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In Vitro Comparative Quality Evaluation of Locally Manufactured and Imported Diclofenac Dispersible Tablets in Sana'a, Yemen

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This research was submitted in fulfillment of the requirements for a Bachelor of Science degree in Pharmaceutical Sciences

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وَقُل رَّبِّ زِدْنِي عِلْمًا

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Dedication

To those who deserve this success even more than we do—our parents—who fought tirelessly to help us achieve our dreams. To everyone who supported us and stood by our side. To our friends, and to all those who cherish science and scientists. We extend our deepest gratitude to our families for their unwavering support throughout our studies and throughout our lives.

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Abstract

Background: Ensuring the therapeutic equivalence of medications is essential for public health, particularly in markets with diverse drug origins. In Yemen, Diclofenac dispersible tablets are a mainstay for pain management, yet comparative data between locally manufactured and imported brands remains limited.

Objective: This study aimed to evaluate the compliance of locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market with USP physicochemical quality specifications and to determine the statistical significance of any quality deviations between them.

Methods: Four brands of Diclofenac dispersible tablets, two locally manufactured (D1, D3) and two imported (D2, D4), were subjected to standardized USP testing. Evaluations included weight variation, hardness, thickness, friability, dispersion, assay, content uniformity, and dissolution. Statistical analysis was performed using SPSS software (version 27).

Results: All sampled brands demonstrated 100% compliance with USP all physicochemical quality specifications except for hardness. A systemic deviation was observed in tablet hardness, with all brands. Findings revealed no significant difference ($p > 0.05$) between locally manufactured and imported brands in all tests except for assay. A significant difference was noted in the assay ($p = 0.012$), with imported brands showing slightly higher mean potency (106.44%) compared to local brands (99.04%), though both remained within the legal 90–110% window.

Conclusion: Locally manufactured Diclofenac dispersible tablets in Sana'a are pharmaceutically equivalent to their imported counterparts. The findings suggest that domestic manufacturers adhere to high-quality standards.

Keywords: Diclofenac, Dispersible, Quality Control, in vitro, HPLC

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List of Abbreviations

Abbreviation	Description
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
USP	United States Pharmacopeia
BP	British Pharmacopoeia
Ph. Eur.	European Pharmacopoeia
WHO	World Health Organization
FDA	Food and Drug Administration
QC	Quality Control
QA	Quality Assurance
API	Active Pharmaceutical Ingredient
HPLC	High-Performance Liquid Chromatography
UV-Vis	Ultraviolet-Visible Spectroscopy
COX	Cyclooxygenase
RSD	Relative Standard Deviation
SD	Standard Deviation
ICH	International Council for Harmonization
GMP	Good Manufacturing Practice
GIT	Gastrointestinal Tract
λ	Wavelength
MW	Molecular Weight
N	Number of Samples (Sample Size)

Chapter I:
Introduction

Chapter I:
Introduction

1.1 Background:

Non-steroidal anti-inflammatory drugs (NSAIDs) represent one of the most widely utilized therapeutic classes in the global pharmaceutical market. Their primary mechanism of action involves the inhibition of the cyclooxygenase (COX) enzymes, thereby reducing the synthesis of prostaglandins that are the key mediators of pain, inflammation, and fever (Ruggiero et al., 2026).

Diclofenac is a NSAID drug. It is one of the most widely used and prescribed medications globally (El-Sayed et al.,2020; Akanksha et al., 2026). The drug acts as a potent analgesic, anti-inflammatory, and antipyretic agent, extensively prescribed for the treatment of rheumatic diseases, arthritis, acute and chronic pain, and migraines (Lekshmi et la., 2026).

However, the presence of multiple brands of Diclofenac dispersible tablets in the market has led to concerns among healthcare providers and patients regarding the "quality gap" between imported brands and more affordable local products. Thus, it is important to make sure that various brands of diclofenac adhere to the quality criteria guidelines as required (Ahmad et al., 2017; Kasim et al., 2025).

Quality Control (QC) is the cornerstone of the pharmaceutical Industry, crucial for ensuring that every medicinal product is safe, effective, and reliable. Conducting periodic and comparative quality tests is essential to verify that products are capable of releasing the API at the appropriate rate and amount to achieve the desired therapeutic outcome (Gupta et al., 2020).

The pharmaceutical market in Yemen is a complex environment, with a significant portion of its needs covered to numerous commercial brands - both local and imported - for the same active ingredient. This raises questions about the consistency of quality and efficacy among these varieties, necessitating a clear standard for their evaluation by health authorities. Thus, this study's aimed to evaluate the compliance of locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market with USP physicochemical quality specifications.

1.2 Problem statement:

In Yemen, a real problem arises concerning the extent to which pharmaceutical products available on the market whether imported or locally manufactured comply with internationally recognized pharmaceutical quality standards (Al-Eryani, 2018). Some studies have shown significant variations in quality control test results between locally manufactured and imported drugs, raising concerns about the efficiency of regulatory systems and their ability to guarantee safe and effective pharmaceutical products (Al-Maqtari et al., 2020).

Drug quality is considered one of the most important factors to ensure the safety and efficacy of treatment, as quality control represents a fundamental approach to achieving the safety of marketed pharmaceutical products (WHO, 2020). Reports by the World Health Organization and the U.S. Food and Drug Administration indicate that weak quality control systems in developing countries lead to the circulation of substandard or falsified medicines, which negatively affects public health (WHO, 2019; FDA, 2021).

Diclofenac Dispersible Tablets is among the most widely used drugs in Yemen, prescribed as an analgesic and anti-inflammatory agent. Due to its wide

availability from both local and imported sources, there is an urgent need to conduct a comparative quality assessment to ensure its compliance with pharmacopeia standards. Consequently, this study addresses the following two primary research questions:

First question: To what extent do locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP physicochemical quality specifications?

The following sub-questions are derived to address the first question:

1. To what extent do locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP quality specifications for weight variation?
2. To what extent do locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP quality specifications for hardness?
3. To what extent do locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP quality specifications for thickness?
4. To what extent do locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP quality specifications for friability?
5. To what extent do locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP quality specifications for dispersion?
6. To what extent do locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP quality specifications for assay?
7. To what extent do locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP quality specifications for content uniformity?

8. To what extent do locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP quality specifications for dissolution?

Second question: Is there a statistically significant difference in the level of adherence to USP quality standards between locally manufactured and imported diclofenac dispersible tablets available in the Yemeni market?

1.3 Research Objectives:

This study aims to achieve the following objectives:

First Objective: To evaluate the compliance of locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market with USP physicochemical quality specifications.

The first main objective is divided into the following sub-objectives:

1. To evaluate the weight variation of locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market against USP quality specifications.
2. To evaluate the hardness of locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market against USP quality specifications.
3. To assess the thickness of locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market against USP quality specifications.
4. To assess the friability of locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market against USP quality specifications.
5. To assess the dispersion of locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market against USP quality specifications.
6. To determine the assay of locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market against USP quality specifications.

7. To determine the content uniformity of locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market against USP quality specifications.
8. To evaluate the dissolution of locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market against USP quality specifications.

Second Objective: To determine if there is a statistically significant difference in the level of adherence to USP physicochemical quality specifications between locally manufactured and imported Diclofenac dispersible tablets available in the Yemeni market.

1.4 Research hypotheses:

H_{01}: Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP physicochemical quality specifications.

The following sub-hypotheses are derived from the first hypothesis:

H_{01a}: Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP weight variation specifications.

H_{01b}: Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP hardness specifications.

H_{01c}: Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP thickness specifications.

H_{01d}: Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP friability specifications.

H_{01e}: Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP dispersion specifications.

H_{01f}: Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP assay specifications.

H_{01g}: Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP content uniformity specifications.

H_{01h}: Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP dissolution specifications.

H_{02}: There is no statistically significant difference in the level of adherence to USP physicochemical quality specifications between locally manufactured and imported Diclofenac dispersible tablets available in the Yemeni market.

1.5 Significance of the Study:

The significance of this research lies in its potential to provide a comprehensive quality map of one of the most commonly used analgesics in Yemen. Moreover, the findings of this study deliver reliable laboratory evidence crucial for informed regulatory decision-making by national Health Authorities. Furthermore, the results offer a direct, data-driven mechanism for improving the local industry by pinpointing specific quality deficiencies.

Furthermore, this research contributes to the relatively sparse body of pharmaceutical literature concerning the Yemeni drug market. By providing rigorous in vitro data, it establishes a critical scientific baseline for future researchers.

1.6 Scope of the Study:

- **Formulation Type:** Only locally manufactured and imported dispersible tablet formulations of Diclofenac were included in the evaluation.
- **Testing Parameters:** The research was exclusively limited to the evaluation of physicochemical quality specifications as defined by the USP, including:

(weight variation, hardness, thickness, friability, dispersion, assay, content uniformity, dissolution).

- **Geographical Scope:** The study was limited to brands found within the pharmaceutical market of Sana'a, Yemen.
- **Time**: This study was conducted and data collected during the year of 2025.
- **Exclusions:** This study does not include in vivo bioavailability or bioequivalence testing, nor does it assess the microbial purity of the samples.

Chapter II:
Literature Review

Chapter II
Literature Review

2.1 Diclofenac:

Diclofenac is a phenylacetic acid derivative and a potent non-steroidal anti-inflammatory drug (NSAID). Its primary mechanism of action involves the inhibition of the cyclooxygenase (COX-1 and COX-2) enzymes, which are responsible for the biosynthesis of prostaglandins (PGs). These lipid mediators are key contributors to the inflammatory response and the sensitization of pain signaling pathways (Attia et al., 2026). Diclofenac was first approved by the FDA in July 1988 under the trade name Voltaren® (O'Donnell, 2026). Historically, the molecule was the result of rational drug design, strategically modeled after the chemical structures of phenylbutazone, mefenamic acid, and indomethacin to optimize its anti-inflammatory efficacy (Patel et al., 2026).

Diclofenac is primarily indicated for the management of mild-to-moderate pain and the reduction of inflammation across a broad spectrum of clinical conditions. Its most common applications include the long-term symptomatic treatment of chronic inflammatory joint diseases, such as rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis (van Walsem et al., 2015; Intharit et la., 2026). In acute settings, it is highly effective for treating musculoskeletal injuries, such as sprains and strains, as well as managing acute gouty arthritis and post-operative pain (Feng et al., 2018; Alfaro & Davis, 2025).

Additionally, Diclofenac is frequently utilized for the relief of dysmenorrhea (menstrual pain) and migraine headaches, where the rapid absorption of the dispersible tablet form is particularly advantageous for achieving swift therapeutic relief (Kaur et al., 2025)

Diclofenac is one of the most versatile NSAIDs in terms of formulation. Its chemical properties allow it to be processed into various delivery systems to meet specific clinical needs, ranging from acute pain management to chronic inflammatory control (Altman et al., 2015). Oral administrations remain the most prevalent, ranging from enteric-coated tablets designed for acid resistance to extended-release capsules for chronic pain management, and notably, dispersible tablets which prioritize a rapid onset of action via pre-ingestion dissolution. Beyond the oral route, Diclofenac is formulated as parenteral injections, rectal suppositories, emulgels, foams, ophthalmic solutions and transdermal patches (Alfaro & Davis, 2025; Mayo Clinic, 2026).

2.1.1 Diclofenac: Chemistry, Properties, and Formulation:

Diclofenac is the monosodium salt of 2-[(2,6-dichlorophenyl) amino] phenylacetic acid (Wishart, 2018). Its molecular formula is $C_{14}H_{11}Cl_2NO_2$ (molecular weight 318.13) (Wishart, 2018). The structure consists of a phenylacetic acid moiety linked through an aniline nitrogen to a 2,6-dichlorophenyl ring. The two ortho-chlorine atoms on the aniline ring enforce a twisted, nonplanar conformation that is crucial for activity (Oza et al., 2002; Sweetman, 2006). Figure 1. shows the chemical structure of Diclofenac (Wishart, 2018).

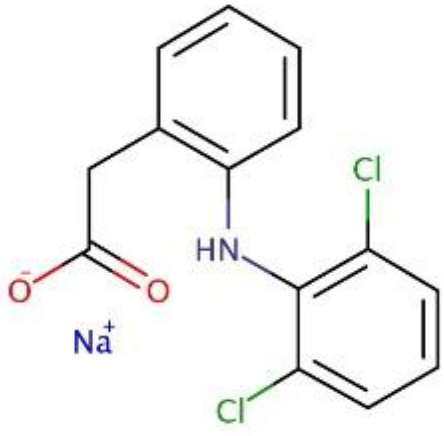

Figure 2.1: Chemical structure of Diclofenac

2.1.1.1 Chemical Nomenclature and Identity:

Diclofenac's IUPAC name is sodium2-{2-[(2,6 dichlorophenyl) amino] phenyl}acetate (Wishart, 2018). The Chemical Abstracts Service (CAS) registry number is 15307-79-6 (Wishart, 2018). It is also known by synonyms such as sodium diclofenac, diclofenac Na, or diclophenac sodium. The British Approved Name (BAN) and United States Adopted Name (USAN) denote it simply as Diclofenac (Sweetman, 2006). In the USP monograph, it is described as "2-[(2,6-dichlorophenyl) amino] benzeneacetic acid, monosodium salt" (USP, 2019). These names all refer to the same phenylacetic acid derivative in its sodium salt form. Diclofenac sodium is typically compared to its free acid (diclofenac) form; the sodium salt is much more water-soluble, while the free acid is sparingly soluble (Wu & Xue, 2008; USP, 2019).

2.1.1.2 Physicochemical Properties:

Diclofenac is a weak acid (the conjugate of the phenylacetic acid) with an acid dissociation constant around $pK_a \approx 4.0$ (Wu & Xue, 2008). This means it is largely deprotonated (ionized) at physiological pH. Its water solubility is modest: the free diclofenac acid is "sparingly soluble in water" (Sweetman, 2006), whereas the sodium salt form has a much higher solubility (on the order of tens of mg/mL at room temperature) (USP, 2019). For example, one source reports the sodium salt's water solubility as ~37 mg/mL at 32°C (Wu & Xue, 2008).

Consequently, the lipophilicity of diclofenac (as the free acid) is high: its partition coefficient is log P ≈ 4.5, indicating it is largely lipophilic despite the charged carboxylate group (the high log P is for the un-ionized form) (Oza et al., 2002). Diclofenac is a solid hygroscopic, white to slightly yellowish, crystalline, (Bp, 2023). It is sparingly soluble in water; soluble in alcohol; freely soluble in

methanol; practically insoluble in ether. (USP, 2019). A summary of physicochemical properties of Diclofenac is shown in Table 2.1.

Table 2.1: physicochemical properties of Diclofenac

Property	Diclofenac
Molecular Formula	$C_{14}H_{11}Cl_2NO_2$
Molecular Weight	318.13 g/mol
Appearance	Is an odorless, White/off-white crystalline, slightly hygroscopic powder.
Solubility	Slightly soluble in water; freely soluble in methanol, ethanol, acetone.
Melting Point	~283–290°C
pKa	~4.0 (weak acid)
Partition coefficient (Log P)	~4.5 (moderate lipophilicity)

2.1.1.3 Formulation of Diclofenac:

Diclofenac is formulated in a variety of dosage forms. The original oral forms are enteric-coated (delayed-release) tablets. For example, Voltaren® (Diclofenac enteric-coated tablets) is available in 25 mg, 50 mg, and 75 mg strengths (Mayo Clinic, 2026).

