FORMULATION AND EVALUATION OF FAST DISINTEGRATING TABLETS OF DICLOFENAC POTASSIUM USING A BLEND OF SUPER DISINTEGRANTS

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CERTIFICATION

This is to certify that this work was carried out by **OMONEHIZENA AKHIDENO,** in the Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, University of Benin, Benin City, Edo State, Nigeria, in partial fulfilment for the award of the Pharm. D degree of the University.

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DEDICATION

This work is dedicated to Almighty God, whose grace, wisdom, and strength have guided me through every stage of my journey in pharmacy school.

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Thank you all

ABSTRACT

Background: Fast-disintegrating tablets (FDTs) are tablets designed to dissolve rapidly when placed on the tongue resulting in quick disintegration of the drug into solution when in contact with saliva. This study aimed to formulate and evaluate fast disintegrating tablets of diclofenac potassium using different concentrations of sodium starch glycolate (SSG) and croscarmellose sodium (CCS) as superdisintegrants.

Method: Six formulations (F1–F6) were prepared by direct compression with varying ratios of SSG and CCS. The powder blends were assessed for pre-compression parameters, while the tablets were evaluated for weight uniformity, hardness, friability, disintegration time, and drug content according to USP standards. Dissolution tests were conducted in 0.1N HCl using a USP paddle apparatus, and absorbance was measured spectrophotometrically at 276 nm.

Result: All formulations complied with USP specifications for mechanical and physical parameters. Disintegration time ranged from 71.5 ± 4.14 s to 270.7 ± 6.90 s, while formulations F1 and F2 showed the fastest drug release, exceeding 90% within 40 minutes. Formulations F3–F5 exhibited slower dissolution, reflecting the effect of superdisintegrant ratio on tablet performance.

Conclusion: The findings from this study show that formulations containing optimized amounts of sodium starch glycolate and croscamellose sodium can provide a balance between mechanical strength and rapid drug release.

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CHAPTER ONE

1.0 INTRODUCTION

Oral drug delivery remains the most preferred and widely accepted route for the administration of therapeutic agents due to its simplicity, safety, and patient convenience. Among the numerous dosage forms developed for oral administration, tablets have gained significant prominence because of their accurate dosing, stability, and ease of production (Jivraj *et al.,*2000). However, despite these advantages, conventional tablets often pose swallowing challenges, especially among pediatric, geriatric, and dysphagic patients, thereby affecting adherence and therapeutic outcomes (Parkash *et al*., 2011).

In modern therapeutics, improving patient compliance and dosage form innovation has become a crucial focus of pharmaceutical formulation research. The increasing demand for more convenient and user-friendly dosage forms has led to the evolution of orally disintegrating dosage systems that aim to overcome the limitations associated with conventional solid forms (More & Ghadge, 2013). These novel systems are designed to disintegrate rapidly in the oral cavity, eliminating the need for water and enhancing patient acceptability (Deepak *et al*., 2012). In this regard, the fast-disintegrating tablet (FDT) technology represents a remarkable advancement in oral drug delivery.

Fast disintegrating tablets (FDTs), also referred to as orally disintegrating tablets (ODTs), are solid dosage forms that disintegrate and dissolve rapidly in the mouth within seconds upon contact with saliva (Pahwa & Gupta, 2011). They combine the advantages of both liquid and conventional solid dosage forms by providing rapid drug action and ease of administration without compromising mechanical strength (Sharma & Sonawane, 2017). FDTs have gained increased attention due to their ability to improve the onset of therapeutic action and

bioavailability of drugs that require prompt pharmacological response (Parkash *et al*., 2011; Momeni *et al*., 2024).

The development of FDTs has been supported by the integration of superdisintegrants and novel excipient technologies. Studies have demonstrated that proper selection and optimization of superdisintegrants significantly influence disintegration time, mechanical strength, and drug release profile (Dhiman, 2022; Shihora & Panda, 2011). For instance, Eraga *et al*. (2018) successfully formulated paracetamol FDTs using a blend of croscarmellose sodium and Pleurotus tuber-regium powder, achieving rapid disintegration and satisfactory mechanical integrity. Such innovations underscore the importance of excipient design in achieving balance between fast disintegration and adequate tablet strength.

Diclofenac potassium serves as an ideal model drug for FDT formulation due to its rapid analgesic and anti-inflammatory activity, which requires prompt systemic absorption (Comoglu *et al*., 2011). Although conventional diclofenac tablets are effective, they are associated with delayed onset of action and potential gastrointestinal irritation (Chuasuwan *et al*., 2009). The fast-disintegrating formulation of diclofenac potassium can therefore enhance patient compliance and ensure faster pain relief, particularly in acute pain conditions (Karthikeyan *et al*., 2012; Chen *et al*., 2015).

Consequently, the formulation and evaluation of diclofenac potassium as an FDT using a blend of superdisintegrants is a promising approach to achieving optimal therapeutic efficacy, improved bioavailability, and enhanced patient adherence (Thapa *et al*., 2021; Eraga *et al*., 2017). The continuous exploration of novel excipients and co-processing technologies further advances the potential of this dosage form in modern drug delivery systems (Eraga *et al*., 2014; Enadeghe *et al*., 2024).

1.1 AN OVERVIEW OF DICLOFENAC POTASSIUM

1.1.1 Pharmacological Profile

Diclofenac potassium is a non-steroidal anti-inflammatory drug (NSAID) belonging to the phenylacetic acid derivatives, widely employed for the management of pain and inflammation. Its therapeutic action primarily results from the inhibition of cyclo-oxygenase (COX-1 and COX-2) enzymes, thereby suppressing prostaglandin synthesis which mediates pain, fever, and inflammatory responses (Comoglu *et al*., 2011).

The potassium salt of diclofenac is preferred over the sodium form because of its higher aqueous solubility and faster absorption, leading to a quicker onset of analgesic effect (Chuasuwan *et al*., 2009).

Pharmacokinetically, diclofenac potassium is rapidly absorbed following oral administration, with peak plasma concentration typically achieved within 0.5–1.5 hours (Chen *et al*., 2015). It is extensively bound to plasma proteins (about 99%) and undergoes first-pass hepatic metabolism, producing hydroxylated and conjugated metabolites which are excreted predominantly in urine and bile. Its relatively short elimination half-life, usually 1–2 hours, supports its use in conditions requiring prompt but short-term pain relief (Abbas *et al*., 2017).

Clinically, diclofenac potassium is indicated in the management of musculoskeletal pain, rheumatoid arthritis, osteoarthritis, migraine, dysmenorrhea, dental pain, and postoperative inflammation (Comoglu *et al*., 2011; Karthikeyan *et al*., 2012). Its rapid pharmacodynamic response makes it particularly useful where immediate analgesia is desired.

1.1.2 Biopharmaceutical and Formulation Considerations

From a biopharmaceutical perspective, diclofenac potassium exhibits high permeability but limited solubility, classifying it as a Biopharmaceutics Classification System (BCS) Class II drug (Chuasuwan *et al*., 2009). Its weakly acidic nature (pKa ≈ 4.0) favors dissolution in alkaline environments but hinders solubility in the acidic gastric milieu, leading to variability in absorption and potential gastrointestinal irritation. Conventional tablets often show delayed

onset of action and may cause mucosal injury due to prolonged gastric residence and local prostaglandin inhibition (Chen *et al*., 2015).

