16, 20, and 24 µg/mL were prepared in 10 mL volumetric flasks and analyzed at 276 nm. A calibration curve was plotted from the absorbance values to determine the regression equation and correlation coefficient.

Precision was evaluated at three concentration levels by performing triplicate measurements within a single day and across three separate days. Results were expressed as relative standard deviation. Accuracy was assessed using the standard addition method at low (2 mg/mL), intermediate (12 mg/mL), and high (24 mg/mL) concentrations prepared in triplicate. Recovery percentages and %RSD were used to confirm accuracy. The LOD and LOQ were obtained according to FDA calculations, where LOD and LOQ were derived as the blank response plus three times and ten times the standard deviation, respectively. The LOQ was cross-checked using the highest calibration standard divided by the third lowest concentration.

The physicochemical quality of the extended-release diclofenac sodium tablets was evaluated by assessing dimensional properties, weight uniformity, hardness, friability, disintegration, dissolution, and active ingredient content. Visual inspection was conducted to assess shape and color, and the thickness of ten tablets per brand was measured using a Dr. Schleuniger Tablet Tester 8M. Uniformity of weight was determined by individually weighing twenty tablets using a top-loading balance and calculating the mean, standard deviation, and percentage deviation. Tablet hardness was measured using a Monsanto hardness tester, and values were recorded for ten tablets per brand. Friability testing was carried out on twenty tablets using a DBK friabilator operated at 25 rpm for 4 minutes; the percentage weight loss was computed to determine friability.

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Disintegration time was determined for six tablets from each brand using a disintegration apparatus operated at 37 ± 0.5°C, with water as the medium. Dissolution testing was performed using the USP paddle method with 900 mL phosphate buffer (pH 6.8) at 37 ± 0.5°C and 50 rpm paddle speed. Samples of 10 mL were withdrawn at predetermined intervals and analyzed at 276 nm, replacing each aliquot with fresh buffer. Compliance with pharmacopeial requirements was assessed based on achieving at least 70% drug release within 45 minutes. To compare dissolution profiles across different pH conditions, multipoint dissolution testing was conducted in media of pH 1.2, 4.5, and 6.8, with 5 mL samples withdrawn at 5–60 minutes and immediately replaced with pre-warmed medium.

Assay of active content for each brand was carried out by non-aqueous titration following the British Pharmacopoeia (2010). Reagents including 0.1 M perchloric acid and potassium hydrogen phthalate buffer were prepared according to pharmacopeial procedures. Ten tablets from each brand were crushed, and 125 mg of powdered sample was titrated with standardized 0.1 M perchloric acid using crystal violet as the indicator. Percentage purity was calculated according to the pharmacopeial formula.

Bioanalysis was performed to quantify diclofenac sodium in dog plasma. Six healthy female dogs (1–2 years old, 12–18 kg) were selected due to their higher microsomal enzyme activity. Ethical approval was obtained from the University of Zambia Animal Ethics Committee. A three-sequence, single-dose design was used, with dogs pre-treated with 2 mg loperamide to slow gastrointestinal transit. Each dog received a 100 mg extended-release diclofenac tablet after an overnight fast, with a 7-day washout between doses. Blood samples were collected from 15 minutes up to 10 hours post-dosing and stored at −20°C after processing.

A 100 µg/mL working stock of diclofenac sodium was prepared in methanol and diluted to 2–24 µg/mL. Quality control samples were produced by spiking blank plasma and analyzed to account for matrix effects. Validation included evaluating linearity, specificity, precision, accuracy, and sensitivity in accordance with US-FDA guidelines. Sample preparation involved acidifying 0.7 mL plasma with 0.1 mL of 1 M HCl followed by liquid–liquid extraction using ethyl acetate. Two sequential extractions were performed, the organic layer was evaporated to dryness at 45°C, and residues were reconstituted in 80 µL methanol. Extraction was repeated three times for reproducibility before UV-Visible analysis.