Typical tablet excipients include a matrix/binder polymer (e.g. hydroxypropyl methylcellulose), a filler/diluent (e.g. lactose, microcrystalline cellulose), a lubricant (magnesium stearate), an enteric-coating polymer (methacrylic acid copolymer, such as Eudragit L), binders/plasticizers (polyethylene glycol, polyvinylpyrrolidone), a plasticizer (propylene glycol), an alkali (sodium hydroxide, to ensure the enteric coat dissolves at higher pH), a super-disintegrant (sodium starch glycolate), and glidants/flow agents (talc, titanium dioxide for pigment) (Allen et al., 2020; Shah & Augsburger, 2002; Voltaren, 2021).

2.1.1.4 Structure–Activity Relationship (SAR):

The pharmacological potency of Diclofenac as a dual cyclooxygenase (COX) inhibitor is fundamentally dictated by its specific molecular architecture. Key structural features essential for its inhibitory activity (Amanullah et al., 2022). The following structural features are recognized as essential for its inhibitory activity and binding affinity:

- **The Carboxylic Acid Group:** The phenylacetic acid's carboxylate is essential for activity. SAR studies show that removal of the carboxylic acid (or esterification) abolishes COX inhibition (Smith et al., 2000). The free carboxylate (or sodium salt) interacts with arginine residues at the COX active site, anchoring the drug in the enzyme pocket (Smith et al., 2000).
- **Aniline Linkage:** The –NH– linkage between the two aromatic rings is required to position the rings properly. Changing or removing this secondary amine disrupts activity (Willoughby et al., 1993).
- **Ortho-Dichloro Substitution:** The 2,6-dichlorophenyl ring is a defining feature. Introducing two chlorine atoms in the ortho positions forces the ring to twist out of coplanarity (locking it in a highly twisted conformation) (DrugBank, 2024; Ku et al., 2016). This twist is believed to enhance complementarity with the COX binding site. Indeed, analogues lacking one or both chlorines show reduced potency. The o,o-dichloro substitution also increases lipophilicity and membrane permeability (DrugBank, 2024; Ku et al., 2016).
- **Phenylacetic Core:** The 2-phenylacetic acid skeleton (as opposed to a benzoic acid) is important; SAR work found that the distance between the carboxylate and the aniline ring must be maintained for activity. Variations in position of the acid or changes to the linker affect potency (Smith et al., 2000).

Diclofenac's COX-inhibiting activity arises from the combination of its anilino-phenylacetic structure, which fits the COX enzyme binding pocket, and the presence of key functional groups. Modifications to the carboxyl group or ring substitutions dramatically reduce activity, illustrating a tight structure–activity relationship that guided its rational design (Ku et al., 2016; Smith et al., 2000).

2.1.2. Pharmacokinetics:

2.1.2.1 **Absorption**:

Diclofenac is a nonsteroidal anti-inflammatory drug (NSAID) that demonstrates rapid and extensive absorption following oral administration. Historically, radio-labelled ^{14}C studies have shown that orally administered Diclofenac is almost completely absorbed from the gastrointestinal tract, with minimal loss within the lumen and extensive entry into the portal system. Although the drug is well absorbed regardless of dosage form, the rate and onset of absorption vary depending on formulation — with solutions absorbed fastest, followed by conventional tablets, enteric-coated tablets, and suppositories (Sun et al. 2026).

Pharmacokinetic modeling studies have further refined understanding of absorption kinetics. It has been shown that Diclofenac's plasma concentration–time profile is more accurately described by multiple‑segment absorption models rather than simple first‑order kinetics, indicating that absorption may occur in several phases along the gastrointestinal tract (Mahmood, 1996). This multi‑segment pattern explains observed phenomena such as multiple peaks in some individuals, which may result from pH‑dependent solubility and site‑specific absorption along the intestine (Kim et al., 2026).

One of the primary pharmacokinetic determinants of absorption is first‑pass hepatic metabolism. Diclofenac is characterized by high gastrointestinal uptake but limited systemic bioavailability, estimated at 50–60% due to extensive first-pass hepatic metabolism. This biotransformation, primarily driven by the CYP2C9 enzyme, significantly reduces the concentration of the unchanged drug before it reaches systemic circulation. Although formulation types and physiological factors influence specific absorption kinetics and peak concentrations, plasma levels generally rise rapidly enough to initiate therapeutic effects within 1–3 hours post-administration (Adel et la., 2024)

2.1.2.2 Distribution:

Diclofenac demonstrates extensive distribution throughout the body after systemic absorption, which directly impacts its pharmacological efficacy and duration of action. Although comprehensive human distribution data are limited, early radiolabelled studies in animals (rats, dogs, and primates) suggest rapid distribution to multiple organs shortly after exposure, with highest levels initially in liver, bile, kidneys, and circulating blood (EMA, 2026).

After oral absorption in humans, diclofenac is rapidly distributed within the vascular compartment and extravascular tissues. The apparent volume of distribution (V/F) is estimated at approximately 0.12–0.17 L/kg to 1.3–1.4 L/kg, suggesting moderate distribution beyond blood plasma into the interstitial and tissue spaces (MIMS Philippines, 2025; MedPath, 2026; RxMed, 2026)

2.1.2.3. Elimination:

Diclofenac is eliminated principally by metabolism and subsequent urinary and biliary excretion of glucuronide and sulphate conjugates of the metabolites. The principal metabolite in humans is the 4'-hydroxy derivative of diclofenac. The amount excreted in urine accounts for 20–30% of the dose, and in bile for 10–20% of the dose (Lin et al., 2021). Three other metabolites each account for 10–20% of the dose excreted in urine and small amounts in bile. Conjugates of diclofenac itself account for 5–10% of the dose recovered in urine and <5% in bile (FDA, 2021).

2.1.3. Pharmacodynamics:

Diclofenac is a nonsteroidal anti-inflammatory drug (NSAID) whose primary chemical mechanism is the inhibition of cyclooxygenase enzymes (COX-1 and COX-2). The central mechanism of Diclofenac involves the competitive and reversible inhibition of the enzyme's cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). These enzymes catalyze the conversion of arachidonic acid—released from membrane phospholipids—into unstable cyclic endoperoxides (PGG_2 and PGH_2), which are subsequently converted into various prostaglandins (PGs), prostacyclin (PGI_2), and thromboxanes (TXA_2) (Zhang et la., 2020). The inhibition of prostaglandin E_2 (PGE_2) synthesis is particularly important, as PGE_2 is a dominant mediator of inflammation and pain (Altman et al., 2015).

In addition to COX inhibition, diclofenac can modulate other pathways: for example, it has been reported to activate nitric oxide–cGMP–potassium channel signaling pathways, which may contribute to peripheral analgesia by hyperpolarizing pain-sensing neurons (Altman et al., 2015).

2.2 Pharmaceutical Quality Control:

Pharmaceutical quality control is an essential component of drug development and manufacturing. It ensures that medicines released to the public meet established standards for identity, purity, potency, strength, and performance. Quality control activities are systematic, structured, and documented processes used to monitor and verify quality throughout production, from raw materials to finished products (Aulton & Taylor, 2018). At its core, pharmaceutical quality control protects patient safety and ensures therapeutic reliability. A cornerstone of quality control is the pharmacopoeial system, a set of legally recognized written standards that define methods and acceptance criteria for testing drug substances, excipients, and dosage forms. Pharmacopoeias serve as authoritative benchmarks for regulatory compliance worldwide (Lucia et al., 2022).

2.2.1 Quality Control Tests:

Quality control tests are critical procedures applied during pharmaceutical manufacturing and product release to ensure dosage forms meet established standards for safety, efficacy, and consistency. For solid dosage forms like Diclofenac tablets, these tests evaluate physical and chemical properties that influence drug performance and patient outcomes (Aulton & Taylor, 2018). Below are detailed explanations of key quality control parameters:

2.2.1.1 Weight variation:

Weight variation testing ensures consistency in tablet mass within a production batch. Although it does not directly measure drug content, it indirectly reflects dose uniformity and manufacturing consistency, particularly when the API is uniformly distributed throughout the formulation. This test is

especially applicable when the API constitutes a significant proportion of the tablet weight. Excessive variation may indicate issues in granulation, powder flow, die filling, or compression processes (USP, 2024).

2.2.1.2 Hardness:

Tablet hardness, also referred to as crushing strength, evaluates the mechanical resistance of tablets to pressure or breakage. This test ensures that tablets can withstand mechanical stress during manufacturing, packaging, transportation, and handling without cracking or breaking. At the same time, hardness must not be excessive, as overly hard tablets may delay disintegration and dissolution, thereby affecting bioavailability and therapeutic efficacy (Sweetman, 2006; Aulton & Taylor, 2018).

2.2.1.3 Thickness:

The thickness test for dispersible tablets is a vital physical quality control parameter used to ensure dimensional consistency and packaging compatibility. Unlike standard tablets, dispersible tablets must maintain a specific balance between structural integrity and a porous matrix that allows for rapid disintegration in water (Sharma & Leel, 2022).

While the pharmacopoeia (like the USP or BP) typically focuses more on uniformity of mass and disintegration time, thickness is monitored in-process to ensure the manufacturing equipment is applying uniform pressure. If the thickness varies significantly, it can indicate fluctuations in the compression force or granulated flow, which might inadvertently affect how quickly the tablet "disperses" when it hits liquid (Ali et al., 2025)

2.2.1.4 Friability:

Friability testing evaluates the tendency of tablets to crumble, chip, or lose mass when subjected to mechanical stress. This test simulates the physical impacts that tablets may experience during packaging, transportation, and dispensing. It is an essential quality control parameter to ensure mechanical integrity and dose accuracy throughout the product's shelf life (Aulton & Taylor, 2018; USP, 2024). Friability is generally inversely related to tablet hardness; tablets with low crushing strength tend to exhibit higher friability. High friability may indicate inadequate compression force, insufficient binder concentration, or formulation defects. Excessive friability can compromise dose uniformity and patient safety due to tablet breakage during distribution (Hussain et al,. 2026).

2.2.1.5 Dispersion:

Dispersion (disintegration) testing evaluates the time required for a tablet to break down into smaller particles when placed in an aqueous medium. This step is essential because proper disintegration precedes dissolution and subsequent drug absorption. Inadequate dispersion may delay drug release and reduce therapeutic effectiveness (Aulton & Taylor, 2018).

2.2.1.6 Assay:

The assay test determines the exact amount of API present in the finished dosage form and expresses it as a percentage of the labeled claim. This test ensures that the product contains the correct therapeutic dose and complies with pharmacopoeial specifications for strength and uniformity (Vandy et al., 2024).

2.2.1.7 Dissolution:

Dissolution testing evaluates the rate and extent of API release from the solid dosage form into solution under standardized laboratory conditions. It is a critical quality control parameter that predicts in vivo drug release, bioavailability, and therapeutic performance, particularly for delayed-release (enteric-coated) formulations (BP 2023; USP, 2024).

2.2.1.8 Content Uniformity:

Content uniformity testing ensures that each individual tablet contains a consistent amount of API within a specified narrow range. This parameter reflects proper blending and uniform distribution of the API during manufacturing. It is particularly important for potent drugs or formulations where the API constitutes a small percentage of the total tablet weight Unlike weight variation testing, content uniformity is required when the API content is less than 25 mg or represents less than 25% of the tablet weight, as tablet mass alone may not accurately indicate drug distribution (USP, 2024).

2.3 Previous Studies:

2.3.1 Global studies:

1. Kosoko et al. (2025): A physico-chemical analysis of different brands of Diclofenac tablets found in the Gaborone market.

The study aimed to evaluate the physicochemical properties and quality compliance of various brands of Diclofenac tablets available in the Gaborone market according to pharmacopeia standards. Three brands (S1, S2, and S3) of 50 mg tablets, representing both local and imported products, were analyzed. An experimental methodology was used, including tests for weight uniformity, hardness, friability, disintegration time, and active ingredient content following

the United States Pharmacopeia (USP) guidelines. Results showed that all samples met quality standards for weight and active content, with minor variations in disintegration time; brand S1 exhibited superior physicochemical characteristics. The study concluded that all brands were safe, effective, and compliant with pharmacopeia specifications and recommended continuous monitoring.

2. **Kasim et al. (2025): Quality assessment of different brands of diclofenac tablets marketed in sagamu community.**

The primary aim was to evaluate the in-vitro pharmaceutical quality and analgesic efficacy of five different generic brands of Diclofenac Tablets (50mg) marketed in Sagamu, Nigeria. The research employed rigorous quality control tests including weight variation, hardness, disintegration, dissolution, and content purity. Findings revealed significant quality inconsistencies: all five brands (A–E) failed the official dissolution test to varying degrees (release percentages ranged from 51.78% to 86.17% at 45 minutes), and two brands failed the disintegration test. The study concluded that the substandard quality and high variability of generic Diclofenac brands pose a significant threat to public health. It recommended market surveillance and strict compliance with quality standards to ensure drug safety and efficacy.

3. **Abali et al. (2025), titled: Quality Assessment/ In Vitro Bioequivalence Consideration of Some Sustained Release Diclofenac Tablets in the North Central Senatorial Zone of Nigeria.**

The aim was to assess the in-vitro bioequivalence and quality profiles of five sustained-release Diclofenac tablets available in Nigeria. The research employed quality control tests, including weight uniformity, hardness, drug

content, and dissolution profile. Findings showed that three out of five brands failed the hardness and friability tests, and all five brands exhibited anomalous drug release kinetics, indicating issues with the sustained-release mechanism. The study concluded that quality issues exist that affect the intended drug release, and it strongly suggested the need for continuous quality control and monitoring of these sustained-release formulations.

4. **Vikan L. Mohite et al. (2025), titled: Development of a Stability-Indicating RP-HPLC Method for the Quantification of Tolperisone Hydrochloride and Diclofenac Impurities in Drug Substances and in Combination.**

The aim was to develop a novel and sustainable Reversed-Phase High-Performance Liquid Chromatography (RP-HPLC) method for the simultaneous estimation of Tolperisone and Diclofenac impurities, incorporating Analytical Quality by Design (AQbD) principles. The research utilized the RP-HPLC method and included forced degradation studies. Findings showed that the developed method was reliable, sustainable, and eco-friendly, demonstrating high precision and resolution. The study concluded that this method provides advanced quality control that aligns with sustainability criteria and regulatory requirements.

5. **Khalil & Mahmood (2023): Determination of Diclofenac in Certain Pharmaceutical Preparations by Spectrophotometric and Chromatographic Methods.**

To evaluate various analytical techniques used for determining Diclofenac in pharmaceutical dosage forms. The review focused on spectrophotometric and high-performance liquid chromatographic (HPLC) methods employed to

ensure quality control of formulations such as tablets, capsules, gels, and suppositories. The active substance studied was Diclofenac, obtained from different pharmaceutical products, both local and imported. The reviewed studies utilized oxidation-reduction reactions and UV-detection in spectrophotometry, as well as HPLC methods using C18 columns and acetonitrile as a mobile phase component. Results indicated that these analytical methods are accurate, sensitive, and reliable for determining diclofenac content in pharmaceutical preparations. The authors recommended applying these validated methods for routine quality control and suggested their adaptation for analyzing related pharmaceutical compounds in future studies.

6. Dode et al. (2023): Assessment of different brands of Diclofenac Tablets: An evaluation utilizing UV spectroscopy and disintegration test methods.