The fast-disintegrating tablet (FDT) approach provides a strategic solution to these challenges by enhancing disintegration and dissolution within the oral cavity prior to swallowing. This facilitates pre-gastric absorption, reduces gastrointestinal side effects, and ensures rapid onset of pharmacological activity (Comoglu *et al*., 2011; Abbas *et al*., 2017).

Incorporating superdisintegrants such as croscarmellose sodium, sodium starch glycolate, or natural polymeric agents has been shown to markedly improve the performance of FDTs by promoting water uptake, swelling, and rapid matrix disintegration (Pahwa & Gupta, 2011; Sharma & Sonawane, 2017; Dhiman, 2022).

Eraga *et al*.,(2017) further demonstrated that acid-modified millet starch can act as an effective natural superdisintegrant in diclofenac tablet formulations, providing comparable disintegration efficiency to synthetic agents. Likewise, blending disintegrants—synthetic and natural—can synergistically reduce disintegration time while maintaining adequate mechanical strength (Eraga *et al*., 2018; Thapa *et al*., 2021).

Hence, developing FDTs of diclofenac potassium using optimized blends of superdisintegrants holds the potential to enhance bioavailability, accelerate therapeutic onset, and improve patient compliance, particularly in populations with swallowing difficulties.

1.2 FAST DISINTEGRATING TABLETS (FDTS)

1.2.1 Definition and Characteristics

Fast disintegrating tablets (FDTs), also known as orally disintegrating tablets (ODTs), are solid unit dosage forms designed to disintegrate or dissolve rapidly in the mouth, usually within 30 to 60 seconds, without the need for water (Deepak *et al*., 2012). According to the United States Food and Drug Administration (FDA), an FDT is “a solid dosage form

containing a medicinal substance that disintegrates rapidly, usually within a few seconds, when placed upon the tongue" (Parkash *et al*., 2011). Similarly, the European Pharmacopoeia defines an orodispersible tablet as "a tablet that disperses or disintegrates in the mouth within 3 minutes" (More & Ghadge, 2013).

The key performance characteristics of an ideal FDT include rapid disintegration, uniform drug distribution, pleasant mouthfeel, adequate mechanical strength, and acceptable taste (Bharawaj *et al*., 2010; More & Ghadge, 2013). These tablets are particularly beneficial for patients who have difficulty swallowing conventional dosage forms. The incorporation of superdisintegrants such as croscarmellose sodium, sodium starch glycolate, or crospovidone is critical to achieving rapid disintegration through mechanisms like wicking, swelling, and particle repulsion (Shihora & Panda, 2011; Sharma & Sonawane, 2017).

Recent technological advancements have expanded the use of natural polymers and co-processed excipients to enhance disintegration efficiency while maintaining acceptable tablet hardness. For instance, Eraga *et al*., (2018) formulated fast disintegrating paracetamol tablets using a blend of croscarmellose sodium and Pleurotus tuber-regium powder, demonstrating that synergistic use of natural and synthetic disintegrants can improve both mechanical integrity and disintegration time. Similarly, Momeni *et al*., (2024) developed a machine learning model capable of predicting disintegration time and hardness, reflecting the growing role of artificial intelligence in FDT optimization.

1.2.2 Advantages of FDTs

Fast disintegrating tablets offer distinct therapeutic and patient-centered benefits. One of their main advantages is improved patient compliance, particularly among pediatric, geriatric, bedridden, psychiatric, and dysphagic populations who experience difficulty swallowing conventional tablets (Parkash *et al*., 2011; Deepak *et al*., 2012). The elimination of the need

for water enhances their suitability for on-the-go administration, making them convenient for active individuals and travelers (More & Ghadge, 2013).

From a pharmacokinetic standpoint, FDTs enable rapid onset of therapeutic action due to pre-gastric absorption through the buccal mucosa, which bypasses first-pass metabolism (Shirsand *et al*., 2010; Comoglu *et al*., 2011). For drugs like diclofenac potassium, which require quick relief of pain, the FDT platform can significantly enhance bioavailability and therapeutic responsiveness (Comoglu *et al*., 2011; Karthikeyan *et al*., 2012).

Additionally, the possibility of improved drug dissolution in the saliva, as reported by Bolhuis, *et al*., (1997), further underscores the role of FDTs in enhancing the dissolution of poorly soluble drugs. Overall, FDTs combine the pharmacological benefits of rapid drug release with the patient-centered advantages of convenience, ease of administration, and improved compliance.

1.2.3 Challenges in FDT Formulation

Despite their advantages, FDT formulation presents several technological challenges. The foremost is achieving a balance between mechanical strength and disintegration rate (Nadaf *et al*., 2024). Tablets that disintegrate too rapidly often lack adequate hardness and may crumble during packaging or transport. Conversely, enhancing mechanical strength can retard disintegration due to increased compaction forces and reduced porosity (Zheng *et al*.,2022).

Another critical issue is taste masking, particularly for bitter drugs like diclofenac potassium, where unpleasant taste can negatively influence patient acceptability (Comoglu *et al*., 2011). Various techniques, including the use of flavoring agents, coating, and inclusion complexes, have been adopted to overcome this limitation (Soni & Raju, 2015). Additionally, hygroscopicity and stability are concerns, as FDTs readily absorb moisture from the

environment, potentially altering disintegration and drug release profiles (Deepak *et al*., 2012; Meko *et al.,* 2018).

Packaging and handling also require careful consideration. Specialized moisture-protective packaging materials are often necessary to preserve tablet integrity and prevent premature disintegration (Parkash *et al*., 2011). Emerging research trends, including the dual approach of porous starch and sublimation for creating robust yet highly porous tablets, demonstrate innovative strategies to overcome these formulation challenges (Nadaf *et al*., 2024).

Therefore, while FDTs offer significant therapeutic promise, their successful development demands precise optimization of formulation parameters, selection of suitable excipients, and a clear understanding of material interactions under different processing conditions.

1.3 SUPERDISINTEGRANTS IN FAST DISINTEGRATING TABLET FORMULATION

1.3.1 Overview and Mechanism of Action

Superdisintegrants are specialized excipients incorporated in tablet formulations to promote rapid tablet breakup when in contact with aqueous fluids. Their primary role is to accelerate the disintegration process, allowing faster drug release and subsequent absorption (Pahwa & Gupta, 2011; Dhiman, 2022). In fast disintegrating tablets (FDTs), this function is critical because drug liberation occurs within seconds in the oral cavity without additional water (Parkash *et al*., 2011).

The effectiveness of a superdisintegrant depends on its mechanism of action, which may involve one or more physicochemical processes. The principal mechanisms include:

1. Swelling – expansion of hydrophilic polymeric chains generates internal pressure that disrupts the tablet matrix (Sharma & Sonawane, 2017).

2. Wicking or Capillary Action – rapid water uptake through the porous network decreases cohesive forces and promotes particle separation (Shihora & Panda, 2011).