2.5 Data analysis

Pharmacokinetic and bioequivalence analyses were performed using non-compartmental methods. The area under the concentration–time curve (AUC) was calculated using the linear trapezoidal rule up to the time of maximum concentration and the logarithmic trapezoidal rule thereafter. Terminal elimination rate constants and half-lives were determined using linear regression of terminal points. Statistical comparisons, including ANOVA and F-tests, were used to evaluate AUC, Cmax, and other pharmacokinetic parameters. Bioequivalence was concluded when the 90% confidence intervals for geometric mean ratios of key parameters fell within the accepted 80–125% range.

3.0 Results

Pharmaceutical and bio-equivalence of three different brands of Extended-Released (ER) diclofenac sodium 100mg tablets were compared. Pharmaceutical equivalence of physicochemical properties, drug release profiles, and drug blood plasma concentration of diclofenac sodium extended-release after dissolution and subsequently absorption was assessed as shown in Table 3.

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Table 3: Results of dimensional properties of diclofenac sodium 100mg tested

S/N	Parameter	Brand A	Brand B	Brand C
1	Shape	Disk like	Disk like	Disk like
2	Colour	Orange	Orange	White
3	Edges	Intact	Intact	Intact
4	Surface	Flat	Flat	Flat

Diclofenac Sodium Products Identification and Verification

The standard solution of diclofenac sodium in methanol (10µg/ml) was scanned in the range of 200 nm and 400 nm on the UV-vis spectrophotometer PerkinElmer lambda 35. The absorption maximum was 276 nm, as shown in figure 1

Analytical Method Validation

The method validation was done as per the US FDA guidelines. The linearity, precision, accuracy and LOD and LOQ parameters were tested.

Linearity: Beer Lambert's law was obeyed in the concentration range of 2-24 µg/ml as shown in Figure 2.

Precision

Table 4 and 5 show the intermediate precision and repeatability respectively.

Table 4: Intermediate Precision (Inter-Day Precision) of The Developed UV Method

Concentration (µg/ml)	1ST day (µg/ml)	2nd day (µg/ml)	3rd day (µg/ml)	SD	%RSD
4	3.759	3.763	3.767	0.004	0.106
8	7.653	7.656	7.663	0.005	0.067
16	15.425	15.432	15.439	0.070	0.458

Table 5: Repeatability (intra-day precision) of the Developed UV Method

Concentration (µg/ml)	1ST day (µg/ml)	2ND day (µg/ml)	3RD day (µg/ml)	SD	%RSD
4	3.769	3.768	3.766	0.002	0.04
8	7.649	7.648	7.647	0.0032	0.041
16	15.425	15.422	15.424	0.002	0.013

Accuracy

Recovery of diclofenac sodium matrix to evaluate the accuracy of the UV method as shaown in Table 6.

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Table 6: Recovery Vs Relative Standard Deviation Of Diclofenac Sodium From Spiked Plasma. Diclofenac Sodium with Recoveries Between 98.13- 99.64% and with RSD <20% Are Framed

Theoretical Concentration (µg/ml)	Obtained Concentration (µg/ml)	Residue Concentration (µg/ml)	%Mean Recovery	% RSD
12	11.80	0.2		
12	11.75	0.25		
12	11.78	0.22	98.13	0.002
22	21.86	0.14		
22	21.79	0.21		
22	21.84	0.16	99.22	0.0013
34	33.89	0.11		
34	33.86	0.14		
34	33.88	0.12	99.64	0.00045

Table 7 shows the Limit of Detection and Limit of Quantification (LOD and LOQ)

Table 7: Limit of Detection LOD and LOQ

Parameter	Quantification
ʎ max	276nm
Beer's-law limit(µg/ml)	0.2-24
Correction coefficient	0.998
Slope	0.0086
LOD	0.731
LOQ	2.4

Physicochemical Analysis

Physicochemical properties of diclofenac sodium comprising weight uniformity, friability, hardness, uniformity content of the drug, disintegration time tests, and dissolution for the three brands were tested and calculated.