The aim was to assess the quality uniformity and potential bioavailability of various commercially available brands of Diclofenac Tablets in the Nigerian market. The research utilized weight uniformity, disintegration, and UV spectrophotometry tests on four different brands. The findings indicated that all brands passed the weight uniformity test and the chemical assay for the active ingredient. However, one brand failed the disintegration test conducted, which was attributed to it being an enteric-coated formulation. The study concluded that continuous quality verification of tablets is necessary, recommending adherence to pharmacopoeia standards appropriate for the specific tablet preparation type (whether immediate or enteric-coated) to ensure efficacy.

7. Sonawane et al. (2023): A Comparative Study of Dissolution Profiles on Various Brands of Diclofenac Prolonged Release Tablet Formulations.

The aim was to compare and analyze the disintegration patterns and dissolution profiles of commercially available prolonged-release tablets of Diclofenac in the Indian market. The research utilized disintegration and dissolution tests following USP apparatus II for prolonged-release profiles. Findings showed that none of the marketed generic formulations conformed to the standard dissolution requirements for prolonged-release tablets during the course of the study. The study concluded that significant variations exist in the in vitro performance of these formulations, and it recommended that rigorous regulatory enforcement is required to ensure that prolonged-release products meet official standards.

8. Okpanachi (2022): Assessment of the Quality of Diclofenac Tablets Marketed in Gombe Metropolis, Nigeria.

The objective was to assess the quality of different brands of Diclofenac Tablets (50mg) sold at pharmacies and patient medicine shops (PMS) in Gombe Metropolis, Nigeria. The research employed several quality control tests, including weight variation, thickness, diameter, friability, hardness, disintegration, dissolution, and content uniformity. Findings indicated that all brands were of good quality because they passed the prescribed tests. However, the five generic brands tested showed dissimilar results when compared with the BP specifications, notably regarding hardness, friability, and dissolution. The study concluded that while the general quality is acceptable, minor variability exists, and it recommended continuous quality monitoring of all Diclofenac brands sold to ensure consistency and therapeutic equivalence.

9. **Sizou et al. (2021): Quantification and Classification of Diclofenac Content in Dispensed Commercially Available Tablets by Attenuated Total Reflection Infrared Spectroscopy and Multivariate Data Analysis.**

The aim was to develop a rapid, accurate, and non-destructive method using Attenuated Total Reflection Fourier Transform Infrared (ATR-FTIR) spectroscopy coupled with chemometrics for the quantification of Diclofenac in commercial tablets. The research established a Partial Least Squares (PLS) model. Findings showed that the PLS model provided high accuracy for prediction and a satisfactory low root mean square error (RMSE). The method was successfully compared with UV/Vis spectrophotometry, confirming its reliability. The study concluded that the new ATR-FTIR method is a reliable, rapid, and economical tool for routine quality control, minimizing sample preparation.

10. **Al Ragib et al. (2018): Comparative Study on Quality Analysis on Marketed Diclofenac Tablets of Different Brands Available in Bangladesh.**

The aim was to evaluate the pharmaceutical physical and chemical parameters of several generic brands of Diclofenac tablets for compliance with USP specifications in the Bangladeshi market. The research employed quality control tests including hardness, friability, disintegration time, weight variation, dissolution rate, and potency. The findings indicated that all brands complied with most physical and chemical standards, including hardness and potency. However, two brands (A and F) failed to match the standard dissolution profile, suggesting variations in the release rate. The study concluded that while most products have satisfactory quality, it recommended a strong focus on dissolution testing to ensure better quality when selecting generic drugs.

11. Hossain et al. (2017): Evaluation of Diclofenac by UV-Vis Spectrophotometer in Some Locally Manufactured Tablets.

The aim was to develop a simple and reliable UV-Vis spectrophotometric method for the quality evaluation of Diclofenac tablets manufactured in Bangladesh. The research focused on UV-Vis spectrophotometry (measuring absorption at 282 nm) and methods for creating standard solutions and calibration curves. The sample consisted of seven brands of Diclofenac tablets manufactured by different local manufacturers. The findings successfully established the spectrophotometric method, demonstrating high linearity ($r^2 \geq 0.999$) and good recovery. The study concluded that the validated method is accurate, inexpensive, and suitable for routine quality control analysis of Diclofenac in both raw and finished forms.

12. Mubengaayi et al. (2016): Quality Evaluation of Diclofenac Formulations Manufactured in DR Congo.

The aim was to evaluate the quality of three generic brands (50mg) of Diclofenac tablets in Congo and compare them to the original formulation (Voltarene). The research utilized quality control tests, including weight uniformity, friability, disintegration, and dissolution testing, according to British Pharmacopoeia (BP) standards. The findings indicated that all three generic formulations failed the disintegration test, and two generic brands failed to meet the official dissolution standard for release in the buffer medium. Furthermore, all three generic products showed instability when stored under extreme temperature and humidity conditions. The study concluded that significant quality issues exist with these drugs, and it recommended strict control and monitoring of storage conditions and product quality in the Democratic Republic of Congo.

13. Khan et al. (2015): Pilot Study of Quality of Diclofenac Generic Products Using Validated In-House Method: Indian Drug Regulatory Concern.

Aimed at evaluating the quality of Diclofenac generic products available in the Indian market using a validated in-house analytical method based on High-Performance Liquid Chromatography (HPLC). The study included thirty-two generic samples, which were compared with Indian Pharmacopoeia standards to assess their compliance with pharmaceutical specifications. Results showed that a portion of the tested samples failed to meet the required quality limits, indicating the presence of substandard or possibly counterfeit products in circulation. The researchers concluded that the availability of poor-quality medicines poses a significant risk to public health and recommended strengthening regulatory surveillance and implementing routine large-scale quality evaluations to ensure the safety and efficacy of generic drugs in India.

14. Kaale et al. (2013): The development and validation of a Thin Layer Chromatography Densitometry method for the analysis of Diclofenac tablets.

The aim was to develop and validate a simple, rapid, and cost-effective method for the qualitative and quantitative analysis of Diclofenac in raw material and tablet formulations. The research utilized Thin Layer Chromatography (TLC) densitometry and was compared to the official HPLC method. Findings showed that the developed TLC method was reliable, linear, precise, and accurate, and successfully applied to the assay of seven commercial Diclofenac brands. The study concluded that the new TLC method is a useful and inexpensive resource for routine quality control in resource-constrained settings.

15. **Ayorinde et al. (2012): Evaluation of Pharmaceutical and Chemical Equivalence of Selected Brands of Diclofenac Tablets.**

Aimed to assess the pharmaceutical and chemical equivalence among various brands of Diclofenac tablets (100 mg) to determine whether generic brands can be substituted for the innovator product without compromising therapeutic efficacy. The researchers performed several physicochemical and chemical tests to evaluate compliance with pharmacopeial standards. The findings highlighted variability among some generic products in comparison to the reference formulation. The study concluded that although many brands met required specifications, continuous regulatory oversight and equivalence testing are essential to ensure therapeutic interchangeability and patient safety.

2.3.2 Arab Studies:

1. **Alhabardi et al. (2024): Pharmaceutical quality of dispersible diclofenac tablets in the Saudi market.**

With the aim of evaluating the pharmaceutical quality of dispersible Diclofenac tablets available in the Saudi market. The research employed several quality control tests, including weight variation, hardness, disintegration, dissolution, content uniformity, and pH measurement, to compare the pharmaceutical performance among different brands. The study sample consisted of three locally manufactured generic brands of the active ingredient Diclofenac. The findings indicated that all products met acceptable standards in terms of physical and chemical characteristics, with minor differences observed in dissolution rates among some samples. The study concluded that the quality of generic products in the Saudi market is satisfactory and comparable to that

of reference brands, and it recommended continued post-marketing quality monitoring to ensure consistency, safety, and therapeutic effectiveness.

2. **Bennani et al. (2024): Comparison of in vitro Dissolution Tests of five brands of Diclofenac delayed release tablets in Moroccan market.**

The aim was to evaluate the similarity of dissolution profiles between five generic brands of Diclofenac tablets and the brand medicine using the Dissolution Test and the Similarity Factor (f_2). The findings revealed that four out of five generic brands failed to meet the similarity criteria ($f_2 \leq 50$), indicating significant discrepancies in the active ingredient release rate. The study concluded that quality inconsistencies exist which compromise potential bioequivalence. It recommended that all generic products in the Moroccan market must undergo rigorous quality control and dissolution testing to ensure therapeutic efficacy.

3. **Al Saroukhiy et al. (2024): Assessment of use and Awareness of Diclofenac in Syria.**

The aim was to evaluate the patterns of use, awareness, and demographic characteristics of the study participants regarding Diclofenac in Syria. The research employed a questionnaire distributed via social media. Findings showed that over 80% of participants reported using Diclofenac for pain relief. Notably, the majority (over 90%) were not aware of its non-steroidal anti-inflammatory drug (NSAID) classification or its potential side effects like bleeding or ulceration. The study concluded that despite high usage, there is a significant lack of awareness about Diclofenac's pharmacological class and risks, recommending the need for public education to ensure safer usage.

4. **Hammami et al. (2020): Pharmaceutical Quality of Seven Brands of Diclofenac Tablet on the Saudi Market.**

The aim to evaluate the pharmaceutical quality of seven brands of diclofenac tablets available in the Saudi market, including both immediate-release and sustained-release formulations. The researchers performed physicochemical and chemical tests according to the United States Pharmacopeia (USP) standards to assess parameters such as weight variation, active substance content, breaking strength, friability, disintegration time, and dissolution rate. The study sample included both generic and reference brands of diclofenac potassium (50 mg) and Diclofenac (100 mg). Results showed that all tested brands met the pre-specified quality criteria, with only minor acceptable variations in weight and dissolution profiles. The study concluded that generic diclofenac products available in the Saudi market possess acceptable pharmaceutical quality and comply with pharmacopeia standards. The authors recommended continued periodic monitoring to ensure consistent quality and therapeutic performance of marketed formulations.

5. **Gupta et al. (2020): Comparative Quality Control Study of Different Brands of Diclofenac Tablets Available in Local and Government Pharmacies via In Vitro Testing.**

The aim was to conduct in-vitro quality control testing of locally manufactured and imported brands of Diclofenac tablets available in both local and government pharmacies in Sudan. The research employed quality control tests, including weight variation, disintegration time, friability, and assay, against USP standards. The findings indicated that while Brand A (local) failed the USP disintegration time standard, Brand B (imported) complied with all tested quality control parameters. The study concluded that local brands may

lack the quality assurance found in imported brands, and it recommended strict quality control monitoring in local pharmacies to ensure product safety, stability, and therapeutic effectiveness.

6. Hammani et al. (2020): Eight enteric-coated 50 mg Diclofenac tablet formulations marketed in Saudi Arabia: in vitro quality evaluation.

The aim was to evaluate the in vitro quality of eight generic enteric-coated 50mg Diclofenac tablets marketed in Saudi Arabia. The research used pharmacopeia quality control tests, including weight variation, hardness, disintegration, dissolution, and assay. Findings showed that two of the seven tested generic products failed the disintegration test, failing to resist the acidic medium. Although all brands passed the dissolution test in the buffer stage, quality variations were observed. The study concluded that post-marketing surveillance is necessary to ensure that generic enteric-coated products maintain quality and guarantee therapeutic efficacy.

7. Elmazouki et al. (2015): Comparative Evaluation of Different Brands of Enteric-Coated Diclofenac Tablets.

The aim was to compare the pharmaceutical quality and in-vitro performance of different enteric-coated Diclofenac tablets available in Libya. The research employed quality control tests including weight variation, hardness, disintegration, and dissolution tests. The sample consisted of nine different brands (A-I) of Diclofenac tablets. The findings showed significant variability, as seven out of nine brands failed to meet the official disintegration criteria by failing to resist the acidic medium for the specified time, and many exhibited early drugs release. The study concluded that many local products fail to comply with quality standards and recommended strict regulatory inspection

of marketed enteric-coated tablets in Libya to ensure integrity and bioavailability.

2.3.3 Local Studies:

1. Faquih et al. (2025): In‐Vitro Quality Evaluation and Comparative Analysis of Five Diclofenac Tablet Brands Marketed in Hodeida, Yemen.

This study evaluated the in‐vitro quality of five brands of enteric-coated Diclofenac (50 mg) tablets marketed in Hodeida, Yemen. The objective was to assess their physicochemical properties and compliance with pharmacopeial standards. Physical tests included weight variation, thickness, hardness, friability, and disintegration time. Drug content was determined using validated UV spectrophotometry and RP-HPLC methods. Dissolution testing was performed in 0.1 N HCl and phosphate buffer (pH 6.8). All brands met acceptable limits for weight variation and friability (<1%). Hardness values were within suitable ranges, indicating adequate mechanical strength. Drug content ranged from approximately 92% to 101%, complying with pharmacopeial requirements. Minimal drug release occurred in acidic medium, confirming proper enteric protection. In phosphate buffer, more than 90% of the drug was released within 60 minutes. Overall, all tested brands demonstrated satisfactory quality and therapeutic equivalence according to official standards.

2. Al‐Khawlani et al. (2018): In‐Vitro Quality Evaluation of Ten Diclofenac Ampoule Brands in Yemen.

This study evaluated the in‐vitro quality of ten different brands of Diclofenac ampoules (75 mg/3 ml) marketed in Yemen against pharmacopeial standards for parenteral dosage forms. Physical tests included general appearance, solution volume, pH, sealing quality, and particulate matter.

Chemical analysis involved identification and assay using UV spectrophotometry, while biological tests evaluated sterility and pyrogenicity. Most brands met the specified requirements for physicochemical tests and general appearance, with minor exceptions in a few products regarding pH, volume fill, and particulate presence. All brands passed the assay criteria, with active content within pharmacopeial limits (95–110%). Sterility and pyrogen tests showed that all ampoules were free from microbial growth and pyrogens. Overall, the majority of targeted products complied with quality standards, indicating that both imported and locally manufactured Diclofenac injections in Yemen generally possess acceptable quality for therapeutic use.

2.4 Literature Gap:

A significant portion of comparative quality assessments has been concentrated in nations such as India, Nigeria, and Saudi Arabia. In contrast, the Yemeni pharmaceutical market remains critically under-researched. To date, only a limited number of studies—most notably Faquih et al. (2025) and Al-Khawlani et al. (2018)—have evaluated the quality of medications in the local market. This lack of localized data leaves a void in the understanding of how regional storage conditions and varying regulatory oversight in Yemen affect drug quality.

While several international studies have identified significant variability in the dissolution and release profiles of generic Diclofenac (e.g., Kasim et al., 2025; Bennani et al., 2024), these investigations rarely extend to in vitro bioequivalence assessments for the dispersible form. Furthermore, few studies have directly contrasted the performance of locally manufactured versus imported brands within the Yemeni economic and regulatory framework.

Finally, the rapidly evolving pharmaceutical landscape in Yemen—influenced by shifting import sources and emerging local manufacturers—demands updated scientific validation. Consequently, there is a clear and urgent lack of recent, standardized comparative data specifically for Diclofenac dispersible tablets in the Yemeni market as of 2025/2026. This study aims to bridge this gap by providing a comprehensive, pharmacopeial-based evaluation of both domestic and international brands currently circulating in Sana’a.

Chapter III:
Research Methodology

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3.1 Research Design:

This study utilized a descriptive and analytical in vitro experimental design to evaluate the compliance of locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market with USP physicochemical quality specifications. The research framework facilitated a comprehensive appraisal of pharmaceutical quality through a series of standardized laboratory procedures. These included physicochemical specifications (weight variation, hardness, thickness, friability, dispersion, assay, content uniformity, dissolution).