3. Deformation and Recovery – particles deformed during compression recover their original shape upon wetting, producing disintegrating stress (Dilebo & Gabriel, 2019).

4. Particle Repulsion or Electrostatic Mechanism – repulsive forces generated by ionic interactions cause disintegration, particularly in low-density matrices (Bolhuis *et al*., 1997).

Recent investigations demonstrate that the performance of superdisintegrants can also be influenced by temperature and compaction pressure, which alter swelling kinetics and porosity (Zhen *et al*., 2022). Consequently, optimal functionality requires a delicate balance between tablet hardness and rapid water penetration.

1.3.2 Commonly Used Superdisintegrants

Superdisintegrants can be synthetic or naturally derived, each with distinctive physicochemical profiles that affect disintegration efficiency and compatibility with drug substances.

The most widely employed synthetic superdisintegrants include croscarmellose sodium (CCS), crospovidone (CP), and sodium starch glycolate (SSG) (Pahwa & Gupta, 2011; Sharma & Sonawane, 2017). CCS and SSG act primarily through swelling and wicking, whereas CP operates by capillary action with minimal swelling, resulting in a clean mouthfeel desirable in FDTs (Sheshala *et al*., 2011).

Natural alternatives have attracted considerable attention as safe, biodegradable, and cost-effective options. Starches from plant sources such as bitter yam, cassava, millet, and avocado seed have been shown to possess significant disintegrant activity (Eraga *et al*., 2017; Enadeghe *et al*., 2024). Acid-modified millet starch, for example, exhibited superdisintegrant

behavior in diclofenac potassium tablets comparable to croscarmellose sodium, validating its potential as a natural substitute (Eraga *et al*., 2017). Similarly, avocado seed starch demonstrated a dual role as binder and disintegrant, offering flexibility in formulation design (Enadeghe *et al*., 2024).

Studies on co-processed excipients combining starch with other polymers, such as microcrystalline cellulose or gelatin, have shown improved compressibility and disintegration synergy, making them particularly suited for direct-compression FDT manufacture (Nnamani & Eraga, 2022; Eraga *et al*., 2015).

1.3.3 Blends of Superdisintegrants

The use of blends of superdisintegrants has emerged as an efficient approach to achieve synergistic improvement in tablet disintegration and dissolution. The rationale lies in combining materials that exhibit complementary mechanisms—for example, a swelling disintegrant with one that acts via capillary action—to produce faster water ingress and structural breakdown (Nagendrakumar *et al*., 2010).

Eraga *et al*., (2018) demonstrated this concept by formulating paracetamol FDTs using a blend of croscarmellose sodium and Pleurotus tuber-regium powder. The blend resulted in tablets with superior disintegration time and mechanical strength compared with individual disintegrants, confirming the existence of a synergistic disintegration effect. Similarly, Thapa *et al*., (2021) compared natural and synthetic superdisintegrants in diclofenac potassium FDTs and reported that mixed systems optimized both disintegration time and dissolution rate.

Further enhancement in performance has been reported with novel co-processed systems, such as starch-polymer composites, which integrate the compressibility advantage of synthetic excipients with the rapid water uptake of natural polymers (Eraga *et al*., 2016;

Eraga *et al*, 2019). These approaches not only improve functionality but also simplify formulation by reducing the total number of excipients required.

1.4 FORMULATION APPROACHES FOR FAST DISINTEGRATING TABLETS

1.4.1 Methods of Preparation

The formulation of fast disintegrating tablets (FDTs) has evolved with the objective of producing dosage forms that rapidly disintegrate in the oral cavity, ensuring patient convenience and enhanced drug bioavailability (Parkash *et al*., 2011; Deepak *et al*., 2012). Several manufacturing techniques have been developed to achieve this goal, each offering distinct advantages and limitations in terms of tablet strength, disintegration rate, and scalability.

(a) Direct Compression Technique:

Direct compression remains the most widely utilized method for preparing FDTs due to its simplicity, cost-effectiveness, and suitability for heat- and moisture-sensitive drugs (Jivraj *et al*., 2000; Eraga *et al*., 2014). It involves the uniform blending of the drug with excipients—especially superdisintegrants—and compressing the mixture into tablets. The technique benefits from improved compressibility and flow when co-processed or multifunctional excipients are used (Eraga *et al*., 2015; Nnamani & Eraga, 2022). Co-processing enhances the binding and disintegration synergy between excipients such as microcrystalline cellulose, gelatin, and starch derivatives, leading to robust tablets with rapid disintegration.

(b) Molding and Mass Extrusion:

Molding techniques are employed to create porous structures that readily absorb saliva, resulting in fast disintegration (Shirsand *et al*., 2010). Mass extrusion involves softening the active blend with a solvent or polymeric solution, extruding it through a syringe or die, and drying the extrudate to form tablets. These methods produce highly porous tablets but often

suffer from poor mechanical strength, necessitating the use of suitable binders (El Maghraby & Elsergany, 2014).

(c) Lyophilization (Freeze-Drying):

The lyophilization method involves freezing an aqueous suspension of the drug and excipients, followed by sublimation of water under reduced pressure. This creates a porous matrix that disintegrates almost instantly upon contact with saliva (Parkash *et al*., 2011). Although this method yields excellent disintegration and dissolution characteristics, it is expensive, time-consuming, and results in fragile tablets that require specialized packaging (More & Ghadge, 2013).

(d) Spray Drying, Sublimation, and Phase Transition Techniques:

Advanced FDT preparation techniques such as spray drying, sublimation, and phase transition aim to create highly porous matrices. Spray drying yields powders with improved compressibility and disintegration profiles (Deepak *et al*., 2012). The sublimation method introduces volatile substances such as camphor or menthol into the tablet matrix, which are later removed through sublimation to leave behind pores that enhance disintegration. Recent innovations, such as combining porous starch with sublimation, have further accelerated disintegration while maintaining mechanical stability (Nadaf *et al*., 2024).

While lyophilization and spray drying ensure superior disintegration, direct compression remains the most feasible industrial method due to its simplicity, lower production cost, and compatibility with multifunctional excipients (Eraga *et al*., 2014; Nnamani & Eraga, 2022).

1.4.2 Selection of Excipients

The selection of appropriate excipients plays a pivotal role in optimizing the mechanical integrity, disintegration time, and palatability of FDTs (Jivraj *et al*., 2000; Parkash *et al*.,

2011). Each excipient class—diluents, binders, lubricants, sweeteners, and flavoring agents—contributes uniquely to the physicochemical and sensory properties of the final product.

Diluents such as microcrystalline cellulose, lactose, and directly compressible starch are commonly employed to provide bulk and enhance compressibility. Studies by Eraga *et al*., (2015) and Nnamani and Eraga (2022) demonstrated that co-processing diluents with polymers like gelatin and cellulose improves powder flow, reduces segregation, and enhances tablet strength without compromising disintegration efficiency.

Binders are selected to provide cohesive strength during compression and handling. Natural polymers such as millet starch mucilage, avocado seed starch, and cassava starch have shown promise as multifunctional binders and disintegrants (Meko *et al*., 2018; Enadeghe *et al*., 2024). These materials offer eco-friendly and cost-effective alternatives to synthetic binders while improving the mechanical resilience of FDTs.

