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Formulation and Evaluation of Fast Disintegrating Sustained Release Formulation of Diclofenac Sodium

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ABSTRACT-

This study aimed to formulate and evaluate fast disintegrating tablets (FDTs) to improve patient compliance and achieve rapid drug onset. A model drug was incorporated into multiple formulations using various superdisintegrants, including Crospovidone and Sodium Starch Glycolate, at different concentrations. The tablets were prepared by the direct compression method and subjected to comprehensive evaluation of pharmaceutical parameters such as hardness, friability, weight variation, disintegration time, drug content uniformity, and in vitro dissolution profile. Among all formulations, the tablet containing Crospovidone at an optimized concentration exhibited the shortest disintegration time along with a superior drug release profile. The results demonstrated that the type and concentration of superdisintegrants play a crucial role in determining the disintegration efficiency and drug release behavior of FDTs. This study highlights the potential of Crospovidone-based formulations for developing effective fast disintegrating tablets, which could enhance patient compliance and provide improved therapeutic outcomes.

Keywords- Fast Disintegrating Tablets, Super disintegrants, Crospovidone, Direct Compression, Disintegration Time, Drug Release.

1.INTRODUCTION

The oral route remains the most widely used and convenient method for drug administration due to its simplicity, patient acceptance, and accurate dosing. However, drugs that are rapidly absorbed and have short half-lives tend to be quickly eliminated from the bloodstream. To address this, controlled-release oral formulations have been developed, allowing for the slow release of drugs to maintain a steady concentration in the blood over extended periods.

Among oral dosage forms, tablets and capsules dominate because they are easy to administer, cost-effective, and offer precise dosing. These forms have evolved to include novel delivery systems such as nanoparticles and microspheres, improving drug targeting and release profiles. Drug delivery technologies now often use carriers to control drug release rates or target specific sites in the body, enhancing therapeutic outcomes.

Despite these advances, delivering drugs through the skin via transdermal delivery systems has limitations, especially for drugs meant to act locally on the skin. Research is ongoing to develop systems that deliver drugs directly and controllably to the epidermis without significant systemic absorption.Fast disintegrating tablets (FDTs) represent a significant advancement in oral drug delivery. These tablets dissolve or disintegrate rapidly in the mouth, typically within 30 to 60 seconds, without the need for water. This feature greatly benefits patients who have difficulty swallowing traditional tablets, such as pediatric, geriatric, or mentally challenged individuals, and those who lack access to water, such as travelers. Upon disintegration, the drug is either absorbed through the oral mucosa or swallowed, enabling quick therapeutic action.The advantages of FDTs include accurate dosing, rapid onset of action, improved bioavailability due to partial absorption in the mouth and upper gastrointestinal tract, enhanced patient compliance, and better taste masking through the use of flavors and sweeteners. Additionally, FDTs reduce the risk of choking and improve convenience for special populations. They can be manufactured using conventional equipment at low costs, making them commercially viable.However, FDTs also present challenges. Their porous nature can make them brittle and sensitive to moisture, requiring careful formulation and packaging to maintain stability. Patients with dry mouth may experience difficulty with these formulations due to insufficient saliva to aid disintegration.The development of FDTs faces several hurdles: ensuring rapid disintegration, maintaining adequate mechanical strength, preventing residue in the mouth, protecting from moisture, and achieving compatibility with taste masking agents. Various preparation techniques exist, including direct compression, lyophilization (freeze drying), sublimation, spray drying, tablet molding, and mass extrusion. and excipients, FDTs are poised to expand their role in modern pharmaceutical therapy.

VARIOUS TECHNIQUES FOR "FDTs" PREPARATION:

Many techniques are used for the preparation of fast disintegrating tablets which are as follows

Disintegrant Addition: This technique involves adding superdisintegrants like sodium starch glycolate, crospovidone, or cross-carmellose in optimal amounts to ensure fast disintegration and good mouthfeel. The tablets are similar to conventional ones but have higher disintegrant content, lower hardness, and higher friability.

Freeze Drying (Lyophilization): The drug is dissolved or dispersed in a solution, frozen, and then dried by sublimation at low temperatures. This

produces highly porous tablets with a large surface area, leading to rapid dissolution and improved bioavailability.

Tablet Molding: Powder blends are moistened with a hydroalcoholic solvent, molded under low pressure, and then air-dried. These tablets are less compact, porous, and dissolve faster than conventional compressed tablets.