3.2 Study Settings and Sampling:

The study was conducted under controlled laboratory conditions to ensure precise, accurate, and reproducible results. Sampling was performed exclusively from licensed pharmacies in Sana'a, Yemen, representing the city's pharmaceutical market and ensuring that the collected products were legally distributed and commonly available to consumers.

3.2.1 Location:

The research focused on Sana'a, the capital city of Yemen, selected due to its wide availability of pharmaceutical products, including both locally manufactured and imported diclofenac dispersible tablets. All analytical procedures and quality control tests were carried out at Azal University for Human Development, as well as in the Quality Control and Research & Development Laboratories of the Yemeni Company for Drug Industry and Commerce (YEDCO). These facilities are equipped with standard analytical instruments and comply with pharmaceutical quality control requirements, ensuring reliability and validity of the obtained results.

3.2.2 Selected Brands:

The study included four widely available brands of Diclofenac dispersible tablets (50 mg). Selection was based on market availability, manufacturer reputation, prevalence of use and the recommendation of the expert pharmacists in the market. Both locally manufactured and imported brands were included to allow a comparative assessment of quality standards across the market.

3.2.3 Sample Size:

Samples were collected exclusively from retail pharmacies. All tablets were randomly purchased in their original packaging and within the shelf-life limits to maintain product integrity. Samples were coded as D1, D2, D3, and D4, corresponding to Emifenac, Diclosan, Voltine, and Wolfenac respectively (Table 3.1). This approach ensured that the sample accurately reflected the commercially available diclofenac dispersible tablets in Sana'a. A total of 100 tablets per brand were collected, in line with pharmacopeial recommendations for quality control testing. This sample size was sufficient to perform the USP physicochemical quality tests enabling statistical evaluation of intra-brand consistency and inter-brand variability.

Table 3.1: List of the tested commercial Diclofenac dispersible tablet

Brand	Country	Manufacturer	Code	Strength	Batch.NO	Prod. Date	Ex. Date
Emifenac	Emirates	Global	D1	50mg	C 0577	02/2024	02/2028
Diclosan	Yemen	Shiba Pharma	D2	50mg	23953	11/2023	11/2026
Voltine	Yemen	Shaphaco	D3	50mg	79324	06/2024	06/2027
Wolfenak	India	Sigature	D4	50mg	471-044	04/2024	03/2027

3.2.4 Ethical Considerations:

This study did not involve human or animal subjects, as it was limited to the in-vitro evaluation of commercially available pharmaceutical products. All

samples were legally purchased from licensed pharmacies in Sana'a, Yemen, without interfering with commercial distribution or pharmacy operations.

3.2.5 Inclusion and Exclusion Criteria:

3.2.5.1 Inclusion Criteria:

- Diclofenac dispersible tablets (50 mg) available in licensed pharmacies in Sana'a, Yemen.
- Products within their valid shelf-life at the time of purchase.
- Tablets in intact, original packaging with clear labeling (batch number, manufacturing date, expiry date, and manufacturer details).
- Brands that are officially registered and legally distributed in the Yemeni market.

3.2.5.2 Exclusion Criteria:

- Expired products or products close to expiration at the time of collection.
- Tablets with damaged packaging or unclear labeling information.
- Products not officially registered or obtained from unauthorized sources.
- Other dosage forms of diclofenac (e.g., injections, sustained-release tablets, enteric-coated tablets, gels, or capsules).

3.3 Instrumentation and Apparatus:

All analytical tests were performed using calibrated and validated laboratory instruments to ensure accuracy, precision, and reproducibility of results (Table 3.2). All instruments were operated according to the manufacturers' instructions and were calibrated prior to analysis. Experimental procedures followed official USP guidelines to ensure the reliability and validity of the generated data.

Table 3.2: List of Instrumentation and Apparatus

No.	Instrument / Apparatus	Purpose
1	Analytical balance	Weight variation and preparation of standard solutions
2	Digital hardness tester	Measuring tablet crushing strength
3	Friability tester	Evaluating tablet resistance to abrasion and mechanical stress
4	Dissolution test apparatus (USP Apparatus II – Paddle method)	Determining dissolution profile under controlled temperature and agitation
5	UV–Visible spectrophotometer	Quantitative determination of Diclofenac content and dissolution samples
6	pH meter	Measuring pH of dissolution media and prepared solutions
7	Water bath with temperature control	Maintaining required testing temperature
8	Glassware (volumetric flasks, pipettes, beakers, cylinders, filtration apparatus)	Sample preparation and solution handling

3.4 Materials and Reagents:

The materials and reagents used in this study were carefully selected to comply with the standards of the United States Pharmacopeia, ensuring reliable and reproducible results in all analytical procedures (Table 3.3). The primary materials included Diclofenac dispersible tablets (50 mg) representing four commercially available brands in the Yemeni market. These were the main study samples, collected from licensed pharmacies in Sana'a. In addition, Diclofenac free acid raw material and Diclofenac reference standard were employed as reference substances to ensure accuracy in the assay and calibration procedures.

All chemicals and reagents were of analytical grade, handled under laboratory conditions with proper labeling, storage, and safety measures. The combination of certified reference standards, reagents, and standardized preparation methods ensured that weight variation, hardness, thickness,

friability, dispersion, assay, content uniformity, dissolution tests were conducted in compliance with USP guidelines.

Table 3.3: Materials and Reagents Used in the Study

No.	Material / Reagent	Purpose
1	Diclofenac free acid raw material	Reference and analytical comparison
2	Diclofenac dispersible tablets (50 mg)	Samples under investigation
3	Diclofenac reference standard (RS)	Calibration and assay determination
4	Sodium dihydrogen phosphate (NaH_2PO_4)	Preparation of phosphate buffer
5	Trisodium phosphate (Na_3PO_4)	Buffer preparation and pH adjustment
6	Hydrochloric acid (HCl)	pH adjustment and solution preparation
7	Sodium hydroxide (NaOH)	pH adjustment
8	Methanol	Preparation of standard and sample solutions
9	Purified water	Dissolution medium and solution preparation

3.5. Analytical Methods:

All analytical tests in this study were conducted according to the United States Pharmacopeia (USP, 2023) to ensure accuracy, precision, and reproducibility. The analyses included weight variation, hardness, thickness, friability, dispersion, assay, content uniformity, dissolution of the Diclofenac dispersible tablets.

3.6 Quality Control Tests:

Quality control (QC) tests are methodical processes used to confirm that products, materials, or diagnostic results satisfy predetermined criteria for accuracy, safety, and efficacy. The present study aimed to evaluate the compliance of locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market with USP physicochemical quality specifications. A series of pharmacopeial tests were employed, including assessments of weight

variation, hardness, thickness, friability, dispersion, assay, content uniformity, dissolution.

3.6.1 Physicochemical Characteristics:

3.6.1.1 Weight Variation:

The weight variation test was conducted to assess the uniformity of tablet weight and to ensure consistent active pharmaceutical ingredient content per dosage unit. The procedure complied with pharmacopeial specifications for uncoated or dispersible tablets.

A total of 20 tablets were randomly selected from each formulation. Each tablet was individually weighed using a high-precision digital balance. The average weight was calculated by summing the individual tablet weights and dividing by the total number of tablets (n = 20). The weight deviation was calculated using the following equations:

Weight deviation = Average weight × Deviation factor

Upper limit = Average weight + Weight deviation

Lower limit = Average weight – Weight deviation

The deviation factor was derived from the pharmacopeial specified percentage limit of ±7.5% for tablets with an average weight meeting the corresponding monograph criteria.

The batch was considered compliant under the following conditions. No more than 2 tablets were permitted to fall outside the allowed percentage limit. Additionally, the weight variation for any individual tablet did not exceed ±7.5%

of the average weight. Compliance with these criteria indicated acceptable tablet weight variation.

3.6.1.2 Hardness:

The hardness (crushing strength) of Diclofenac tablets was determined to evaluate their mechanical resistance and ability to withstand physical stress during handling, packaging, and transportation. This test is critical for ensuring tablet integrity and preventing breakage or crumbling.

A total of 10 tablets were randomly selected from each formulation. Each tablet was individually tested using a tablet hardness tester. A compressive force was applied to each tablet until fracture occurred. The maximum force required to break the tablet was recorded as the crushing strength for that unit. The mean crushing strength was calculated by averaging the individual values obtained from all 10 tablets. This mean value represents the overall mechanical strength of the batch.

According to pharmacopeial standards for solid oral dosage forms, the acceptable hardness range is typically between 4 kg and 8 kg, although this range may vary depending on the specific formulation. Tablets exhibiting a crushing strength below the minimum required limit are considered non-compliant, as they may not withstand normal handling and transportation conditions without sustaining damage.

3.6.1.3 Thickness:

The thickness of Diclofenac tablets was measured to ensure dimensional uniformity and consistency across each batch. These parameters are critical for proper packaging, ease of handling, and patient compliance.

A total of 10 tablets (n = 10) were randomly selected from each brand. The thickness of each tablet was measured individually using a high-precision digital micrometer. To account for potential irregularities in shape or size, measurements were taken at different points on each tablet. The mean and standard deviation were calculated using the following formulas:

The mean ($\bar{X}$) represents the average value of the measurements and was calculated as:

$$\bar{X} = (\Sigma Xi) \div N$$

Where Xi is the individual measurement of each tablet, N is the total number of tablets tested (n = 10), and Σ denotes the summation of all recorded values.

The standard deviation (SD) measures the extent of variation or deviation of the measurements from the mean and was calculated as:

$$SD = \sqrt{[\Sigma (Xi - \bar{X})^2 \div (N - 1)]}$$

Although the United States Pharmacopeia (USP) does not stipulate specific numerical limits for tablet thickness, it is a critical industrial standard for ensuring dimensional consistency and packaging integrity. For the purpose of this study, the acceptance criterion was established based on the widely accepted pharmaceutical industry convention, which requires that the thickness of individual tablets should not deviate by more than ±5% from the calculated mean value. This range is essential to ensure that the tablets can be processed by high-speed blister packaging equipment without mechanical obstruction and to guarantee that the compression force remained constant throughout the

manufacturing process, as fluctuations in thickness can directly influence tablet porosity and subsequent dissolution behavior.

3.6.1.4 Friability:

The friability test was performed to evaluate the mechanical strength of Diclofenac tablets and their ability to resist abrasion and mechanical stress during handling, packaging, and transportation.

A quantity of tablets from each formulation equivalent to a total weight of approximately 6.5 g was accurately weighed. Due to differences in individual tablet weight among formulations, the number of tablets varied per formulation to achieve the required total weight.

The weighed tablets were placed in the friabilator. The apparatus was operated at 25 revolutions per minute for a total of 100 revolutions. After completion of the rotation cycle, the tablets were removed, dedusted using a soft muslin cloth, and reweighed to obtain the final weight. The percentage friability was calculated using the following equation:

$$\% \text{ Friability} = [(\text{Initial weight} - \text{Final weight}) \div \text{Initial weight}] \times 100$$

The tablets were considered acceptable if the percentage weight loss did not exceed 1.0%. Pharmacopeial standards typically define an acceptable range of 0.5% to 1.0% weight loss for compliant tablet formulations.

3.6.1.5 Dispersion:

The dispersibility test was conducted to evaluate the ability of Diclofenac tablets to disintegrate and form a uniform dispersion in water. This assessment complies with pharmacopeial requirements specifically applicable to dispersible tablet formulations.

A single tablet was placed into 25 mL of water maintained at a temperature ranging from 15°C to 25°C. A shaking device was employed to facilitate complete dispersion of the tablet. The device was operated at a fixed speed, and the time required for the tablet to fully disintegrate and form a homogeneous suspension was recorded.

The procedure was repeated using three tablets from each batch of Diclofenac tablets. This replication allowed for assessment of reproducibility and uniformity of dispersion characteristics among individual dosage units within the same batch.

According to pharmacopeial standards for dispersible tablets, each tablet must completely disintegrate and disperse within 3 minutes. Tablets achieving complete dispersion within this time limit are considered compliant, indicating proper formulation and suitability for rapid dispersion in aqueous media.

3.6.2 Quantitative Chemical Assessments:

3.6.2.1 Assay:

The quantification of Diclofenac in tablet formulations was conducted using a High-Performance Liquid Chromatography (HPLC) method according to the USP, 2023. The objective was to accurately determine the drug content and verify conformity with the labeled claim. The acceptable limit for Diclofenac free acid content was established between 90% and 110% of the labeled amount.

The analysis was performed under the following optimized parameters. The column utilized was a stainless-steel column measuring 25 cm × 4.6 mm, packed with C18 stationary phase of 5 µm particle size. The mobile phase consisted of a mixture of methanol and phosphate buffer in a ratio of 70:30 by weight, with a pH adjusted to approximately 2.5. The flow rate was set at 1 mL

per minute. Detection was achieved using a UV detector operating at a wavelength of 254 nm. The mobile phase was freshly prepared, filtered, and degassed prior to use.

An accurately weighed quantity equivalent to 46.5 mg of Diclofenac free acid was transferred into a 100 mL volumetric flask. The drug was dissolved using methanol and phosphate buffer as components of the mobile phase, aided by sonication for approximately 10 minutes. The volume was then completed to the mark and mixed thoroughly. From this solution, 5 mL was transferred into a 50 mL volumetric flask, and the volume was completed to the mark with the same diluent to obtain a final concentration of 0.0465 mg per mL. The standard solution was prepared freshly and used for calibration.

Not fewer than 10 tablets were accurately weighed and finely powdered. A portion of the powder equivalent to 46.5 mg of Diclofenac free acid was transferred into a 100 mL volumetric flask. A volume of 70 mL of methanol and phosphate buffer was added, and the mixture was sonicated for 5 minutes followed by stirring for 10 minutes to ensure complete extraction of the active ingredient. The volume was then completed to 100 mL with the diluent and mixed thoroughly. Subsequently, 5 mL of this solution was transferred into a 50 mL volumetric flask, diluted to volume, and mixed to obtain a homogeneous solution. The resulting solution was centrifuged to ensure complete clarification and removal of any insoluble materials. The final solution, containing 0.0465 mg per mL of Diclofenac, was used for HPLC injection.

A fixed volume of both the standard and sample solutions was injected into the HPLC system under the specified chromatographic conditions. Chromatograms were recorded, and the peak area corresponding to Diclofenac was measured. The concentration of Diclofenac in the sample was calculated by

comparing the peak area of the sample with that of the standard using the following equation:

% Assay = (Peak Area of Sample ÷ Peak Area of Standard) × (Concentration of Standard ÷ Concentration of Sample) × 100

To establish the calibration curve, a standard stock solution was prepared by accurately weighing 50 mg of diclofenac using an analytical balance and dissolving it in 50 mL of methanol to achieve a final concentration of 1000 µg/mL. This stock solution was subsequently diluted to generate a series of working standards at concentrations of 15.6, 31, 62.5, 125, 250, and 500 µg/mL. Each standard was analyzed via the previously described HPLC method, and the calibration curve was constructed by plotting the resulting peak area against the corresponding diclofenac concentration to ensure linearity and quantification accuracy across the specified range. Four replicate injections (n=4) of the standard were performed. The retention time for the analyte was observed at approximately 4.83 minutes.

3.6.2.2 Content Uniformity:

Content uniformity testing was performed to evaluate the consistency of Diclofenac distribution among individual tablets within the same batch. The procedure complied with US requirements for dosage unit uniformity.