Lubricants and Glidants like magnesium stearate and colloidal silica are incorporated to reduce friction and enhance flowability, ensuring uniform die filling during compression (Jivraj *et al*., 2000). However, excessive use may impair disintegration; hence, optimization is crucial.

Sweeteners and Flavoring Agents are essential for patient compliance, particularly in pediatric and geriatric formulations. They improve mouthfeel and mask the bitter taste of drugs such as diclofenac potassium, which is frequently used in FDT formulations for rapid pain relief (Comoglu *et al*., 2011).

Overall, successful FDT formulation depends on the synergistic interaction among excipients, where components such as multifunctional starches or co-processed systems simultaneously serve as fillers, binders, and disintegrants, simplifying formulation and enhancing product performance (Eraga *et al*., 2014; Eraga *et al*., 2015).

1.4.3 Evaluation Parameters of Fast Disintegrating Tablets (FDTs)

The evaluation of fast disintegrating tablets (FDTs) involves assessing both pre-compression and post-compression parameters to ensure optimal manufacturability, mechanical strength, and patient performance. Additionally, specialized tests are employed to assess the rapid disintegration and dissolution behavior, while *in vivo* evaluations confirm pharmacokinetic performance and patient acceptability (Parkash *et al*., 2011)

The flow and compression characteristics of the powder blend are crucial determinants of the uniformity and mechanical properties of FDTs (Eraga *et al*., 2014; Nnamani & Eraga, 2022). Parameters such as angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio are routinely evaluated to predict flowability and compressibility.

A low angle of repose (<30°) and Carr's index below 15% typically indicate good flow properties, essential for consistent die filling during tablet compression (Eraga *et al*., 2015). Studies by Eraga *et al*. (2017) demonstrated that the modification of native starches, such as acid-modified millet starch and pre-gelatinized yam starch, improves powder flow and compaction, enhancing the quality of tablets produced by direct compression. Similarly, the co-processing of excipients, as explored by Nnamani and Eraga (2022), improves both flow and compressibility due to enhanced particle size distribution and surface characteristics.

After compression, FDTs are evaluated for weight variation, hardness, friability, thickness, and drug content uniformity to ensure consistency and mechanical integrity. The hardness of FDTs should be optimized to maintain sufficient mechanical strength without compromising disintegration (Eraga *et al*., 2016). Friability values below 1% indicate good mechanical resistance, which is particularly important since FDTs are often handled without the use of water or protective packaging (Eraga *et al*., 2015).

Weight variation and content uniformity tests are critical for dosage accuracy. According to Eraga *et al*. (2018), blending natural and synthetic disintegrants, such as Pleurotus tuber-regium powder and croscarmellose sodium, yielded tablets with uniform weight and satisfactory hardness while maintaining rapid disintegration characteristics.

Given that the key feature of FDTs is rapid disintegration, specialized tests are used to assess their functional performance. These include wetting time, water absorption ratio, *in vitro* disintegration time, and *in vitro* dissolution profile.

Wetting time and water absorption ratio assess how quickly saliva can penetrate the tablet structure, which directly correlates with disintegration behavior (Eraga *et al*., 2018). A short wetting time indicates high porosity and efficient capillary action, both of which are desirable for FDTs.

The *in vitro* disintegration time is a critical quality attribute, and it should ideally be below 60 seconds (Pahwa & Gupta, 2011; Shihora & Panda, 2011). Eraga *et al*., (2017) observed that acid-modified millet starch exhibited excellent superdisintegrant activity, reducing the disintegration time of diclofenac tablets significantly. This highlights the functional superiority of modified natural starches as cost-effective alternatives to synthetic superdisintegrants.

The *in vitro* dissolution profile determines the rate and extent of drug release. Faster dissolution ensures a quicker onset of therapeutic action, particularly important for analgesic drugs such as diclofenac potassium (Comoglu *et al*., 2011).

Additional tests like taste evaluation, moisture uptake, and stability studies are conducted to assess patient compliance and storage stability. According to Eraga *et al*. (2015), the inclusion of excipients such as Pleurotus tuber-regium powder and mucin-based polymers can improve both palatability and environmental stability of FDTs.

While *in vitro* evaluations provide valuable insight into tablet performance, *in vivo* studies confirm bioavailability, pharmacokinetic behavior, and patient acceptability. The rate and extent of absorption of FDTs depend on rapid drug release and pre-gastric absorption (Chuasuwan *et al*., 2009; Chen *et al*., 2015).

Comoglu *et al*. (2011) reported that diclofenac potassium FDTs produced rapid onset of analgesic effect in migraine patients, demonstrating clinical relevance of optimized disintegration and dissolution profiles. Pharmacokinetic evaluation, therefore, remains essential to correlate *in vitro* disintegration and dissolution with *in vivo* performance. Moreover, Eraga *et al*., (2017) demonstrated that excipient modification and use of polymeric binders can modulate drug release and improve therapeutic consistency.

Patient acceptability, particularly for geriatric and pediatric populations, is also an important consideration. FDTs designed with appropriate excipients, pleasant taste, and minimal residue improve compliance and therapeutic outcomes (Ranganathan & Yoong, 2017; Pahwa & Gupta, 2011).

1.5 PREVIOUS RESEARCH ON DICLOFENAC POTASSIUM FAST DISINTEGRATING TABLETS (FDTS)

Over the past two decades, substantial progress has been made in developing fast disintegrating tablets (FDTs) of diclofenac potassium, aimed at improving the drug's onset of action, patient compliance, and bioavailability. Diclofenac potassium, a non-steroidal anti-inflammatory drug (NSAID), is commonly prescribed for the management of pain, inflammation, and musculoskeletal disorders. Its rapid absorption and potent analgesic profile make it a suitable candidate for formulation into fast disintegrating systems (Chuasuwan *et al*., 2009; Karthikeyan *et al.,* 2012).

Several formulation strategies have been employed to enhance the disintegration and dissolution of diclofenac potassium. Comoglu *et al*. (2011) developed fast-disintegrating diclofenac potassium tablets using various superdisintegrants, including croscarmellose sodium and sodium starch glycolate, demonstrating improved disintegration times and clinical efficacy in migraine patients compared to conventional tablets. Similarly, Karthikeyan *et al*. (2012) formulated rapid-release diclofenac tablets employing a combination of crospovidone and sodium starch glycolate, achieving a notable reduction in disintegration time and a faster onset of analgesic activity.

Thapa *et al*. (2021) further compared the performance of natural and synthetic superdisintegrants in diclofenac potassium FDTs, showing that natural agents such as plant-derived mucilage and modified starches exhibited comparable, and in some cases superior, disintegration efficiency relative to synthetic ones. Their findings emphasized the growing interest in eco-friendly and biocompatible excipients for sustainable tablet design.

In another approach, Abbas *et al*. (2017) designed a bilayer tablet combining an orodispersible diclofenac potassium layer with a sustained-release diclofenac sodium core. This innovative system demonstrated a dual benefit — rapid onset from the outer layer and prolonged therapeutic coverage from the inner matrix, highlighting the versatility of diclofenac formulations in addressing both acute and chronic pain.