Physicochemical Parameters

Table 8 shows the results of physicochemical parameters of diclofenac sodium extended-release tablets. results expressed as mean ± SD and %CV, results expressed as mean ± SD

Table 8: Physicochemical parameters of diclofenac sodium extended-release tablets. results expressed as mean ± SD and %CV, results expressed as mean ± SD

Brand	Weight Variation (mg) *	Hardness (Kg/F) *	% Mean Friability	Disintegration (Min)	Drug Content (%w/w)
A	298.75 ± 5.38 1.78	10.7±0.823	2.0	14	96.14
B	366.71±5.44 1.48	12.4±0.49	1.9	18	102.89
C	378.46±1.96 0.50	11.2±0.92	2.1	20	95.41
Official Specification	USP	USP	USP	USP	BP

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Dissolution test

Figure 3 shows the plots of percent drug dissolved against time for three brands of diclofenac sodium 100mg tablets to determine compliance with official specifications. Results were reported in micrograms**.**

Bioanalysis: Bio-analytical Method Validation

Linearity: figure 3 shows the calibration curve and linear regression equation for diclofenac sodium in plasma at 276nm

Precision: Table 9 shows the Intraday of Diclofenac Sodium in Plasma and repeatability (Table 10)

Table 9: Intraday of Diclofenac Sodium in Plasma

Concentration (µg/ml)	Amount Recovered (µg/ml)	% Recovery	SD	%RSD
4	3.84	96		
	3.79	94.75		
	3.78	94.5	0.032	0.84
8	7.82	97.75		
	7.85	98.81		
	7.69	96.12	0.096	1.23
12	11.6	96.66		
	11.7	97.5		
	11.6	96.6	0.026	0.023

Table 10: Repeatability (Inter-day) of Diclofenac Sodium in Plasma

Concentration (µg/ml)	**Amount Recovered (µg/ml)**	**% Recovery**	**SD**	**%RSD**
4	3.81	95.25		
	3.74	93.5		
	3.77	94.25	0.035	0.9
8	7.79	97.38		
	7.82	97.75		
	7.65	95.63	0.09	0.012
12	11.3	94.16		
	11.4	95		
	11.3	94.16	0.07	0.62

Accuracy: Table 11 shows the recovery of diclofenac sodium in plasma.

Table 11: Recovery of Diclofenac Sodium in Plasma

Standard Concentration (µg/ml spiked)	Obtained Mean Concentration (µg/ml)	%Recovery	Mean %Recovery ± RSD
2	1.85	92.50	92.50 ±0.01
12	11.07	92.33	92.33±0.006
24	22.71	94.63	94.63±0.001

Limit of Detection and Limit of Quantification

Table 12 shows the Limit of Detection (LOD) and Limit of Quantification (LOQ) For Diclofenac Sodium in Plasma Spiked With 2.4 µm/Ml Diclofenac Sodium

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Table 12: Limit of Detection (LOD) and Limit of Quantification (LOQ) For Diclofenac Sodium in Plasma Spiked With 2.4 µm/ml Diclofenac Sodium

Amount Recovered	%Recovery	SD	Mean ±%RSD
2.45	102		
2.39	99.58		
2.35	97.92		
2.36	98.33		
2.36	98.33		
2.38	99.17	0.03	2.38 ± 1.43

Pharmacokinetics parameters

The pharmacokinetic analysis of different diclofenac sodium brands in dogs (n=2). The curves of the two brands were similar and overlapped as shown in Figure 5. Plasma concentrations returned to initial values around 8 hours after oral administration, while after 10 hours, the levels were almost undetectable in Table 13. Thu, the AUC10 was determined as shown in Figure 5.

Table 13: ANOVA Drug Plasma Concentration of Three Brands of Extended-Release Diclofenac Sodium

PARAMETER	InCmax
Sum Square Total (SST)	1081.13
Degree of Freedom	33
The sum of Square Within the Group (SSW)	1031.46
Between the Group (SSB)	49.67
Variance Between	24.84
Variance Within	38.2
P	1.23
F	0.05
Critical Value	2.83

The validated analytical method for diclofenac sodium at 276 nm showed excellent sensitivity and linearity within the 2–24 µg/mL range, following Beer-Lambert's law (r = 0.9962, regression equation Y = 0.0301x + 0.0136). Precision and recovery were confirmed to be within acceptable limits via replicate analyses at six concentrations. Additionally, the limits of detection (LOD) and quantification (LOQ) were determined, underscoring the method's robustness. Overall, this simple, reproducible, cost-effective method is highly suitable for bioequivalence studies, and the physicochemical parameters for all three tested brands met the required standards.