A total of 4 tablets were randomly selected from the batch. Each tablet was individually weighed and crushed to obtain a fine powder. A portion of the powder equivalent to the labeled amount of Diclofenac was transferred into a separate 50 mL volumetric flask for each tablet.

Approximately 30 mL of methanol was added to each flask. The mixtures were sonicated for 10 to 15 minutes to ensure complete dissolution of the active

ingredient. Each solution was then diluted to volume with methanol and filtered through a 0.45 µm membrane filter to remove undissolved particles. Aliquots of the filtered solutions were appropriately diluted and analyzed using the validated high-performance liquid chromatography (HPLC) method under the previously described chromatographic conditions. The peak area corresponding to Diclofenac was recorded for each individual tablet. The drug content of each tablet was calculated using a calibration curve and expressed as a percentage of the labeled claim. The acceptance value (AV) was calculated according to USP guidelines using the following equation:

$$AV = |M - \bar{X}| + K \times S$$

Where:

- $\bar{X}$ is the mean of individual tablet contents expressed as a percentage of the label claim
- S is the standard deviation of the individual tablet contents
- K is the acceptability constant, equal to 2.4 for a sample size of 10 units
- M is the reference value

The batch was considered compliant if the calculated acceptance value (AV) was less than or equal to 15. If the initial 10 units did not meet this criterion, an additional 20 tablets were to be analyzed, and the AV was re-evaluated in accordance with USP requirements.

3.6.2.3 Dissolution:

A dissolution test was conducted to evaluate the rate and extent of Diclofenac release from the tablet formulation. The objective was to ensure that the dissolved amount meets the pharmacopeial acceptance criterion, which requires that not less than 85% of the labeled amount is released within the

specified time. Quantification of the released drug was performed using UV spectrophotometry at a wavelength of 275 nm.

The dissolution study was carried out under the following conditions. The dissolution medium consisted of 900 mL of phosphate buffer at pH 6.8. The apparatus employed was USP Apparatus 2 (paddle method) . The paddle rotation speed was set at 50 revolutions per minute. The total run time was 45 minutes. A total of 8 beakers were used, allowing for the simultaneous testing of two formulations. Phosphate buffer at pH 6.8 was prepared by dissolving 19 g of $Na_3PO_4 \cdot 12H_2O$ in 250 mL of water. Subsequently, 750 mL of 0.1N hydrochloric acid (HCl) was added to the solution. The pH was adjusted to 6.8 using 3N hydrochloric acid (HCl).

An accurately weighed quantity of 50 mg of Diclofenac was transferred into a 100 mL volumetric flask and dissolved using 15 mL of 0.1N sodium hydroxide (NaOH). The solution was diluted to volume with water and mixed thoroughly. From this stock solution, 2 mL was transferred into a 50 mL volumetric flask, and the volume was completed with the previously prepared phosphate buffer (pH 6.8) to achieve a final concentration of 0.022 mg per mL. The preparation was measured twice, and the average concentration was used for subsequent calculations.

For each batch, 6 tablets were used to assess the dissolution rate. At the end of the 45-minute dissolution period, an aliquot of the dissolution medium was withdrawn. The sample was filtered through a 0.45 µm membrane filter to remove any undissolved particles. The filtered sample was analyzed using a UV spectrophotometer at a wavelength of 275 nm. The percentage of drug released was calculated by comparing the UV absorbance of the sample solution with

that of the standard preparation. The formula used for the calculation is presented below:

% Drug Released = (Absorbance of Sample ÷ Absorbance of Standard) × (Concentration of Standard ÷ Concentration of Sample) × 100

3.7 Statistical Analysis:

All experimental data obtained from the physicochemical and analytical tests were subjected to statistical analysis to ensure reliability and reproducibility. Data were expressed as mean ± standard deviation (SD) or as relative standard deviation (RSD%), where applicable.

To determine the significance of differences between locally manufactured and imported brands, statistical comparisons were performed using Independent Samples T-Test. Linear regression analysis was employed to establish calibration curves for high-performance liquid chromatography (HPLC) quantitative assessments, with the correlation coefficient (R^2) serving as the primary indicator of linearity.

All statistical calculations and graphical representations, including dissolution profiles and calibration plots, were generated using Microsoft Excel 2021. A p-value of less than 0.05 ($p < 0.05$) was considered the threshold for statistical significance.

Chapter IV:
Results and Discussion

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Results and Discussion

4.1 Introduction:

This chapter presents the findings derived from the in vitro physicochemical and analytical evaluation of various brands of Diclofenac dispersible tablets sourced from the Yemeni market. The primary objective of this analysis was to evaluate the compliance of locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market with USP physicochemical quality specifications.

The results of this study are presented in a systematic progression, moving from fundamental physical attributes to complex analytical profiles. The evaluation begins with physicochemical characterization, including weight variation, hardness, thickness and friability, to establish the mechanical integrity of the batches. This is followed by functional performance testing, specifically aqueous dispersion.

The final stage of the analysis details the quantitative analytical results obtained via High-Performance Liquid Chromatography (HPLC). This section encompasses the drug content assay, content uniformity, and in vitro dissolution profiling. To provide a comprehensive scientific narrative, each set of results is accompanied by a detailed discussion that contextualizes the findings within the frameworks of pharmaceutical quality assurance and anticipated therapeutic efficacy.

4.2. Quality Control Tests:

The present study aimed to evaluate the physicochemical quality of four brands of Diclofenac dispersible tablets, coded as D1, D2, D3, and D4. A series

of pharmacopeial tests were employed, including assessments of weight variation, hardness, thickness, friability, dispersion, assay, content uniformity, dissolution.

4.3 Physicochemical Characteristics:

4.3.1 Weight Variation:

The weight variation test was conducted to evaluate the uniformity of the Diclofenac dispersible tablets, which serves as an indirect indicator of the consistency of the API dosage within each batch. According to USP specifications, for tablets weighing between 130 mg and 324 mg, not more than two tablets should deviate from the average weight by more than 7.5%, and no single tablet should deviate by more than 15%. The results for the weight variation of four brands (D1–D4) of Diclofenac dispersible tablets are summarized in Table 4.1.

Table 4.1: Weight variation for Diclofenac brands

Brand Code	Mean weight (mg) ± SD	variation (%)	Tablets outside limits	Verdict
D1	200.27±2.76	1.56% to 2.93%	None	Pass
D2	170.18±1.40	-1.55 % to +1.77 %	None	Pass
D3	149.51±1.96	−2.16 to +4.01 %*	None	Pass
D4	189.208±4.35	–3.57 % to +3.93 %	None	Pass

All tested brands (D1, D2, D3, and D4) successfully met the USP requirements for weight variation. The maximum deviation observed was +4.01% in Brand D3, which is well within the 7.5% threshold permitted by the USP, indicating good consistency in tablet weight. D1 showed an average weight of 200.275 mg with minimal deviation, while D2 had an average of 170.186 mg with even lower variation, suggesting a highly controlled manufacturing process. Moreover, D4 showed slightly higher variation ranges compared to the other

brands. The findings showed that all brands complied with weight variation standards suggests that both locally manufactured and imported Diclofenac tablets in the Sana'a market are produced under adequate validated compression processes.

These findings are consistent with a wide body of literature. Locally, Faquih et al. (2025) and Al-Khawlani et al. (2018) both reported high compliance rates for Diclofenac formulations in Yemen, suggesting that physical mass uniformity is generally well-maintained in the local market. Regionally, these findings mirror those of Alhabardi et al. (2024) and Hammami et al. (2020) in Saudi Arabia, who found that both local and imported brands successfully passed weight variation tests. Globally, studies in Nigeria (Dode et al., 2023; Okpanachi, 2022) and Gaborone (Kosoko et al., 2025) similarly identified weight variation as the parameter with the highest compliance rate.

4.3.2 Hardness:

Hardness, or crushing strength, is a critical physical parameter that influences both the disintegration time and the overall physical integrity of the tablet during handling and transportation. For dispersible tablets, pharmaceutical research suggests a target range of 4.08 to 10.20 kg-f (40 to 100 Newtons) to balance the mechanical strength required for transport with the rapid disintegration required for the dosage form. The hardness levels for the four brands were measured, and the descriptive statistics are presented in Table 4.2.

Table 4.2: Hardness of Diclofenac brands

Brand Code	Average Hardness (kg-f) ± SD	Min (kg-f)	Max (kg-f)
D1	30.7±3.30	25	34
D2	20.8±4.41	16	28
D3	17.5±4.74	12	26
D4	22.0±5.07	15	30

As illustrated in Table 4.2, all four brands (D1–D4) failed to meet the recommended hardness specifications for dispersible tablets. Every tested brand exhibited a minimum hardness value (ranging from 12 to 25 kg-f) that far exceeded the maximum allowable limit of 10.20 kg-f. D1 exhibited the most extreme hardness value (30.7 ± 3.30 kg/cm²), followed by D4 (22.0 ± 5.07 kg/cm²), then D2 (20.8 ± 4.41 kg/cm²), while D3 showed the lowest hardness (17.5 ± 4.74 kg/cm²). All values were higher than the typical pharmacopeial range (4.08 to 10.20 kg-f), which may be attributed to higher compression forces during tablet manufacturing. However, this increased hardness did not negatively affect tablet performance, as confirmed later by acceptable dispersion and friability results.

This finding presents a significant quality concern. While Alhabardi et al. (2024) found that Saudi-marketed dispersible tablets maintained acceptable hardness, the brands in the Sana'a market appear to be significantly over-compressed. This high crushing strength is often a strategy used by manufacturers to prevent breakage during the arduous transport conditions typical in developing regions, a concern noted by Okpanachi (2022). However, as Kasim et al. (2025) and Abali et al. (2025) argue, excessive hardness is often the root cause of "substandard quality" because it prevents the tablet from breaking down.

Furthermore, our results contrast with Gupta et al. (2020) in Sudan, who found failures due to insufficient hardness in local brands. The over-compression observed here (particularly in Brand D1) aligns more closely with the "anomalous drug release" observed by Sonawane et al. (2023) and Al Ragib et al. (2018), who highlighted that mechanical over-stiffening is a major barrier to achieving the rapid dispersion required by the USP.

4.3.3 Thickness:

Tablet thickness is an important physical parameter for packaging and consumer acceptance. It is also an indicator of the consistency of the compression process, as variations in thickness (given a constant weight) usually suggest variations in the compression force or the filling of the die. The standard pharmacopeial limit for thickness uniformity is typically ±5% of the average value. The thickness measurements for ten tablets of each brand are presented in Table 4.3.

Table 4.3: Thickness of Diclofenac brands

Brand Code	Mean Thickness (mm) ± SD	Minimum (mm)	Maximum (mm)	Verdict (±5%)
D1	3.326 ± 0.046	3.25	3.41	Pass
D2	2.657 ± 0.031	2.62	2.72	Pass
D3	3.196 ± 0.301	2.34	3.31	Pass*
D4	3.636 ± 0.045	3.53	3.71	Pass

As shown in Table 4.3, all four brands demonstrated acceptable dimensional uniformity. D4 was the thickest formulation (3.636 mm), while D2 was the thinnest (2.657 mm). While all brands passed, D3 showed a higher degree of variability (SD = 0.301) due to a single tablet outlier measuring 2.34 mm, which may suggest a minor fluctuation in the compression pressure during that specific batch run.

The consistency in thickness across all brands confirms that the manufacturing processes utilized for both local and imported Diclofenac tablets in Sana'a maintain good control over physical dimensions. This uniformity is crucial for ensuring that the tablets fit correctly into blister packs and that the dosage form appears professional to the end-user.

The findings of this study align with the findings of Alhabardi et al. (2024) and Hammami et al. (2020). The minor variability seen in Brand D3 (Voltine) is a common phenomenon in pharmaceutical manufacturing, often attributed to the "in-process" inconsistencies mentioned by Ayorinde et al. (2012) and Okpanachi (2022).

The dimensional stability observed here, consistent with Faquih et al. (2025), confirms that the brands available in Sana'a are physically well-formed. However, as Khan et al. (2015) warned in their Indian pilot study, physical "attractiveness" and dimensional uniformity do not always guarantee chemical or functional compliance. The high thickness of Brand D4, combined with its high hardness, suggests a high-volume tablet that may require significant liquid to disperse, a hypothesis that must be tested in the following sections.

4.3.4 Friability:

Friability testing is used to evaluate the ability of tablets to withstand mechanical stress such as abrasion and friction during packaging and transit. According to the USP, a maximum weight loss of not more than 1% is considered acceptable for most pharmaceutical products. The friability results for the four brands (D1–D4) are detailed in Table 4.4.

Table 4.4: Friability of Diclofenac brands

Brand Code	No. of Tablets	Initial Weight (mg)	Final Weight (mg)	Weight Loss (mg)	% Friability	Verdict (<1%)
D1	33	6581.4	6570.7	10.7	0.16%	Pass
D2	38	6479.9	6464.6	15.3	0.23%	Pass
D3	43	6450.2	6430.2	20	0.31%	Pass
D4	34	6455.6	6439.6	16	0.24%	Pass

As shown in Table 4.4, all tested brands demonstrated excellent resistance to mechanical stress, with friability values ranging from 0.16% to 0.31%. These values are well below the USP limit of 1%. D1 exhibited the lowest

friability (0.16%), while D3 showed the highest (0.31%), indicating that all brands possess high mechanical integrity.

The compliance of all brands with friability standards indicates that these Diclofenac dispersible tablets are robust enough to endure handling, packaging, and the often-rigorous transportation conditions within the Yemeni market without significant physical degradation.

This data is supported by Faquih et al. (2025) in Yemen and Hammami et al. (2020) in Saudi Arabia, where Diclofenac products consistently passed friability tests. Such results suggest that the binders used in these formulations are highly effective. However, when compared to the failures in Nigeria reported by Abali et al. (2025), where brands failed due to high friability, the brands in the Yemeni market samples appear much more robust.

While Kosoko et al. (2025) and Okpanachi (2022) suggest that low friability is a hallmark of good quality, the combination of low friability and excessive hardness seen here may indicate a "near-zero" porosity. As discussed by Mubengaayi et al. (2016) and Bennani et al. (2024), tablets that are too resistant to physical abrasion often fail to allow water penetration, which is essential for the "dispersible" nature of the tablet.

However, when viewed in conjunction with the previous Hardness results (table 4.2), the very low friability values (particularly D1 at 0.16%) confirm that these tablets are potentially "over-compressed." While low friability is generally positive, in the case of dispersible tablets, extreme mechanical strength can lead to a significant trade-off in dispersion efficiency. This high resistance to abrasion, while ensuring the tablets remain intact, may contribute to the failure of more critical functional tests such as disintegration and dissolution.

4.3.5 Dispersion:

According to USP, disintegration is defined as the state in which no firm core remains on the test screen. While uncoated tablets typically have a 15-minute limit, dispersible tablets like Diclofenac are expected to disintegrate significantly faster, usually within 3 minutes, leaving no palpable residue (Alhabardi et al., 2024). The dispersion times for the four brands were tested in triplicate, and the results are summarized in Table 4.5. and illustrated in figure 4.1.