The efficiency of FDTs largely depends on the type and concentration of superdisintegrants incorporated. Studies have consistently shown that the use of superdisintegrant blends can produce synergistic effects, resulting in faster tablet disintegration and enhanced dissolution profiles (Sharma & Telange, 2011; Shirsand *et al*., 2010). For instance, Shirsand *et al*. (2010) demonstrated that blending croscarmellose sodium with sodium starch glycolate significantly reduced disintegration time and improved wetting characteristics.

In related work on paracetamol FDTs, Eraga *et al*. (2018) reported that a blend of croscarmellose sodium and Pleurotus tuber-regium powder produced superior disintegration and mechanical strength compared to individual disintegrants. Although their study did not directly involve diclofenac, it provides compelling evidence that synergistic blends of synthetic and natural disintegrants could optimize both mechanical and dissolution properties in similar NSAID formulations.

Further contributions by Eraga *et al*. (2017) on acid-modified millet starch demonstrated its efficiency as a superdisintegrant in diclofenac tablet formulations, suggesting that starch modification through acid treatment enhances swelling and wicking abilities, thereby accelerating tablet breakdown. These findings underscore the relevance of natural starches as functional excipients in modern tablet technologies.

Comparative studies have also revealed differences in the mechanical integrity and friability of FDTs depending on formulation method and excipient type. Qandil *et al*. (2013) incorporated diclofenac potassium into Eudragit ERL/ERS matrices for sustained-release orally disintegrating tablets and found that polymer-drug interactions could be harnessed to modulate drug release kinetics. However, these formulations often suffered from poor mechanical strength, especially at higher polymer concentrations.

Despite significant advancements, certain formulation challenges persist, including achieving an optimal balance between tablet hardness and disintegration time, ensuring content uniformity, and preventing drug-excipient incompatibility. Studies such as those by Chen *et al*. (2015) highlighted that even differences in dosage form (oral solution versus tablet) could alter pharmacokinetic behavior due to variations in dissolution rates and gastric emptying times.

While numerous studies have explored the formulation of diclofenac potassium FDTs, gaps remain in understanding the interplay between disintegrant blends and tablet performance parameters. Most studies focused on individual superdisintegrants rather than their synergistic effects. Additionally, there is limited exploration of locally sourced and modified starches as multifunctional excipients for diclofenac potassium formulations, despite evidence of their promising functionality in other drugs (Eraga *et al*., 2015; Enadeghe *et al*., 2024).

The current study, therefore, seeks to build upon these earlier findings by developing and evaluating fast disintegrating diclofenac potassium tablets using a blend of synthetic superdisintegrants. This approach aims to achieve an optimal balance between mechanical strength, rapid disintegration, and effective drug release, contributing to improved therapeutic efficacy and patient convenience.

1.6 JUSTIFICATION OF THE STUDY

The formulation of fast-disintegrating tablets (FDTs) has become a significant advancement in oral drug delivery because it offers rapid onset of action, improved patient compliance, and ease of administration without the need for water (Parkash *et al*., 2011; More & Ghadge, 2013). For analgesic drugs such as diclofenac potassium—whose therapeutic effect depends largely on rapid absorption—developing an FDT ensures faster pain relief and greater patient acceptability (Comoglu *et al*., 2011; Karthikeyan *et al*., 2012).

A major determinant of FDT performance is the choice and combination of superdisintegrants, which govern tablet disintegration and subsequent drug dissolution (Pahwa & Gupta, 2011; Shihora & Panda, 2011). Superdisintegrants such as croscarmellose sodium, sodium starch glycolate, and crospovidone act by distinct mechanisms—swelling, wicking, and strain recovery—to promote rapid breakup of the tablet matrix. However, recent evidence shows

that blending two or more superdisintegrants with complementary mechanisms can produce synergistic effects, leading to superior disintegration efficiency compared with individual agents (Shirsand *et al*., 2010; Sharma & Telange, 2011).

Studies have demonstrated that combining natural and synthetic disintegrants or co-processing excipients can markedly enhance disintegration time, mechanical strength, and overall tablet quality (Eraga *et al*., 2014; 2015; 2018). For instance, the blend of Pleurotus tuber-regium powder and croscarmellose sodium yielded fast-disintegrating paracetamol tablets with improved friability and release characteristics compared to single-agent formulations (Eraga *et al*., 2018). Similarly, co-processed excipients such as those developed by Eraga *et al*. (2015) and Nnamani & Eraga (2022) have shown multifunctional behavior—acting simultaneously as binders, fillers, and disintegrants—thus improving compressibility and uniformity in direct-compression tablet formulations. These findings underscore the scientific rationale for investigating synergistic combinations of disintegrants or co-processed excipients.

Furthermore, previous works by Eraga *et al*. (2017; 2019) revealed that starches derived from local sources such as millet, bitter yam, cassava, and cocoyam possess valuable pharmaceutical properties, including favorable swelling capacity and disintegration efficiency. Utilizing such indigenous starches in combination with established synthetic disintegrants can reduce dependence on imported excipients and foster local pharmaceutical innovation. This aligns with the growing call for the development of region-specific excipient technologies that support sustainability and cost-effectiveness (Enadeghe *et al*., 2024).

Combining superdisintegrants therefore holds scientific and practical significance. Scientifically, it provides an opportunity to investigate how varying physicochemical mechanisms (wicking, swelling, deformation, and capillary action) can act synergistically to

achieve optimal tablet disintegration and dissolution (Dilebo & Gabriel, 2019; Zheng *et al*., 2022). Practically, such formulations enhance patient compliance, reduce manufacturing costs, and support the production of high-quality FDTs using locally available materials (Eraga *et al*., 2015; Meko *et al*., 2018).

The present study is thus justified on the following grounds:

1. To establish a scientific basis for the combined use of synthetic superdisintegrants to achieve rapid tablet disintegration and improved drug release.
2. To contribute to the body of knowledge in excipient technology and formulation design, promoting indigenous capacity in pharmaceutical product development.

By addressing these objectives, the study not only seeks to improve the performance of diclofenac potassium formulations but also aims to strengthen the scientific foundation for co-processing and blending of excipients as a strategy for enhanced formulation performance and patient-centric drug delivery.

1.7 AIM AND OBJECTIVES OF THE STUDY

Aim

The overall aim of this research is to formulate and evaluate fast-disintegrating tablets (FDTs) of diclofenac potassium using a blend of superdisintegrants.

Specific Objectives

1. To formulate fast disintegrating tablets of diclofenac potassium using varying ratios of sodium starch glycolate and croscamellose sodium.
2. To evaluate the pre- compression properties of the powder blends and post-compression parameters of the formulated tablets.

3. To access the disintegration time and *in vitro* dissolution profile of the formulated tablets.

CHAPTER TWO

2.0 MATERIALS AND METHODS

2.1 MATERIALS

Diclofenac potassium powder (BDH Chemicals, London, UK), Microcrystalline cellulose (Avicel PH 102), Sodium starch glycolate (SSG), Croscarmellose sodium (CCS) Lactose powder, Magnesium stearate and Talc (FMC Corporation, USA), Concentrated HCL 37% (BDH Chemicals, London).