4.0 Discussion

Visual inspection plays an important role in reinforcing quality assurance, public health protection, and supply-chain integrity. In this study, all diclofenac sodium extended-release tablet brands demonstrated acceptable packaging, accurate labeling, and complete documentation in line with WHO recommendations. Details such as manufacturing and expiry dates, batch numbers, registration status, and country of origin were clearly indicated, confirming traceability and reducing the likelihood of falsified or substandard products circulating within the distribution chain. These findings reaffirm the importance of routine visual checks as an early screening tool for quality monitoring and recall procedures.

Diclofenac sodium was identified successfully using UV spectrophotometry, showing a clear maximum absorption wavelength at 276 nm. Spectral analysis confirmed that the compound adhered to Beer's law across the linear range

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of 2–24 µg/mL, consistent with earlier reports by Revathi Gunji et al. (2014) and Ball (2006). Methanol was used as the working solvent because it did not interfere with the characteristic absorption peaks of diclofenac sodium. During analytical method development and validation, the UV spectrophotometric method exhibited excellent precision, with percentage relative standard deviations below 0.2%, and high accuracy based on recovery studies aligned with previous literature (Yasir, 2015). Calibration curves generated during validation established strong linearity, while additional optical characteristics—Beer's limit, molar absorptivity, and Sandell's sensitivity—confirmed the suitability of the method. The LOD and LOQ determined using US-FDA bioanalytical guidelines further demonstrated the sensitivity and reliability of the assay.

The physicochemical evaluation of the diclofenac sodium extended-release tablets emphasized the importance of uniformity, disintegration, and dissolution behavior in ensuring product equivalence. Oral drug performance depends on proper gastrointestinal absorption, and interchangeable formulations should therefore exhibit comparable quality attributes. In this study, weight variation, thickness, hardness, friability, dissolution, and content uniformity were assessed to determine whether brands A, B, and C met pharmacopeial requirements.

All three brands complied with the British Pharmacopoeia specifications for weight uniformity. Brand A showed a mean tablet weight of 298.74 mg (coefficient of variation 1.78%), Brand B averaged 366.71 mg (1.4%), and Brand C 379.46 mg (0.5%). These low levels of variability indicate consistent manufacturing processes, as only minimal deviation was observed among tablets of the same batch. In contrast, the friability test revealed that all brands failed the ≤1% limit. Excessive friability was attributed to factors such as high binder content or excessive compression force, leading to chipping, cracking, and tablet fragmentation. The inverse association observed between friability and crushing strength suggests that very hard tablets tended to resist abrasion but also became more brittle, predisposing them to physical damage.

Hardness testing further revealed substantial deviations from recommended standards. All three brands showed hardness values far above the ideal 4–6 kgF range, with Brand A averaging 10.7 kgF, Brand B 12.4 kgF, and Brand C 11.2 kgF. While the values were comparable across brands, the excessive hardness indicates manufacturing issues such as incorrect compression settings or excipient imbalance. Tablets compressed too strongly may hold their shape but risk poor dissolution or lamination defects. These observations explain why tablets may pass weight uniformity yet fail friability and hardness specifications, highlighting the multidimensional nature of tablet quality.

Content uniformity testing showed that all brands met the British Pharmacopoeia (2008) requirement of 95–105% of labeled drug content, with assay values between 95.41% and 102.89%. This confirms adequate potency and uniform distribution of active pharmaceutical ingredient (API), which is essential for achieving therapeutic efficacy.

Disintegration behavior varied among brands but remained within the pharmacopeial limit of 60 minutes for enteric-coated tablets. Brand C disintegrated the fastest at 14 minutes, despite its low crushing strength. This illustrates that disintegration is not solely dependent on hardness; rather, it is influenced by factors such as granule size distribution, moisture content in granules, type and concentration of lubricants, pre-compression parameters, and the nature of disintegrants used. Previous studies (Graham & Summers, 1990) support these findings and emphasize that excessive compression force may produce tablets that are structurally sound but slow to break down, or conversely, tablets that appear hard but contain lamination defects that facilitate faster disintegration.