Sublimation: Volatile substances like camphor or ammonium bicarbonate are mixed with tablet ingredients, compressed, and then removed by sublimation to create a porous structure that enhances dissolution.

Spray-Drying: This method uses gelatin, mannitol, disintegrants, and acidic or alkaline agents in the formulation. The tablets rapidly disintegrate, usually within 20 seconds, when placed in an aqueous medium.

Direct Compression: This is the simplest and most cost-effective method, involving direct compression of powders using standard equipment and excipients, requiring fewer processing steps.

2.Literature Review

Patel et al. (2023) developed FDTs of levocetirizine dihydrochloride using different concentrations of synthetic superdisintegrants such as sodium starch glycolate (SSG) and crospovidone. The study showed that formulations containing 6% crospovidone had the fastest disintegration time of 17 seconds, without compromising tablet hardness or friability. Their findings highlight the significance of selecting the right type and concentration of superdisintegrant for optimum tablet performance.

Singh and Mehra (2022) investigated the role of co-processed excipients in enhancing the flowability and compressibility of the powder blend used in FDTs of amlodipine besylate. Their work emphasized that co-processed lactose-microcrystalline cellulose (MCC) mixtures improved not only mechanical strength but also reduced disintegration time to under 30 seconds, indicating their dual functionality in formulation.

Kumar et al. (2021) focused on the sublimation technique to develop oro-dispersible tablets of domperidone. Camphor and menthol were used as subliming agents, which were later removed by vacuum drying, resulting in porous tablets with a significantly enhanced disintegration profile. The optimized formulation disintegrated in 15–20 seconds, offering a promising strategy for improving bioavailability of poorly soluble drugs.

Sharma and Jain (2020) explored natural superdisintegrants, specifically mucilage of Plantago ovata and powder of fenugreek seeds, in the formulation of FDTs of paracetamol. Compared to synthetic disintegrants, the natural alternatives demonstrated comparable disintegration efficiency with added benefits of biocompatibility and low cost, suggesting their potential use in herbal or green formulations.

Bansal et al. (2019) formulated palatable FDTs of metoclopramide HCl using ion-exchange resins (Tulsion 335) for taste masking. Their study confirmed that ion-exchange complexes significantly improved patient acceptability without affecting disintegration or dissolution profiles. The tablets exhibited excellent disintegration within 25 seconds and uniform drug content.

Rao and Reddy (2018) utilized the lyophilization (freeze-drying) technique to prepare FDTs of risperidone, a drug used for schizophrenia. The resulting tablets had high porosity and low hardness, disintegrating in less than 20 seconds. Their study confirmed that lyophilization produces elegant, fast-acting formulations, though at a higher production cost.

Deshmukh et al. (2017) applied central composite design to optimize the formulation of ODTs of ondansetron. The study evaluated the effect of variables like superdisintegrant concentration and compression force on tablet properties. Results indicated that a combination of 5% crospovidone and 2% MCC yielded the most desirable disintegration time and drug release profile.

3.Materials:

Diclofenac Sodium was obtained as a gift from Schwitz Biotech, Ahmedabad. Microcrystalline cellulose (Avicel), magnesium stearate, sodium alginate, and calcium chloride were supplied by the college. All chemicals were of analytical grade and used without further purification.

Methods:

Microspheres were prepared using the ionotropic gelation technique. Carbopolwas dispersed in cold water with the drug and allowed to swell for 2–3 hours. Separately, sodium alginate was dissolved in water and mixed with the carbopol-drug solution to form a viscous mixture. This solution was then added dropwise via a 21-gauge syringe into a 4% calcium chloride solution under continuous stirring. The formed microspheres were collected by filtration, dried at 30–40°C for 2–3 days, and stored in a sealed container for later use. (Table 1)

Table 1: Formulations of microspheres

Code of Formulation	Drug	Polymer Carbopol (mg)	Sod. Alginate (mg)	Carbopol + Sod. Alginate(mg)	Drug: Polymer Ratio
F1	100	0	100	100	1:1
F2	100	0	200	200	1:2
F3	100	0	300	300	1:3
F4	100	0	400	400	1:4
F5	100	100	100	200	1:2
F6	100	200	100	300	1:3
F7	100	300	100	400	1:4