2.2 PREPARATION OF POWDER BLEND

The formulations of the various batches of diclofenac potassium powder blends and tablets are presented in Table 2.1.

Powder blends sufficient to produce 50 tablets per batch were prepared for a total of six batches (F1–F6).

The accurately weighed quantities of diclofenac potassium, superdisintegrants, lactose, and microcrystalline cellulose were mixed geometrically in a clean, dry mortar for 5 minutes. Magnesium stearate and talc were subsequently added, and the blend was passed through a sieve No. 60 to ensure uniform particle size.

The resulting blend was evaluated for its pre-compression flow properties before compression.

Table 2.1: Formula for the preparation of diclofenac powder blends and tablets

Ingredients (mg)	**Batches**					
	F1	F2	F3	F4	F5	F6
Diclofenac Potassium	50	50	50	50	50	50
Sodium Starch Glycolate	225	225	150	112.5	75	-
Croscamellose Sodium	-	75	150	112.5	225	225
Avicel	110	110	110	110	110	110
Lactose	105	30	30	105	30	105
Magnesium Stearate	5	5	5	5	5	5
Talc	5	5	5	5	5	5
Total	**500**	**500**	**500**	**500**	**500**	**500**

2.3 EVALUATION OF PHYSICOCHEMICAL PROPERTIES OF POWDER BLENDS

2.3.1 Bulk Density (Db)

A weighed amount of the powder blend was transferred into a 50 mL graduated cylinder, and the initial volume (V_0) was recorded. The bulk density was calculated using:

$D_b = m/V_0$……..(1)

where *m* is the mass of the powder and V_0 is the bulk volume.

2.3.2 Tapped Density (Dt)

The cylinder containing the sample was tapped 100 times, and the final volume (V_{100}) recorded. The tapped density was calculated as:

$D_t = m/V_{100}$……(2)

2.3.3 Angle of Repose (θ)

The angle of repose was determined by the funnel method. The powder was allowed to flow through a funnel onto a flat surface until a conical pile was formed. The height (h) and diameter (d) of the pile were measured, and the angle of repose calculated using:

$\tan \theta = 2h/d$…….(3)

Lower values of θ indicate better flow properties.

2.3.4 Carr's Index (CI) and Hausner's Ratio (HR)

These parameters were derived from the bulk and tapped densities as follows:

$CI = (D_t - D_b/D_t) \times 100$……(4)

$HR = D_t/D_b$……..……(5)

Carr's Index values below 15% and Hausner's ratios below 1.25 indicate good flow properties.

2.4 PREPARATION OF DICLOFENAC POTASSIUM TABLETS

Six batches of fast-disintegrating tablets (F1–F6) were prepared by direct compression. Each batch contained at least 40 tablets.

The previously prepared powder blends were compressed using a multi-punch tablet compression machine to obtain tablets weighing approximately 500 mg each.

The tablets were stored in airtight containers until further evaluation.

2.5 EVALUATION OF TABLET PROPERTIES

2.5.1 Weight Uniformity

Twenty tablets were randomly selected and weighed individually using a digital balance. The average weight and percentage deviation were determined.

2.5.2 Hardness Test

The crushing strength of three tablets from each formulation was determined using a Monsanto hardness tester, and results expressed in kg/cm^2.

2.5.3 Friability

Ten tablets were accurately weighed (W_i) and placed in a friabilator rotating at 25 rpm for 4 minutes. The tablets were dedusted and reweighed (Wf). Friability (%) was calculated as:

$$\text{Friability} = (W_i\text{-}Wf/W_i) \text{ X } (100/1) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (6)$$

A friability value below 1% was considered acceptable.

Where

W_i = Initial Weight of tablets before test

Wf = Final Weight of tablets after test.

2.5.4 *In Vitro* Disintegration Time

The disintegration time of six tablets was determined using the British Pharmacopoeia (BP) disintegration apparatus with distilled water maintained at 37 ± 2°C. The time taken for complete disintegration of each tablet with no palpable mass remaining was recorded in minutes.

2.5.5 *In Vitro* Dissolution Study

Dissolution studies were performed using the USP Type II (paddle) apparatus.

Each vessel contained 600 mL of 0.1 N HCl maintained at 37 ± 0.5°C, and the paddle speed was set to 50 rpm. One tablet was placed in each vessel.

At predetermined time intervals, 5 mL aliquots were withdrawn and replaced with an equal volume of fresh medium. The samples were filtered, and the absorbance was measured at 276 nm using a UV–Visible spectrophotometer with 0.1 N HCl as blank.

The cumulative percentage of diclofenac potassium released was calculated using a previously established calibration curve.

All measurements were performed in triplicate, and results expressed as mean ± standard error of mean (SEM).

CHAPTER THREE

3.0 RESULT AND DISCUSSION

3.1 EVALUATION OF PHYSICOCHEMICAL PROPERTIES OF POWDER BLENDS

The powdered blends were evaluated for bulk density, tapped density, angle of repose, Hausner's ratio and Carr's index and the results are shown in Table 3.1.

3.1.2 Bulk Density

The bulk density values of the powder blends ranged from 0.30 to 0.55 g/cm³. According to USP standards, powders with bulk density values between 0.25 and 0.65 g/cm³ generally exhibit acceptable packing properties and flow behavior for tablet formulation. Therefore, the values obtained in this work fall within the acceptable range, suggesting that all the formulations possessed good bulk packing characteristics suitable for direct compression.

The slightly higher bulk density observed in batch F1 (0.55 g/cm³) indicates that the powder particles were more closely packed, which may enhance weight uniformity during tablet compression. Conversely, the lower value in F6 (0.30 g/cm³) suggests a more porous blend, which could contribute to faster water penetration during disintegration but may require careful control to prevent weight variation during tableting.

3.1.3 Tapped Density

The tapped density values for the blends ranged from 0.44 to 0.73 g/cm³, which are within the typical USP acceptable range for granules and powder mixtures (0.40–0.80 g/cm³). These values indicate that the powder blends had satisfactory compressibility and could be compressed into tablets without major issues of capping or lamination. The relatively higher tapped density in F2 (0.73 g/cm³) suggests improved particle rearrangement and packing efficiency upon tapping, which can contribute to good tablet strength

Table 3.1: Physiochemical properties of powder blends

Batch	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Carr's Index (%)	Hausner's Ratio	Angle of repose (^{o})
F1	0.55	0.67	17.89	1.22	34.59
F2	0.54	0.73	26.17	1.35	30.02
F3	0.42	0.53	20.75	1.26	37.87
F4	0.41	0.51	19.02	1.23	38.02
F5	0.31	0.44	28.25	1.39	41.27
F6	0.30	0.44	33.79	1.50	45.0

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3.1.4 Carr's Index

According to the USP, Carr's Index values below 15% indicate excellent flow, 15–20% good, 20–35% fair to passable, and above 35% poor flow. In this study, the Carr's Index values ranged from 17.89% to 33.79%, showing that most batches had fair to good flow properties. Batches F1, F3, and F4 had values below 20%, which signifies good compressibility and flow suitable for direct compression. However, F5 (28.25%) and F6 (33.79%) showed higher values, indicating less efficient particle packing and slightly poorer flow. Despite this, the blends were still within workable limits for tablet production, as no segregation or capping was observed during compression. This implies that all blends possessed acceptable flow and compaction behavior for uniform tablet formation.