Dissolution testing demonstrated that Brands A and B achieved the required 70% drug release within 45 minutes in accordance with British Pharmacopoeia standards, whereas Brand C did not meet this criterion at the 45-minute mark. Nonetheless, all brands achieved at least 80% dissolution within 60 minutes, indicating general in-vitro pharmaceutical equivalence. Earlier studies (Zafar, 2014; Oishi et al., 2007; Ayorinde et al., 2012) have similarly shown acceptable physicochemical and dissolution performance for diclofenac tablet formulations, reinforcing the expectation that extended-release products should exhibit predictable and reproducible drug-release characteristics. The observed dissolution differences are likely attributed to variations in excipient profiles, manufacturing methods, and compression forces.

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Bioanalytical method validation demonstrated strong linearity (r = 0.998) over the working range of 2–24 µg/mL, with high precision (%RSD <2%) and recovery values ranging from 92.33% to 94.44%. Limits of detection and quantification were 0.01 µg/mL and 2.4 µg/mL, respectively, confirming that the method was sensitive enough to detect low plasma concentrations of diclofenac sodium in pharmacokinetic studies. These findings align with other spectrophotometric assays previously used for diclofenac determination in plasma and tablet formulations.

Pharmacokinetic evaluation revealed differences in absorption rates among the three brands. All formulations were absorbed within 30 minutes and maintained plasma levels for up to 10 hours, reflecting the expected profile of extended-release preparations. Brand A achieved the shortest time to peak concentration (Tmax = 2 hours), whereas Brands B and C reached Tmax at 3 hours. Brand A also showed a higher Cmax, suggesting greater initial systemic exposure and potentially stronger analgesic effects. Despite these variations, the pharmacokinetic parameters for all three brands fell within the 80–125% bioequivalence limits for AUC and Cmax, indicating comparable therapeutic performance. The study also highlighted the importance of controlling biological variability by using animals of similar age and weight, as well as the need for larger sample sizes to improve statistical power and generalizability.

Overall, the findings demonstrate that while physicochemical differences existed among the brands—particularly in hardness, friability, and early dissolution profiles—all three formulations were ultimately bioequivalent and pharmacokinetically comparable. The study supports the use of the dog model as a reliable predictor of human bioequivalence and provides a foundation for future clinical investigations.

Conclusion

Three brands of extended-release diclofenac sodium 100 mg tablets were analyzed for physicochemical properties and drug release. All brands exhibited excellent physicochemical characteristics and met nearly all official specifications. However, while brands B and C demonstrated similar bioequivalence in terms of Cmax and AUC, brand A significantly deviated in AUC values. As a result, brands B and C can be used interchangeably without altering the therapeutic effect, whereas brand A may lead to different pharmacological responses and should not be substituted for B or C.

The three brands of extended-release diclofenac sodium 100mg tablets on the market were analyzed, and the selected brands of diclofenac sodium sustained-release 100 mg tablets showed excellent physicochemical characteristics and demonstrated acceptable drug release. Therefore, the three brands tested conformed to almost all the official specifications for physicochemical parameters. Regarding Bioequivalence, brands B and C showed similarities in Cmax and AUC, while brand A was far off the AUC. The differences between brand A and Brands B and C pharmacokinetics parameters show that the brands, though chemically equivalent, are not bioequivalent. Based on the results presented, brands B and C can be interchanged with no expectation of change in therapeutic response. However, brand A could potentially result in a varied pharmacological response and consequently should not be used as a substitute for B and C.

Acknowledgement

The authors duly appreciate the efforts and contributions of our research assistants, Ameerah Yahaya Sambo and Rihana Atitebi, and the laboratory assistants.

Funding

This research received no external funding. All activities were self-supported by the authors.

Conflict of interest

The authors declare no conflict of interest.