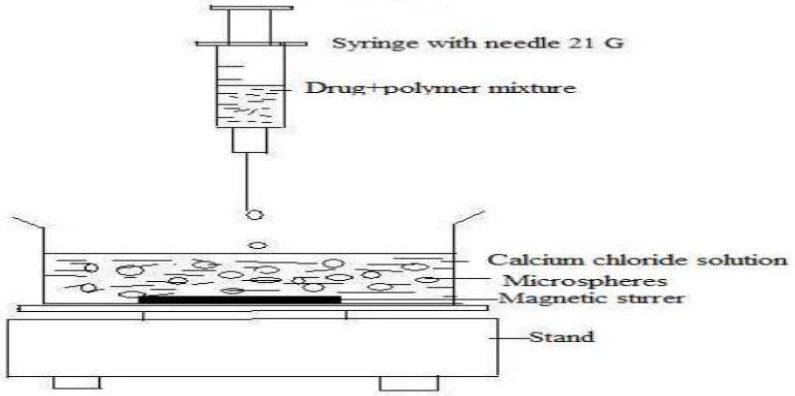

Figure1: Ionic gelation technique

Evaluation of Microspheres

Particle Size Analysis:
Particle size of microspheres was measured using a digital microscope.

Drug Entrapment Efficiency and Loading:
Known amounts of microspheres (containing theoretically 100 mg drug) were crushed and dissolved in phosphate buffer (pH 7.4). After stirring and 24-hour soaking, the solution was filtered and analyzedspectrophotometrically.

- *Entrapment Efficiency (%)* = (Actual drug content / Initial drug content) × 100
- *Drug Loading (%)* = (Amount of drug in microspheres / Weight of microspheres) × 100

Swelling Study:
Microspheres (50 mg) were immersed in distilled water, 0.1N HCl, and PBS (pH 7.4) until equilibrium swelling. The degree of swelling was calculated as:
Degree of swelling (a) = (Weight after swelling − Initial weight) / Initial weight

In Vitro Release Study:
Dissolution was performed using USP paddle method at 75 rpm and 37±0.5°C. Microspheres equivalent to 100 mg drug were tested in 900 ml 2% SLS in 0.1 N HCl for 2 hours, followed by 900 ml 1% SLS in pH 6.8 phosphate buffer for 10 hours. Samples were withdrawn at intervals, filtered, and analyzedspectrophotometrically.

Tablet Formulation:
Fast disintegrating tablets were prepared by direct compression using microspheres mixed with microcrystalline cellulose, superdisintegrants, and mannitol. The best ratio based on disintegration time and hardness was selected. Magnesium stearate was addedbefore compressing into tablets.

Table 2: Formulation of FDT of Diclofenac Sodium

Sr. No.	Ingredients	Formulations					
		S1	S2	S3	S4	S5	S6
1	Microspheres	250	250	250	250	250	250
2	SSG	6	9	12	6	9	12
3	Mannitol	15	15	15	15	15	15
4	MCC	121.5	118.5	115.5	121.5	118.5	115.5
5	Magnesium stearate	7.5	7.5	7.5	7.5	7.5	7.5
	Total weight (mg)	400	400	400	400	400	400

Evaluation of Tablets

Tablets were evaluated for thickness, weight variation, hardness, friability, drug content, wetting time, disintegration time, and in vitro dissolution using standard methods.

Thickness:
Measured using a Vernier caliper.

Weight Variation:
Twenty tablets were weighed individually; none deviated more than ±5% from the mean.

Friability:
Ten tablets were tested in a friabilator at 25 rpm for 4 minutes. Percent friability was calculated by comparing weights before and after the test.

Drug Content:
Powdered tablets were dissolved in phosphate buffer (pH 7.4), stirred, filtered, and analyzed spectrophotometrically. Average values were calculated from three tablets.

Wetting Time:
A tablet was placed on folded tissue paper soaked with simulated saliva (pH 6.8), and the time to complete wetting was recorded. Average time from three tablets was noted.

Disintegration Time:
Tested in phosphate buffer (pH 6.8) at 37±2°C using a tablet disintegration apparatus. Time for complete disintegration of six tablets was recorded.

In Vitro Dissolution:
Dissolution was performed using USP paddle method at 75 rpm and 37±0.5°C. Tablets were tested in 900 ml 2% SLS in 0.1 N HCl for 2 hours, followed by 900 ml 1% SLS in pH 6.8 phosphate buffer for 10 hours. Samples were withdrawn, filtered, and analyzed spectrophotometrically for drug release.