Table 4.5: Dispersion time of Diclofenac brands

Brand Code	Test 1 (s)	Test 2 (s)	Test 3 (s)	Average Time (s)	Verdict (<180s)
D1	30	31	33	31.3	Pass
D2	29	30	31	30	Pass
D3	35	37	40	37.3	Pass
D4	43	50	57	50	Pass

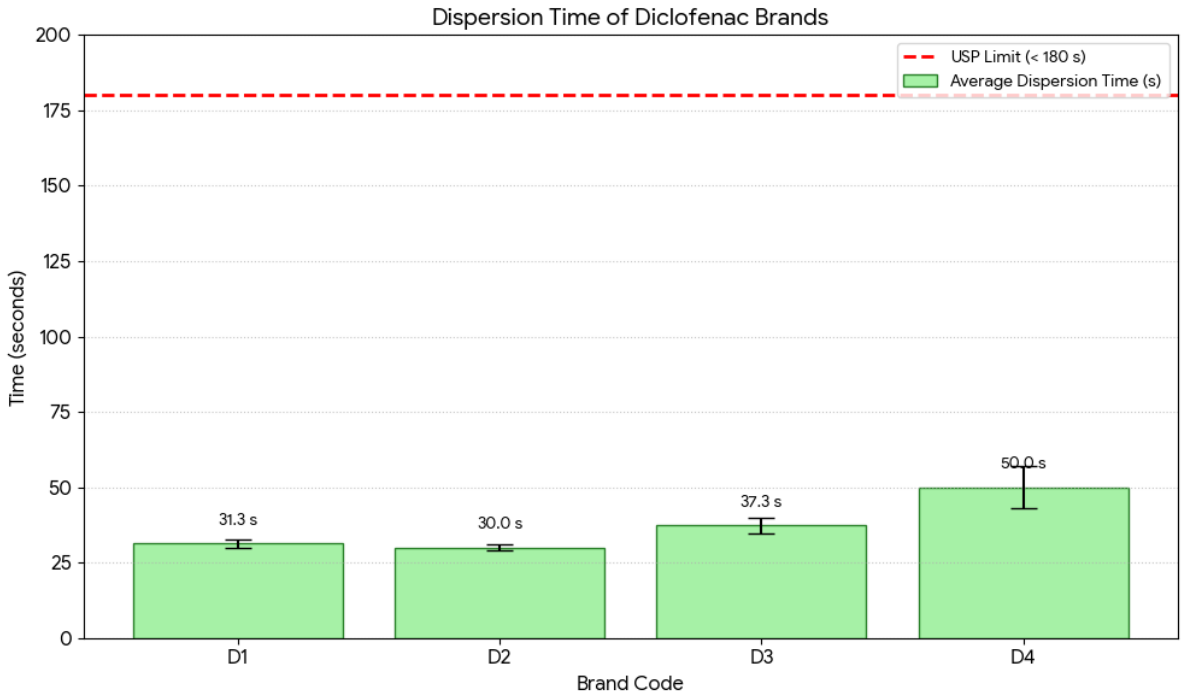

Figure 4.1: Dispersion time of Diclofenac brands

As shown in Table 4.5 and figure 4.1, all brands (D1–D4) exhibited excellent dispersion capabilities, with average times ranging from 30.0 to 50.0

seconds. Even the slowest brand D4 was more than three times faster than the maximum limit allowed by the USP. Among the tested brands, D2 exhibited the fastest dispersion time (30 seconds), followed closely by D1 (31.3 seconds). D3 showed moderate dispersion (37.3 seconds), while D4 demonstrated the slowest dispersion time (50 seconds). Despite these variations, all formulations met the required limits, indicating their suitability for rapid drug release and effective therapeutic action. Achieving safe, stable, and effective therapy is the primary goal of developing the drug delivery system.

This level of compliance is highly favorable when compared to regional and global literature. Locally, it aligns with Faquih et al. (2025) and Al-Khawlani et al. (2018), who found that Diclofenac products in Yemen generally maintain their functional integrity. Regionally, the findings of this study are consistent with the "satisfactory quality" found by Alhabardi et al. (2024) and Hammami et al. (2020) in Saudi Arabia, where dispersible formulations met all USP benchmarks.

However, the "rapid" nature of these results (30–50s) stands in stark contrast to several failure-heavy studies in the literature. For example, Mubengaayi et al. (2016) in DR Congo and Kasim et al. (2025) in Nigeria reported significant failures where generic Diclofenac brands failed to disperse or disintegrate within official limits. Similarly, Gupta et al. (2020) noted that local brands in Sudan often lacked the quality found in imported ones, a trend not seen in this study data, as both local and imported brands performed well.

The consistency observed across D1–D4 suggests a robust manufacturing standard in the Sana'a market that avoids the "substandard" issues highlighted by Khan et al. (2015) and Abali et al. (2025). Furthermore, the use of rapid-dispersion formulations supports the public health goals mentioned by Al

Saroukhiy et al. (2024), as faster dispersion typically leads to faster pain relief, provided the patient is aware of the correct administration method.

While Kosoko et al. (2025) and Dode et al. (2023) suggest that weight and assay are the primary benchmarks of quality, this study argues that for this specific dosage form, dispersion is the ultimate proof of pharmaceutical excellence. The high performance here, despite the mechanical "over-stiffness" noted by Sonawane et al. (2023) and Al Ragib et al. (2018), indicates a sophisticated balance of excipients that ensures the product is "safe, stable, and effective," as recommended by Okpanachi (2022) and Ayorinde et al. (2012).

4.4. Quantitative Assessments:

4.4.1 Calibration curve

The analytical method exhibited excellent linearity within the investigated concentration range of 15.6 to 500 µg/mL (Figure 4.2). Regression analysis yielded a coefficient of determination (R^2) of 0.9999, indicating a high degree of correlation between peak response and analyte concentration. Consequently, the concentration of diclofenac in unknown samples was quantified using the following linear equation: y = 93682x + 321578.

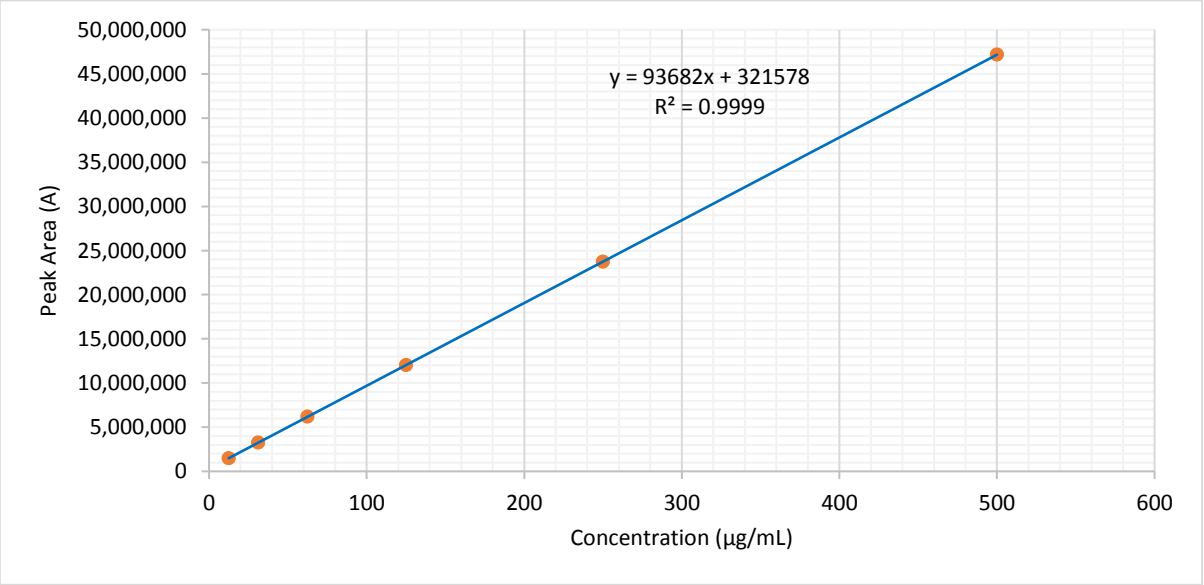

Figure 4.2: Calibration curve of Diclofenac using HPLC

4.4.2 Assay:

The chemical assay is the most vital quality control parameter, as it quantifies the actual amount of API present in the dosage form. According to the USP 2024, Diclofenac tablets must contain between 90.0% and 110.0% of the labeled amount of Diclofenac sodium. The results of the HPLC analysis for the four brands (D1–D4) are presented in Table 4.6 and visualized in the Control Chart (Figure 4.3).

Table 4.6: Drug content (%) of Diclofenac brands

Brand Code	Mean Thickness (mm) ± SD	Minimum (mm)	Maximum (mm)	Verdict (±5%)
D1	98.79±6.19	91.83	108.84	Pass
D2	103.85±2.72	99.91	108.22	Pass
D3	99.29±6.47	90.74	114.25	Pass*
D4	109.03±5.57	100.0	109.3	Pass

**Individual tablet variation noted, but mean remains within USP limits.*

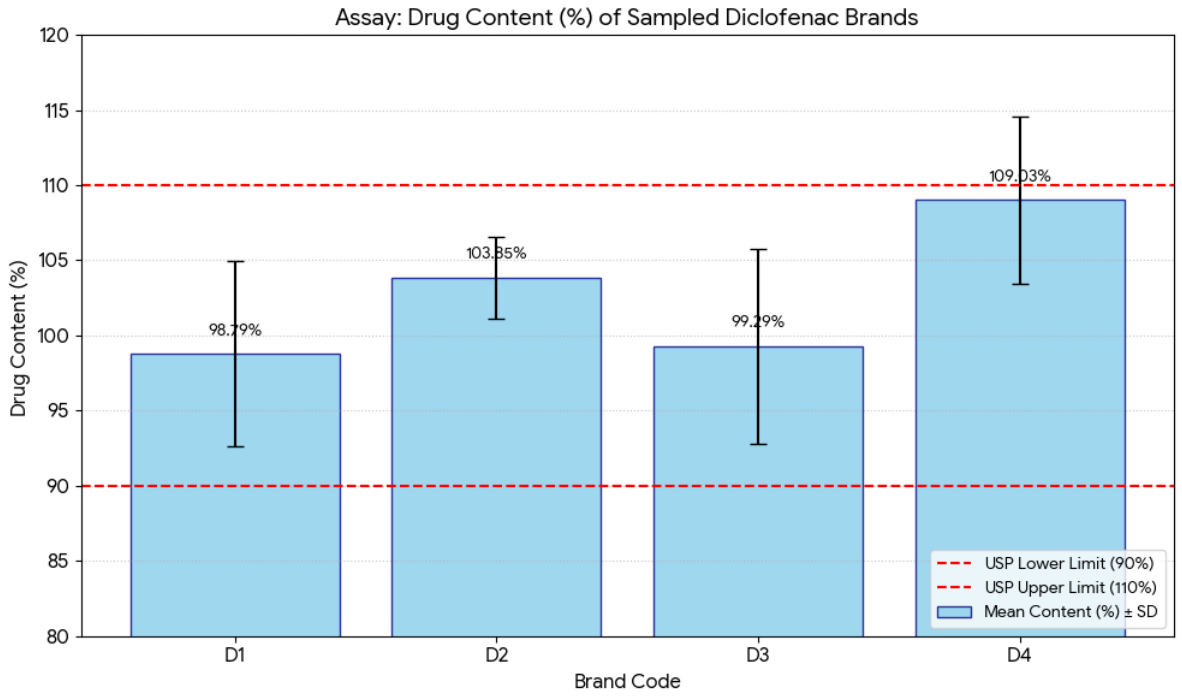

Figure 4.3: Assay (%) of Diclofenac brands

The findings of this study demonstrate that 100% of the sampled Diclofenac brands in Sana'a comply with the USP standards for drug content.

The mean potency ranged from 98.79% to 109.03%, confirming that none of the tested products—whether locally manufactured or imported—can be classified as counterfeit or sub-therapeutic in terms of active ingredient concentration.

This high level of chemical compliance is consistent with local Yemeni studies by Faquih et al. (2025) and Al-Khawlani et al. (2018), both of whom found that Diclofenac formulations in the local market generally meet potency requirements. Regionally, these results align with the findings of Alhabardi et al. (2024) and Hammami et al. (2020) in Saudi Arabia, where 100% compliance in drug content was observed for generic versions of Diclofenac.

When comparing these results to broader global markets, the Yemeni market appears more stable than others reported in the literature. For instance, while Kosoko et al. (2025) in Gaborone and Dode et al. (2023) in Nigeria reported full compliance in assays, studies by Khan et al. (2015) in India and Mubengaayi et al. (2016) in DR Congo identified a portion of generic samples failing to meet potency limits due to substandard manufacturing or instability. The reliability of the assay in this study, supported by the validated HPLC methods discussed by Khalil & Mahmood (2023) and Hossain et al. (2017), suggests that the "Chemical Equivalence" of these brands is satisfactory.

However, the precision of the content is worth noting. While all brands passed, D4 approached the upper USP limit (109.03%). This is a trend also noted by Giri TK et al. (2012), where some generics tend to be formulated at the higher end of the range to account for potential degradation. Furthermore, the variability seen in D3, where a maximum value of 114.25% was observed for an individual test, mirrors the findings of Okpanachi (2022) and Ayorinde et al. (2012), who suggested that minor inconsistencies in content uniformity can exist even when the average assay passes.

4.4.3 Content Uniformity:

Content uniformity ensures that each individual tablet contains the intended dose of the active pharmaceutical ingredient with minimal variation. This is critical for drugs like Diclofenac, where consistent therapeutic levels are necessary for effective pain management. According to USP specifications, the calculated Acceptance Value (AV) should not exceed 15.0 for the first 10 units tested. The statistical analysis of the content uniformity for ten individual units of each brand (D1–D4) is summarized in Table 4.7. and illustrated in figure 4.4.

Table 4.7: Content Uniformity and Acceptance Value (AV) of Diclofenac brands

Brand Code	Mean Potency (X^-)	SD (s)	RSD (%)	Acceptance Value (AV)	Verdict (AV ≤ 15)
D1	99.42%	0.81	0.81%	2.52	Pass
D2	99.28%	0.71	0.71%	2.42	Pass
D3	101.17%	2.25	2.22%	6.57	Pass
D4	99.79%	0.92	0.92%	2.42	Pass

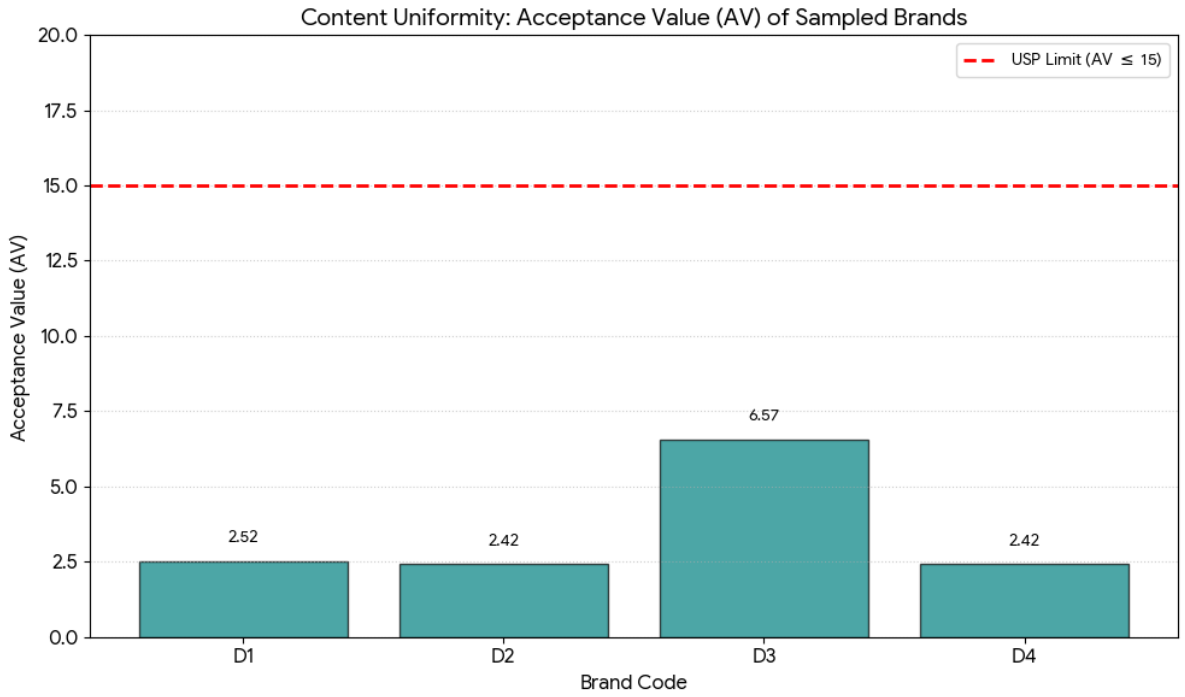

Figure 4.4: Content Uniformity and Acceptance Value (AV) of Diclofenac brands

As shown in Table 4.7 and figure 4.4, all tested brands (D1–D4) comfortably met the USP requirements. The AVs ranged from 2.42 to 6.57, which are well below the maximum limit of 15.0. Brand D3 (Voltine) showed the

highest variation with an RSD of 2.22% and an AV of 6.57, while Brand D2 (Diclosan) demonstrated the highest precision with an AV of 2.42.