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APPENDICES: FIGURES AND TABLES

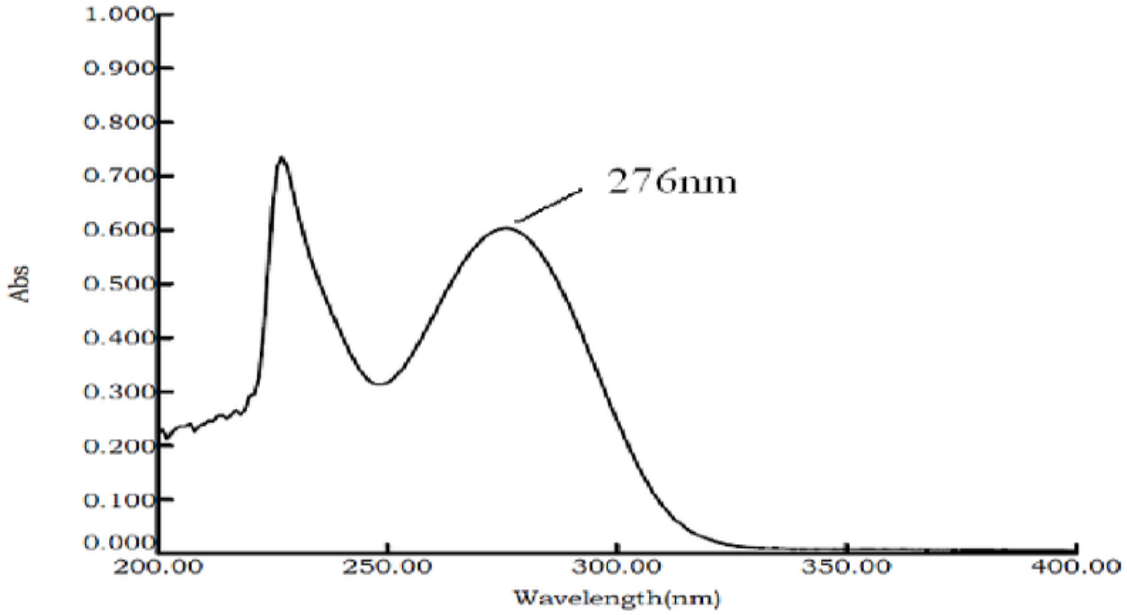

Figure 1: Shows detection of diclofenac sodium at 276nm wavelengths

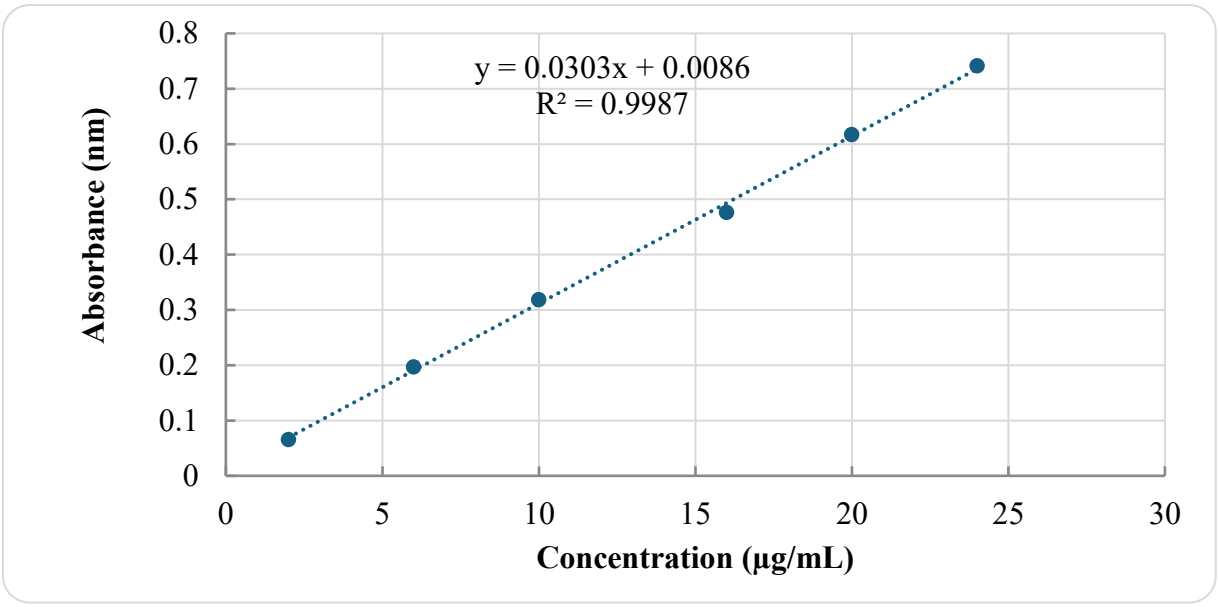

Figure 2. Calibration curve for diclofenac sodium at 276nm (absorbance maximum of diclofenac sodium).