4. Results and Discussion

Evaluation of Microspheres

Particle Size Analysis

Particle size can be determined by using Digital microscope. The mean diameter of Diclofenac Sodium microspheres was found in between 79.36±0.43 to 90.20±0.34 µm (Table 3).

Table 3: Mean particle size of microspheres

Sr. No.	Formulation code	Mean Particle size (µm)
1	F1	84.28±0.68
2	F2	82.12±0.22
3	F3	80.40±0.46
4	F4	79.36±0.43
5	F5	84.32±0.32
6	F6	90.20±0.34
7	F7	89.33±0.54

Drug entrapment efficiency and drug loading

The percent encapsulation efficiency was increased upto 80.4±0.26 % with increasing polymer concentration (Table 4).

Table 4: Drug entrapment efficiency and Drug loading of microspheres

Sr. No.	Formulation code	DEE (%)	DL (%)
1	F1	48.44±0.66	24.22±0.33
2	F2	52.6±0.36	26.3±0.18
3	F3	56.8±0.72	28.4±0.36
4	F4	64.48±0.40	32.24±0.2
5	F5	68.90±0.48	34.45±0.24
6	F6	74.64±0.44	37.32±0.22
7	F7	80.4±0.26	40.2±0.13

Swelling study (Degree of swelling)

Prepared microspheres swell in distilled water, 0.1N HCl and phosphate buffer 6.8 (Table 5).

Table 5: Swelling study of prepared microspheres

Sr. No.	Formulation	Degree of swelling		
		0.1 N HCL	Distilled water	Phosphate buffer 6.8
1	F1	0.27	0.42	0.82
2	F2	0.33	0.49	0.96
3	F3	0.34	0.55	1.13
4	F4	0.45	0.61	1.25
5	F5	0.54	0.70	1.30
6	F6	0.64	0.79	1.41
7	F7	0.71	0.98	1.58

In Vitro Drug Release:

Dissolution was performed using USP paddle apparatus at 75 rpm and 37±0.5°C. Microspheres equivalent to 100 mg Diclofenac Sodium were tested in 2% SLS (0.1 N HCl) for 2 hours, then in 1% SLS (pH 6.8 phosphate buffer) for 10 hours.

Tablet Formulation:

Formulation F7 showed optimal particle size, drug entrapment, swelling, and release, and was selected for fast-disintegrating tablet preparation using Crospovidone and Sodium starch glycolate by direct compression.

Tablet Evaluation:

Six formulations were evaluated for thickness, weight variation, hardness, friability, drug content, wetting time, and disintegration time (see Tables 6 & 7).

Table 6: Evaluation of the tablets (S1, S2, S3)

Sr. No.	Evaluation parameters	Formulations		
		S1	S2	S3
1	Thickness (mm)	4.6	4.6	4.6
2	Weight variation (mg)	398.58	400.2	399.4
3	Hardness (kg/cm2)	4.2±0.6	4.6±0.4	4.5±0.2
4	Friability (%)	0.72±0.4	0.74±0.36	0.56±0.4
5	Drug content (%)	99.7±0.2	100.1±0.3	100.2±0.2
6	Wetting time (sec)	44.3±1.6	42.3±2.4	39.2±2.1
7	In-vitro disintegration time (sec)	66.2±2.1	58.4±2.2	51.2±1.8

Table 7: Evaluation of the tablets (S4, S5, S6)

Sr. No.	Evaluation parameters	Formulations		
		S4	S5	S6
1	Thickness (mm)	4.6	4.6	4.6
2	Weight variation (mg)	399.08	401.44	400.6
3	Hardness (kg/cm2)	4.2±0.3	4.4±0.7	4.6±0.8
4	Friability (%)	0.66±0.09	0.56±0.24	0.67±0.4
5	Drug content (%)	99.8±0.2	100.0±0.4	99.8±0.3
6	Wetting time (sec)	64.2±1.6	60.1±0.8	54.8±1.3
7	In-vitro disintegration time (sec)	80.4±1.6	73.1±1.5	62.1±2.0

5. Conclusion

This study successfully developed stable sustained-release fast disintegrating Diclofenac Sodium tablets, combining prolonged drug release with easy swallowing. This approach benefits patients with swallowing difficulties and ensures steady drug levels, reducing side effects. Formulation F7 showed the best particle size, drug loading, swelling, and release, and was selected for tablet preparation.

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