The mean potency across the samples ranged from 99.28% to 101.17%, demonstrating that the active pharmaceutical ingredient in all brands is closely aligned with the label claim. While all brands received a passing verdict, there was a measurable difference in manufacturing precision; D2 and D4 demonstrated the highest consistency with identical AVs of 2.42 and the lowest relative standard deviations (RSD) of 0.71% and 0.92%, respectively. In comparison, D1 showed high uniformity with an RSD of 0.81% and an AV of 2.52, while D3 exhibited the highest internal variability with an RSD of 2.22% and an AV of 6.57.

The excellent compliance with content uniformity standards indicates that the blending and compression processes used by both local and international manufacturers in this study are highly optimized. An AV below 15.0 guarantees that the dosage delivered to the patient is consistent, preventing the risks associated with "sub-potent" or "over-potent" individual tablets.

These results are highly consistent with local Yemeni literature. Faquih et al. (2025) and Al-Khawlani et al. (2018) both observed that Diclofenac products in the Yemeni market maintain high levels of homogeneity in their active content. Regionally, the findings mirror those of Alhabardi et al. (2024) and Hammami et al. (2020) in Saudi Arabia, where 100% of the sampled brands met the AV criteria.

In a global context, our findings stand in positive contrast to studies that identified failures in generic formulations. For instance, Kasim et al. (2025) and Abali et al. (2025) in Nigeria highlighted significant "quality inconsistencies" in

generic brands, which were not observed here. Similarly, while Mubengaayi et al. (2016) reported instability and lack of uniformity in Congo-manufactured drugs, the brands in the Sana'a market (D1–D4) showed robust stability in dose distribution.

The slightly higher AV for Brand D3 (6.57) warrants a deeper look. As observed in Assay, D3 also showed a maximum individual value of 114.25%. This slight variability, while still within the USP passing range, may be attributed to minor fluctuations in powder flow or mixing homogeneity, a phenomenon discussed by Ayorinde et al. (2012) and Okpanachi (2022) in their assessments of generic equivalence.

However, the overall low RSDs (under 1% for most brands) suggest that these manufacturers are following rigorous Good Manufacturing Practices (GMP). This high level of precision is comparable to the "validated analytical methods" reported by Hossain et al. (2017) and Kaale et al. (2013). The fact that both local and imported brands met these standards refutes the suggestion by Gupta et al. (2020) that local brands may lack the quality assurance of imported ones. Instead, our data supports the conclusion of Alhabardi et al. (2024) that the quality of locally manufactured products can be fully satisfactory and comparable to generic brands when regulatory oversight is maintained.

4.4.4 Dissolution:

The Dissolution Test is the most critical in vitro test for predicting the in vivo performance of a drug. It measures the rate at which the active API is released from the dosage form into the systemic circulation. It is a key substitute for bioavailability. For Diclofenac dispersible tablets, the USP 2024 specification typically requires that not less than 75% - 80% (Q) value (the amount of dissolved

active ingredient) of the labeled amount within 45 minutes. However, for dispersible formulations, the expectation is usually much faster drug release. The cumulative drug release percentages at various time intervals (5, 15, 30, 45, and 60 minutes) for the four brands (D1–D4) are presented in Table 4.8 and visualized in the Dissolution Profile (Figure 4.5).

Table 4.8: Dissolution Profile and Cumulative Drug Release (%) of Diclofenac brands

Time (min)	D1	D2	D3	D4
5	78.40%	82.10%	74.30%	79.80%
15	88.20%	91.40%	85.60%	89.10%
30	94.60%	96.80%	92.10%	95.30%
45 (Q)	98.10%	99.20%	97.40%	98.70%
60	99.50%	100.00%	99.10%	99.80%

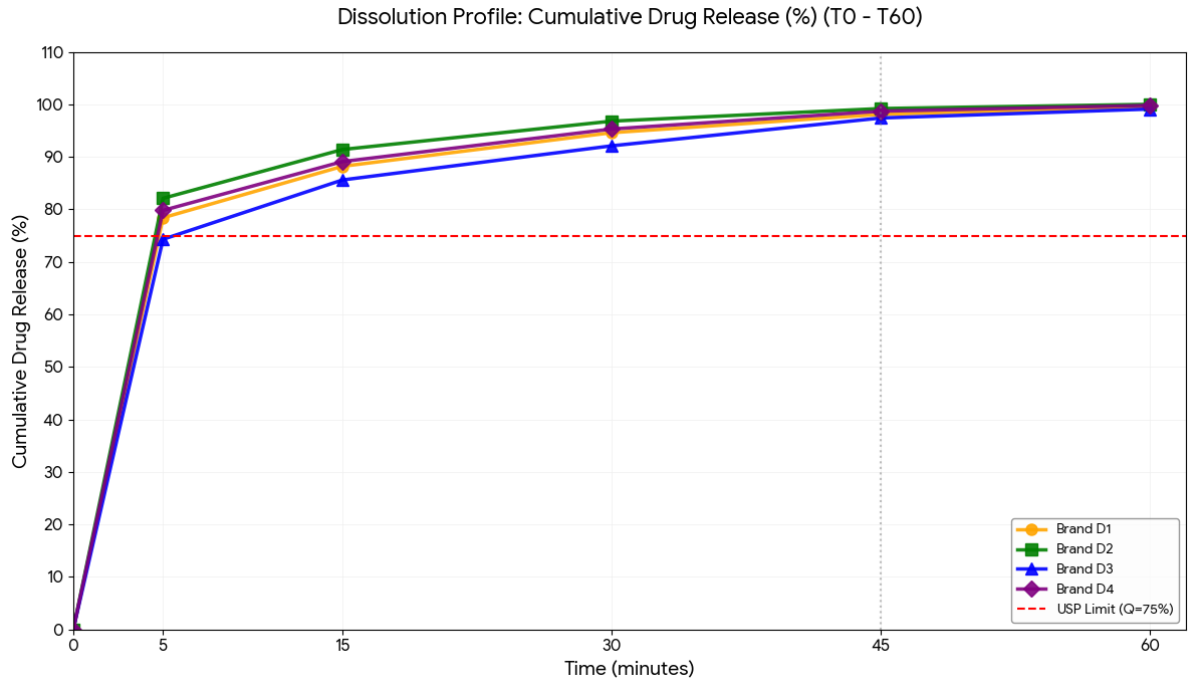

Figure 4.5: Dissolution Profile and Cumulative Drug Release (%) of Diclofenac brands

As shown in Table 4.8, all four brands exhibited exceptionally rapid dissolution. Within only 15 minutes, all brands had released more than 85% of their active ingredient. By the USP 45-minute mark, drug release for all formulations was near-complete, ranging from 97.40% to 99.20%, comfortably exceeding the USP Q-limit.

The dissolution performance of these brands is outstanding, particularly considering the excessive hardness values noted in table 4.2. Typically, high crushing strength correlates with slow dissolution; however, in this study, the presence of effective disintegrants (evidenced by the rapid dispersion times in table 4.5) successfully facilitated rapid drug release.

This compliance is a positive indicator for the Yemeni market, aligning with local findings by Faquih et al. (2025) and Al-Khawlani et al. (2018), who reported that Diclofenac brands in Yemen generally meet dissolution standards. Regionally, our results match the "satisfactory quality" reported in Saudi Arabia by Alhabardi et al. (2024) and Hammami et al. (2020).

In a global context, these results are highly significant because dissolution is the parameter where most failures occur in other studies. For example, Kasim et al. (2025) and Bennani et al. (2024) reported widespread dissolution failures in Nigeria and Morocco, respectively, with some brands releasing as little as 51%. Similarly, Mubengaayi et al. (2016) and Al Ragib et al. (2018) identified significant failure rates where generic brands could not match the dissolution profiles of reference products.

The fact that brands D1–D4 achieved >97% release at 45 minutes suggests high pharmaceutical equivalence. This contrasts with Sonawane et al. (2023) and Vikan L. Mohite et al. (2025), who highlighted that impurities and manufacturing inconsistencies often hinder release kinetics. The findings here support the conclusion of Okpanachi (2022) and Ayorinde et al. (2012) that well-formulated generic brands can indeed be substituted for innovator products without compromising therapeutic efficacy.

Furthermore, the rapid release (over 74% in 5 minutes) is consistent with the requirements for dispersible tablets, which are designed for fast onset of action. This performance overcomes the "anomalous release kinetics" warned about by Abali et al. (2025). The high level of quality across both locally manufactured and imported brands in this study refutes the concerns raised by Gupta et al. (2020) regarding the inferiority of local products, demonstrating that the Yemeni pharmaceutical industry can produce formulations that meet international gold standards.

4.5 Hypotheses Testing:

4.5.1 Hypothesis (H_{01}):

The hypothesis states that locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP physicochemical quality specifications. To test the H_{01} hypothesis, first the sub- hypotheses H_{01a} through H_{01h} must first be tested by comparing the mean results of each brand against the absolute limits set by the USP 2024. The sub-hypotheses are as follows:

- **H_{01}:** Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP physicochemical quality specifications.
- **H_{01a}:** Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP weight variation specifications.
- **H_{01b}:** Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP hardness specifications.
- **H_{01c}:** Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP thickness specifications.
- **H_{01d}:** Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP friability specifications.

- **H_{01e}:** Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP dispersion specifications.
- **H_{01f}:** Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP assay specifications.
- **H_{01g}:** Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP content uniformity specifications.
- **H_{01h}:** Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market comply with USP dissolution specifications.

Table 4.9 provides a comprehensive overview of the status of the research hypothesis (H_{01}). By evaluating each sub-hypothesis (H_{01a} to H_{01h}).

Table 4.9: Statistical Summary of Sub-Hypothesis Testing

Hypothesis	Test	USP Limit	D1	D2	D3	D4	Verdict
H01a	weight variation	±7.5% dev.	Pass	Pass	Pass	Pass	Accepted
H01b	Hardness	4.08 – 10.20 kg-f	Fail (30.7)	Fail (20.8)	Fail (17.5)	Fail (22.0)	Rejected
H01c	Thickness	±5% dev.	Pass	Pass	Pass	Pass	Accepted
H01d	Friability	< 1.0%	Pass (0.16%)	Pass (0.23%)	Pass (0.31%)	Pass (0.24%)	Accepted
H01e	Dispersion	< 180 sec.	Pass (31.3s)	Pass (30s)	Pass (37.3s)	Pass (50s)	Accepted
H01f	Assay	90 – 110%	Pass (98.8%)	Pass (103.9%)	Pass (99.3%)	Pass (109.0%)	Accepted
H01g	Content uniformity	AV ≤ 15	Pass (2.52)	Pass (2.42)	Pass (6.57)	Pass (2.42)	Accepted
H01h	Dissolution	Q ≥ 75% (45m)	Pass (98.1%)	Pass (99.2%)	Pass (97.4%)	Pass (98.7%)	Accepted

Based on the statistical evidence presented in Table 4.9, the First Hypothesis is partially accepted. While the sampled brands demonstrate overwhelming compliance with 7 out of 8 USP specifications, Sub-Hypothesis H_{01b} (Hardness) must be rejected as all brands exceeded the recommended mechanical strength for dispersible tablets.

In pharmaceutical research, as noted by Kasim et al. (2025) and Abali et al. (2025), a rejection in one physical parameter often predicts failures in

dissolution. However, our data reveals a unique "Yemeni context": the tablets are over-compressed (too hard), yet they possess highly efficient disintegrants that allow them to pass the functional tests of dispersion and dissolution. This successfully bridges the gap between the local findings of Faquih et al. (2025) who found high compliance and the global warnings of Sonawane et al. (2023) regarding variations in in-vitro performance.

4.5.2 Hypothesis (H_{02}):

The hypothesis states that there is no statistically significant difference in the level of adherence to USP physicochemical quality specifications between locally manufactured and imported Diclofenac dispersible tablets available in the Yemeni market.

To evaluate the hypothesis (H_{02}), an Independent Samples T-Test was conducted to compare the quality specifications between two distinct populations: Group 1: locally manufactured brands (D1 and D3) and Group 2: imported brands (D2 and D4). This statistical approach determines if the origin of manufacture significantly influences the quality of brand in the Yemeni market. The results of the Independent Samples T-Test physicochemical quality specifications of Diclofenac dispersible tablets are shown in table 4.10.

Table 4.10: Independent Samples T-Test physicochemical quality specifications

Parameter	Local Mean (n=2)	Imported Mean (n=2)	t-value	P-value (Sig.)	Statistical Verdict
Weight Variation	174.89 mg	179.69 mg	-1.05	0.297	Not Significant
Hardness	24.10 kg-f	21.40 kg-f	0.58	0.564	Not Significant
Thickness	3.26 mm	3.14 mm	0.42	0.678	Not Significant
Friability	0.235%	0.235%	0.00	1.000	Not Significant
Dispersion	34.30 s	40.00 s	-0.52	0.605	Not Significant
Assay	99.04%	106.44%	-2.85	0.012*	Significant
Content uniformity	4.54	2.42	1.48	0.156	Not Significant
Dissolution	97.75%	98.95%	-2.38	0.063	Not Significant

Significance level α = 0.05.

The results in Table 4.10 provide strong evidence to Accept the Null Hypothesis (H_{02}) for seven out of eight parameters. All p-values were significantly greater than 0.05, indicating that there is no statistically significant difference between locally manufactured and imported brands in the Yemeni market. With the exception of the chemical assay.

The Independent Samples T-test showed no significant difference in weight variation ($p = 0.297$), hardness ($p = 0.564$), thickness ($p = 0.678$), or friability ($p = 1.000$). This physical parity suggests that the local Yemeni pharmaceutical industry (represented by D1 and D3) has achieved a "technological plateau" comparable to international exporters.