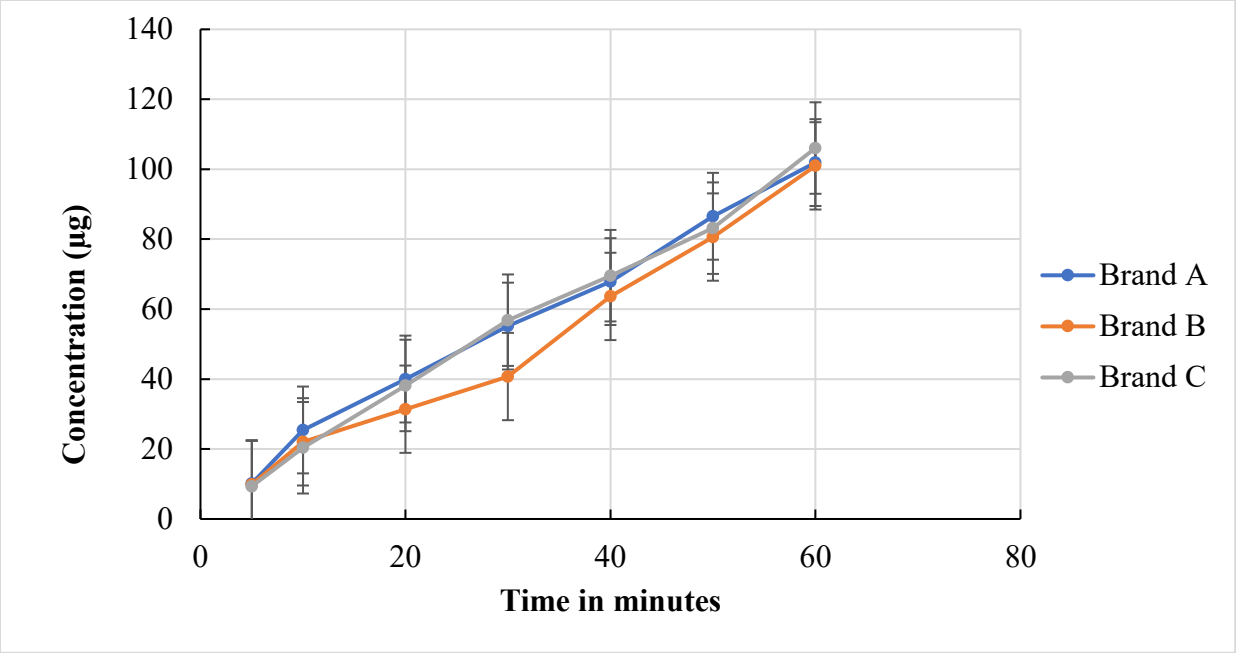

Figure 3: Plots of percent drug dissolved against time for three brands of diclofenac sodium 100mg tablets to determine compliance with official specifications. Results were reported in micrograms**.**