3.1.5 Hausner's Ratio

It is the ratio of tapped to bulk density and is also recognized by the USP as a standard test for flowability. According to the USP, Hausner's ratio values below 1.25 indicate good flow, 1.25–1.5 suggest passable flow, and above 1.5 indicate poor flow. In this study, Hausner's ratio ranged from 1.22 to 1.50, meaning most formulations exhibited good to passable flow properties. The lowest ratio was observed in F1 (1.22), suggesting good flow, while F6 (1.50) approached the upper limit of passable flow, indicating some degree of particle cohesion that might reduce flow efficiency.

3.1.6 Angle of Repose

According to USP guidelines, an angle of repose below 30° indicates excellent flow, 30–40° good, 40–45° passable, and above 45° poor flow. The angles of repose obtained in this study ranged from 30.02° to 45.0°, indicating that the powder blends possessed good to passable flow properties. Specifically, F2 (30.02°) showed the best flow, while F6 (45.0°) had the poorest. The good flow observed in F1–F3 ensured smooth die filling during tablet

compression, contributing to the uniformity in tablet weight and thickness seen in the post-compression results. The slightly higher angle in F5 and F6 could be due to the higher content of croscarmellose sodium, which tends to increase cohesiveness, leading to slower powder flow.

3.2 EVALUATION OF POST COMPRESSION PROPERTIES OF TABLETS

The results obtained from the tests carried out on the tablets in Batches F1-F6 are shown in Table 3.2.

3.2.1 Weight Uniformity

According to the British Pharmacopeia (BP), for tablets weighing 250 mg or more, the permissible percentage deviation should not exceed ±5%.

In this study, the average tablet weights ranged from 483.5 ± 0.79 mg (F5) to 494.0 ± 1.15 mg (F3). All batches fell well within pharmacopoeia limits, indicating excellent weight uniformity and accurate die filling during compression. The low standard deviations also confirm that the powder blends had adequate flow and compressibility, which prevented weight variation from one tablet to another. This uniformity is essential for consistent dosing and therapeutic effectiveness of diclofenac potassium.

3.2.2 Hardness (Crushing Strength)

In this study, hardness values ranged approximately between 8.4 and 8.8 kg/cm² across all batches. These values fall within the generally accepted range for tablets (3–9 kg/cm²). The results indicate that the tablets had adequate mechanical strength to resist mechanical shock without being too hard to disintegrate quickly. The slightly higher hardness in batches containing more croscarmellose sodium (such as F2 and F6) suggests that CCS contributed to better binding within the matrix, providing strength without significantly delaying disintegration.

Table 3.2 Evaluation of Diclofenac potassiumTablets

Batch	Tablet Weight (mg)	Tablet Crushing Strength (KP)	Friability (%)	Disintegration Time (Secs)
F1	491.2 ± 1.268	8.6 ± 0.187	0.06	83.83 ± 5.382
F2	492.5 ± 1.517	8.8 ± 0.123	0.13	71.50 ± 4.137
F3	494.0 ± 1.149	8.5 ± 0.158	0.1	270.70 ± 6.902
F4	483.7 ± 1.317	8.4 ± 0.187	0.12	190.0 ± 1.932
F5	483.5 ± 0.786	8.4 ± 0.187	0.08	206.80 ± 2.007
F6	484.8 ± 1.397	8.4 ± 0.187	0.12	151.30 ± 5.554

3.2.3 Friability

According to USP standards, the acceptable friability limit for compressed tablets is not more than 1% weight loss after testing. The friability results in this study ranged from 0.06% to 0.13%, which are well below the USP limit. This indicates that the tablets had excellent mechanical resistance and could withstand the stress of handling and transportation. The low friability values further confirm that the compression force and binder concentration used were optimal, providing strong, cohesive tablets suitable for packaging and distribution.

3.2.4 Disintegration Time

Disintegration time is the most critical parameter for fast disintegrating tablets (FDTs). The European pharmacopoeia (EP) specifies that FDTs should disintegrate within 30 to 120 seconds when placed in water at 37 ± 2°C.

In this study, disintegration times ranged from 71.50 ± 4.14 seconds (F2) to 270.70 ± 6.90 seconds (F3). Formulation F2 exhibited the fastest disintegration and thus best met the USP specification for FDTs. This rapid disintegration can be attributed to the balanced blend of sodium starch glycolate (which swells rapidly) and croscarmellose sodium (which facilitates wicking and water penetration).

On the other hand, F3, with equal amounts of both superdisintegrants, had the slowest disintegration (270.7 s), which exceeds the EP upper limit. This slower disintegration could be due to excessive swelling that led to gel formation, hindering water penetration.

Formulations F1, F4, F5, and F6 showed intermediate disintegration times (ranging between 83 and 206 seconds), with most still within or close to the EP acceptable range. Overall, the results indicate that F2 achieved the optimal balance between mechanical strength and disintegration efficiency, meeting the EP standard for fast disintegrating tablets.

3.2.5 Dissolution rate

Prior to the dissolution test, a standard calibration curve of the pure active ingredient

was carried out, the plot is shown in Figure 3.1.

The equation of the straight line obtained from linear regression o the data is given by:

$Y = MX + C$…….. (7)

Where;

Y = y-axis (Absorbance)

M = Slope

X = x-axis (concentration)

C = Intercept of curve on the y-axis

The data for the derivation of the standard curve for Paracetamol are listed in Table 5.1.

Analysis of the data yielded the following:

M (Slope) = 0.0006

C (Intercept on y-axis) = 0.0032

Such that the equation of the straight line (Y = MX + C) is

$Y = 0.0006x + 0.0032$

The correlation coefficient (r^2) was 0.994.

The percentage drug released per unit time was calculated using the formula:

$M_t/M_0 \times 100$……(8)

Where;

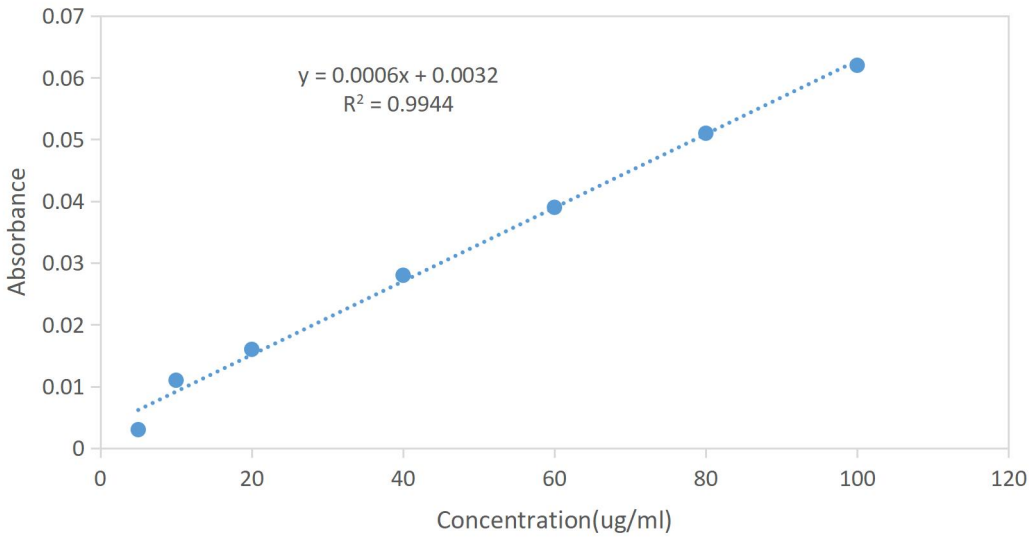

Figure 3.1 Standard Calibration plot of Diclofenac potassium

M_0 = Amount of Drug

M_t = Amount of Drug released at time t.