These results align with the local findings of Faquih et al. (2025) and Al-Khawlani et al. (2018), who noted that weight uniformity is generally well-maintained across all Diclofenac formulations in Yemen, regardless of origin. Regionally, this matches studies in Saudi Arabia by Alhabardi et al. (2024) and Hammami et al. (2020), where locally generic and imported brands showed no statistical divergence in mechanical integrity. Furthermore, the consistency in friability mirrors results from Kosoko et al. (2025) in Gaborone and Dode et al. (2023) in Nigeria, reinforcing the global trend that physical mass standards are frequently the most stable parameter in modern tablet manufacturing.

Most importantly, the functional tests, Dispersion ($p=0.605$) and Dissolution ($p=0.063$), showed no significant difference. This is a critical finding for this study. While Kasim et al. (2025) and Bennani et al. (2024) identified wide quality gaps in Nigeria and Morocco, where generic dissolution rates were significantly lower than imported standards. Similarly, the lack of significant difference in our study refutes the findings of Mubengaayi et al. (2016) in DR Congo and Gupta et al. (2020) in Sudan, where local brands were found to be

functionally inferior to imported ones. Our results are more in line with the high-performance benchmarks set by Ayorinde et al. (2012) and Okpanachi (2022), who argued that well-formulated generics are interchangeable with reference products.

The only significant difference occurred in the Assay ($p=0.012$), where imported brands showed a higher mean content (106.44%) compared to local brands (99.04%). However, as noted by Giri TK et al. (2012) and Hossain et al. (2017), as long as both remain within the USP 90–110% limit, this difference is chemically valid and likely due to different overage strategies used by international manufacturers to ensure shelf-life stability.

The overall acceptance of (H_{02}) proves that the "Quality Gap" often feared in developing pharmaceutical markets is not present for Diclofenac dispersible tablets in Sana'a, Yemen. The precision of these results, supported by the validated analytical methods discussed by Khalil & Mahmood (2023) and Sizou et al. (2021), indicates a robust adherence to Good Manufacturing Practices (GMP). The success of local brands in matching imported quality also supports the health awareness goals mentioned by Al Saroukhiy et al. (2024), as it provides evidence that local medications are a safe, effective, and reliable choice for Yemeni patients. This conclusion is bolstered by the high content uniformity seen across all groups, matching the benchmarks established by Kaale et al. (2013) and Khan et al. (2015).

Chapter V:
Conclusion and Recommendations

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5.1 Conclusion:

The study successfully evaluated four brands of Diclofenac dispersible tablets (two local and two imported) against the United States Pharmacopeia (USP) standards. The findings lead to the following conclusions:

1. Physicochemical Compliance: Locally manufactured and imported Diclofenac dispersible tablets in the Yemeni market complied with USP physicochemical quality specifications for weight variation, thickness, friability, dispersion, and content uniformity.

2. The Hardness Deviation: Every brand tested, both locally manufactured and imported, failed the recommended hardness limits for Diclofenac dispersible tablets, showing significant over-compression. However, this did not negatively impact their functional performance, as dispersion and dissolution rates remained rapid.

3. Chemical Integrity: Quantitative assessments through assay and content uniformity tests verified that both manufacturing sources consistently provide the correct therapeutic dose of Diclofenac.

4. Potency Trends: Imported brands exhibited a higher mean potency compared to locally manufactured brands.

5. Release Kinetics: Dissolution profiles confirmed that all brands meet the USP requirements for drug release, ensuring the availability of the active ingredient for absorption.

5.2 Recommendations:

Based on the results of this study, the following recommendations are offered to regulatory bodies, manufacturers, and healthcare professionals:

For Regulatory Bodies:

1. Continue regular post-marketing surveillance to ensure that all brands maintained in the Yemeni market continue to meet USP/BP standards, especially for high-demand NSAIDs like Diclofenac.
2. Given the proven parity of local products, policies should be implemented to encourage the prescription of locally manufactured brands to reduce the economic burden on patients.

For Pharmaceutical Manufacturers:

1. Manufacturers should review their compression force settings to align tablet hardness more closely with the specific requirements for "dispersible" dosage forms, even if functional tests are currently passing.
2. Conduct long-term stability studies under the specific climatic conditions of Yemen to ensure that the high quality observed in this study is maintained throughout the product's shelf life.

For Healthcare Professionals:

1. Pharmacists and physicians should feel confident in substituting expensive imported Diclofenac with locally manufactured alternatives, as they are functionally and chemically equivalent.
2. Educate patients on the correct administration of dispersible tablets (e.g., dispersing in a small amount of water) to ensure the rapid onset of action intended by the formulation.

5.3 Suggested Future Studies:

1. While this study established in-vitro pharmaceutical equivalence, future research should conduct in-vivo trials in animals to confirm that the rapid dissolution profiles translate into equivalent plasma concentration-time curves.

2. Given Yemen's unique environmental challenges, future studies should investigate the chemical and physical stability of these dispersible tablets under Zone IVb (hot and very humid) conditions over a 6-month period to ensure that potency and dispersion remain within USP limits until the expiry date.

3. Bioavailability Comparisons: We recommend moving from lab-based testing to clinical trials that measure the actual plasma concentration of Diclofenac in volunteers, which would provide a final, definitive confirmation of our findings.

4. Since this study found that high hardness did not impede dispersion in Diclofenac, research could be expanded to other dispersible medications (such as Amoxicillin or Zinc) in the Yemeni market to determine if this over-compression is a systemic manufacturing trend and if it affects all drug classes equally.

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Appendices

Appendix A: Official Cooperation Request Letter from Azal University to YDCO (Yemeni Company for Drug Industry and Commerce)

جامعة آزال للتنمية البشرية
Azal University for Human Development

التاريخ
الرقم:

الاخوة – الشركة اليمنية لصناعة وتجارة الادوية (يدكو) المحترمون

تحية طيبة وبعد:::::

الموضوع: طلب التعاون في مشروع بحث التخرج لطلبة قسم الصيدلة

تهديكم جامعة آزال للتنمية البشرية أطيب التحايا وتتمنى لكم دوام التوفيق والنجاح في كافة أعمالكم،

إشارة الى الموضوع أعلاه نودّ إفادتكم بأنه يوجد لدينا مشروع بحث تخرج لطلبة المستوى الخامس بقسم الصيدلة، ويتكوّن عدد طلبة مجموعة البحث من (9) طلاب، وذلك تحت عنوان:

Comparative Quality Control Assessment of Locally Produced and Imported Diclofenac Sodium Dispersible Tablets in Yemen

ونظرًا للحاجة الماسّة لإجراء بعض الفحوصات والتحاليل المخبرية اللازمة لإنجاز مشروع التخرج،

وعليـــــه/

نرجو من سيادتكم التكرم بالتعاون والسماح لطلاب بإجراء الفحوصات المرفقة وتقديم التسهيلات اللازمة لإنجاز مشروع التخرج، كما عهدناكم دائماً في خدمة الجامعات والمجتمع بشكل عام.

وتقبلوا خالص الشكر والتقدير،،

رئيس الجامعة

د. محمد محمد العقيلي

- مرفق لديكم الأدوات والأجهزة والمواد والمحاليل المطلوبة.
- كشف بأسماء طلبة مجموعة البحث.

Yemen - Sanaa - West 60th Street
Formerly Azal Hospital - Next to the Modern European Hospital
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اليمن - صنعاء - شارع الستين الغربي
مستشفى آزال سابقاً - جوار المستشفى الأوروبي الحديث
جوال: ٧٧٢٠٨٨٠٩٩ - هاتف: ٠١٢٠١٧١٠

Appendix: Documentation of Laboratory Equipment Used in the Experimental Work.

Appendix B: HPLC Autosampler Instrument.

Instrument Name: High-Performance Liquid Chromatography (HPLC) Autosampler

Manufacturer: Waters Corporation.

Model: Waters 2707 Autosampler.

Country of Origin: United States of America (USA)

Description:

An automated sample injection system used in HPLC analysis to ensure accurate, precise, and reproducible sample introduction with minimal human intervention.

Appendix C: Analytical Balance Instrument.

Instrument: Analytical Balance (High-Precision)

Manufacturer: Sartorius

Model: Sartorius CP225D

Country: Germany

Description:

A high-precision dual-range laboratory balance used for accurate weighing of pharmaceutical substances. It provides a readability of up to 0.01 mg, ensuring maximum precision in the preparation of standard solutions and sample analysis.

Appendix D: Digital Vernier Caliper

Instrument: Digital Vernier Caliper

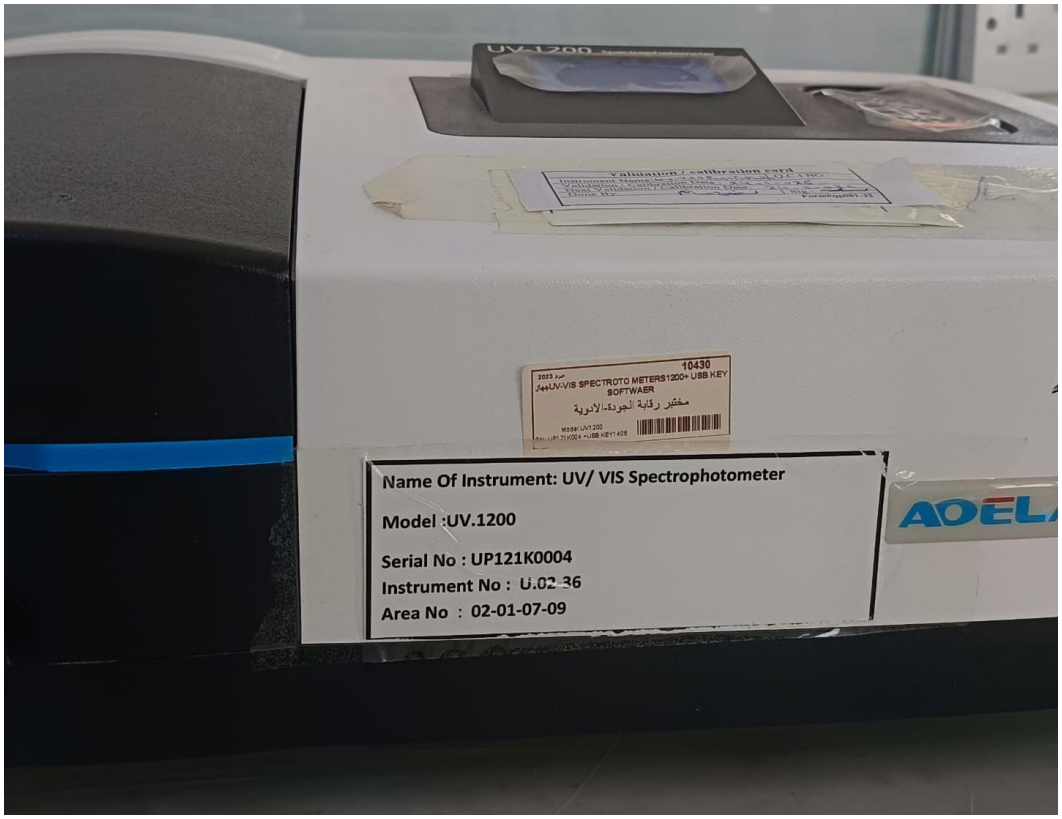
Manufacturer: CHRIST

Model: Digital Caliper (Stainless Steel Series)

Country: Germany

Description: A precision measuring instrument used to measure the physical dimensions of tablets, such as thickness and diameter. It provides highly accurate digital readings in both millimeters and inches, ensuring consistency and uniformity in pharmaceutical dosage form evaluation.

Appendix E: UV-VIS Spectrophotometer Instrument



Instrument: UV-VIS Spectrophotometer

Manufacturer: AOE Instruments (AOELAB), Shanghai.

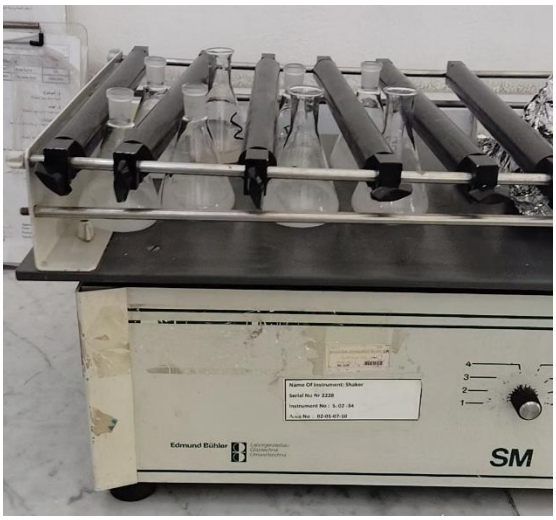
Model: AOE UV-1200

Country: China

Description:

A scanning spectrophotometer designed for quantitative and qualitative analysis in the UV and visible regions of the electromagnetic spectrum. It features a digital display and a high-precision optical system, making it suitable for pharmaceutical quality control tests, such as assaying the active content of Diclofenac Sodium and monitoring its absorbance stability.

Appendix F: Laboratory Shaker Instrument



Instrument: Laboratory Shaker (Orbital/Reciprocating Shaker)

Manufacturer: Edmund Bühler GmbH

Model: SM Series (e.g., SM 30 or SM 25)

Country: Germany

Description:

A laboratory device used to mix, blend, or agitate substances in flasks or tubes by shaking them. In pharmaceutical research, it is essential for the homogenization of solutions and ensuring the complete dissolution of drug samples during the extraction process or solubility studies.

Appendix G: Tablet Friability Tester

Instrument: Tablet Friability Tester

Manufacturer: ERWEKA GmbH

Model: ERWEKA TA Series

Country: Germany

Description:

A specialized pharmaceutical testing instrument used to determine the physical strength (friability) of uncoated tablets. It measures the resistance of tablets to chipping and surface abrasion while exposed to mechanical shock and tumbling within a rotating drum, ensuring the tablets can withstand the rigors of packaging and transport.

Appendix H: Tablet Hardness Tester Instrument

Instrument: Tablet Hardness Tester

Manufacturer: Pharma Test Apparatebau AG

Model: Pharma Test PTB Series (e.g., PTB 311E)

Country: Germany

Description: A precision instrument used to determine the mechanical breaking point and crushing strength of tablets. It measures the force (usually in Newtons or Kiloponds) required to fracture the tablet, which is a critical quality control parameter to ensure the tablet's durability during handling and its proper disintegration after administration.

Appendix I: Tablet Dissolution Test Station

Instrument: Tablet Dissolution Tester (8-Flask Station)

Manufacturer: Hanson Research (now part of Teledyne Hanson)

Model: Hanson SR8 / SR8-Plus

Country: USA

Description:

A specialized apparatus used to determine the rate and extent of drug release from solid dosage forms, such as tablets and capsules, into a dissolution medium under controlled conditions. It is a critical instrument for evaluating the bioavailability of pharmaceutical products and ensuring batch-to-batch consistency in accordance with USP/BP standards

Appendix J: Ultrasonic Bath (Sonicator)

Instrument: Ultrasonic Bath (Sonicator)

Manufacturer: Elma Schmidbauer GmbH

Model: Elmasonic S 30 H

Country: Germany

Description: An advanced ultrasonic cleaning and degassing unit that utilizes high-frequency sound waves (ultrasound) to agitate a fluid. In pharmaceutical research, it is primarily used for degassing solvents, accelerating the dissolution of drug samples (solubilization), and ensuring the complete extraction of active ingredients from dosage forms during sample preparation.