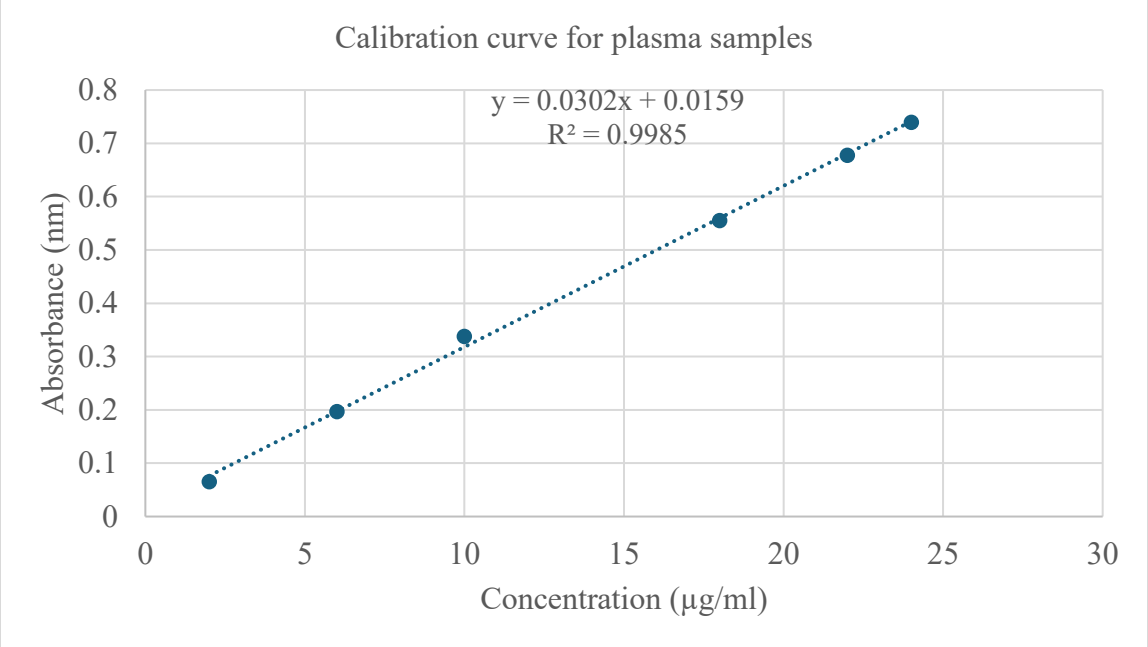

Figure 4: Calibration curve and linear regression equation for diclofenac sodium in plasma at 276nm

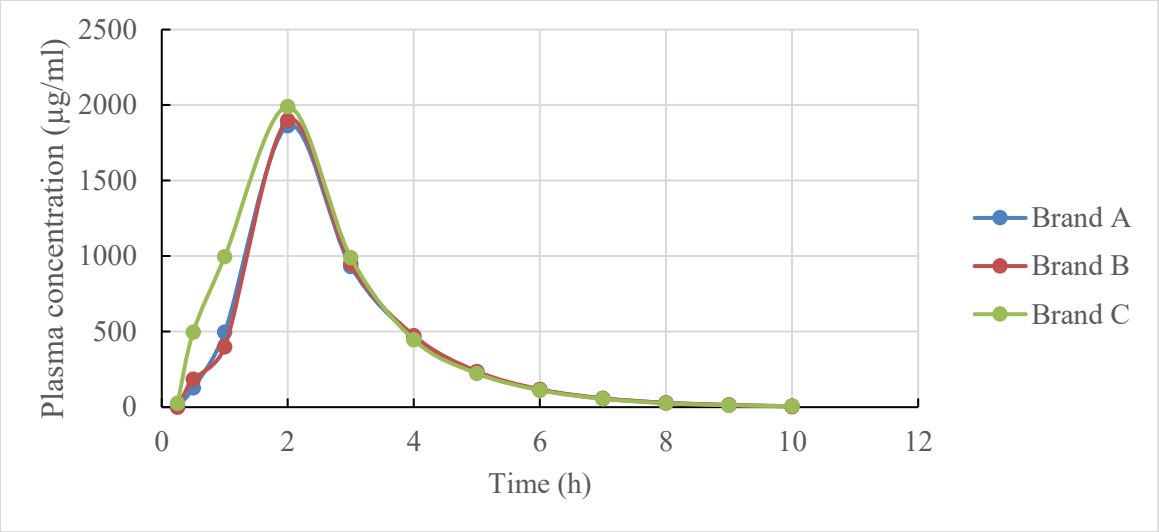

Figure 5: Plasma concentration of diclofenac sodium. Data correspond to 6 dogs which received 100 mg of Brand A, Brand B, and Brand C for diclofenac sodium for each brand of two dogs.