M_t = Concentration of drug × Dissolution factor × Volume of diluent

The standard calibration curve of Diclofenac potassium gave a straight line curve which confirms that Beer - Lambert's law was obeyed within the concentration range used. The law states that the intensity of beam of parallel monochromatic radiation decreases exponentially as it passes through a medium of homogeneous thickness.

The dissolution profile of diclofenac potassium tablets showing the rate of drug release for each batch is shown in Figure 3.2.

The dissolution profile of the six diclofenac potassium formulations (F1–F6) revealed distinct variations in drug release rates due to differences in the type and proportion of superdisintegrants used. Formulations F1 and F2 exhibited the most rapid and complete drug release, achieving over 90% dissolution within 40 minutes, which complies with the USP requirement of at least 80% release within 30 minutes for fast-disintegrating tablets. The enhanced performance of F1 and F2 can be attributed to the effective disintegration and wetting facilitated by sodium starch glycolate and croscarmellose sodium, whose combined swelling and wicking actions promoted rapid matrix breakdown and drug diffusion. F6 also showed satisfactory release (about 78% in 30 minutes), though slightly slower, likely due to higher croscarmellose sodium concentration, which may have caused localized gel formation that delayed medium penetration. In contrast, formulations F3, F4, and F5 demonstrated slower and incomplete drug release, with less than 60% dissolved after 30 minutes, indicating suboptimal superdisintegrant ratios and reduced porosity that limited water uptake.

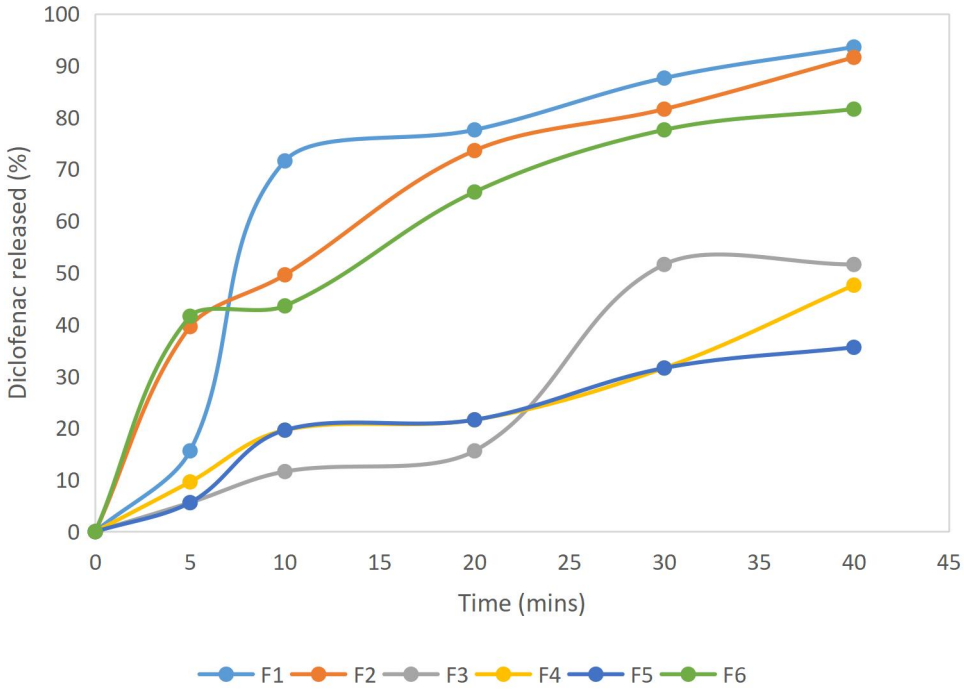

Figure 3.2: Dissolution profile of Diclofenac tablets containing different concentrations of the superdisintegrants.

Overall, the trend in drug release rate followed the order F1 > F2 > F6 > F5 > F4 > F3, confirming that the choice and proportion of superdisintegrants critically affect dissolution efficiency. These findings establish that formulations containing optimized amounts of sodium starch glycolate and croscarmellose sodium can provide a balance between mechanical strength and rapid drug release, making them suitable for fast-disintegrating diclofenac potassium tablets aimed at ensuring quick onset of action and improved patient compliance.

CHAPTER FOUR

4.1 CONCLUSION

This study successfully formulated and evaluated fast-disintegrating tablets (FDTs) of diclofenac potassium using varying concentrations and combinations of sodium starch glycolate (SSG) and croscarmellose sodium (CCS) as superdisintegrants. All pre- and post - compression parameters were within acceptable limits, indicating good powder flow, tablet uniformity, and mechanical strength. The dissolution profile revealed that formulations F1 and F2 exhibited the most desirable characteristics, achieving over 90% drug release within 40 minutes, which meets USP requirements for fast-disintegrating tablets. The rapid disintegration and high dissolution rate of these formulations can be attributed to the synergistic action of the selected superdisintegrants, which enhanced water uptake and tablet breakup. Overall, the study confirms that the direct compression method is an effective and reliable technique for producing diclofenac potassium FDTs with rapid onset of action and improved patient compliance.

4.2 RECOMMENDATIONS

Based on the findings of this study, formulations F1 and F2 are recommended as optimized formulations for fast-disintegrating diclofenac potassium tablets due to their excellent disintegration and dissolution profiles. Further studies should focus on *in vivo* evaluation to confirm the correlation between *in vitro* dissolution performance and actual bioavailability. Additionally, stability testing under various storage conditions should be conducted to determine the shelf life and robustness of the optimized formulations. Future research may also explore the incorporation of taste-masking agents and alternative natural superdisintegrants to improve palatability and cost-effectiveness, thereby enhancing patient acceptance and commercial viability.

4.3 LIMITATIONS OF THE STUDY

The study was conducted using conventional laboratory-scale equipment, some of which were old and lacked advanced precision, which may have influenced certain parameters such as compression force and mixing uniformity. This limitation could affect the reproducibility of results if the study were to be replicated on a large or industrial scale. In addition, the study focused solely on *in vitro* evaluation without conducting *in vivo* bioavailability or pharmacokinetic studies, which are crucial for confirming clinical efficacy. The research also excluded stability testing, which would have provided insights into the long-term behavior of the formulations under various storage conditions. Moreover, only two synthetic superdisintegrants (SSG and CCS) were evaluated, limiting broader comparison with natural alternatives. Despite these constraints, the study provides valuable foundational data that can guide further optimization and industrial development of diclofenac potassium fast-disintegrating tablets.

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