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FORMULATION AND EVALUATION OF FAST DISINTEGRATING TABLET OF DICLOFENAC SODIUM

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ABSTRACT

Diclofenac sodium is among the most extensively used NSAIDS; employed in rheumatoid arthritis and osteoarthritis, affords quick relief of pain and wound edema. Fast disintegrating tablets are gaining prominence as new drug delivery systems. These dosage forms disintegrate within a minute with very less quantity of water. Fast disintegrating tablets of Diclofenac sodium were prepared by direct compression method after incorporating superdisintegrants like Croscarmellose sodium (CCS) and Crospovidone (Polyplasdone XL) in different concentrations. Six formulations comprising superdisintegrants at different concentration levels were prepared to access their efficiency and critical concentration level. Different types of evaluation parameters for tablets were performed. Tablets containing combination of croscarmellose sodium and crospovidone at two different concentrations (3.7% and 2.7%) and (4.2% and 3.2%) show excellent and almost similar in-vitro disintegration time and drug release profile as compared to other formulations.

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Key Words

Diclofenac sodium, Direct
compression method,
Superdisintegrants, Fast
disintegrating agent.

INTRODUCTION

Conventional tablet and hard gelatin capsule dosage forms possess higher disintegration time so patients obtain pharmacological effect after 30 to 45 minutes of dosage form administration that may result in high incidence of non-compliance and variable bioavailability^[1]. Fast disintegrating tablets are gaining prominence as new drug delivery systems. These dosage forms disintegrate within a minute with very less quantity of water. This can be achieved by addition of various superdisintegrants like croscarmellose sodium, crospovidone, sodium starch glycolate alone or in various combinations. Due to the fast disintegration of dosage form, patients obtain quick pharmacological effect of active pharmaceutical ingredient^[1-4].

Diclofenac sodium is a traditional non-steroidal anti-inflammatory (NSAIDs) drug. It is nonselective cyclooxygenase inhibitor. It inhibits the prostaglandin synthesis. Sodium Salt increase stability and reduce side effects. It is used as analgesic, anti-inflammatory and antipyretic. It is well absorbed orally, 99% protein bound, metabolized and excreted both in urine and biles. The plasma $t_{1/2}$ is 2 hours. However it has good tissue penetrability and concentration in synovial fluid is maintained for 3 times longer period then in plasma, exerting extended therapeutic effect within joints. Diclofenac sodium is among the most extensively used NSAIDs; employed in rheumatoid arthritis and osteoarthritis, bursitis, ankylosing spondylitis, toothache, dysmenorrhoea, post-traumatic and

postoperative inflammatory conditions, affords quick relief of pain and wound edema^[5,6]. In this study, an effort has been made to formulate Fast disintegrating tablets of Diclofenac sodium using two different disintegrants. Objective of study was to enhance safety and efficacy of drug molecule, achieve better compliance and enhance onset of action.

MATERIALS AND METHODS

Materials:

Diclofenac sodium, Crospovidone and Talc (Seva fine chemicals, Ahmedabad), Croscarmellose sodium (Thrien enterprise, Ahmedabad), Mannitol (Rankem chemicals, New Delhi), Aerosil and Lactose DCL 11 (C D H labo. Mumbai), Saccharin sodium and Menthol (Loba chemicals, Mumbai), Citric acid (S D fine chemicals Ltd., Mumbai), Magnesium stearate (Chemdyes corporation, Rajkot), Microcrystalline cellulose PH 101 (MCC) (Astron chemicals, Ahmedabad).

Preparation of tablets:

Weigh all the ingredients accurately according to Table 1 and pass through sieve # 40. Mix all the ingredients geometrically except Aerosil, Talc and Magnesium Stearate. Then lubricate the blend with Aerosil, Talc and Magnesium Stearate. Powder mixture was compressed on eight station rotary tableting machine (Hardik engineering works, Ahmedabad, India). Tablets, each weighing 260 mg, were prepared. Table 1 illustrates the formulation design of tablets^[7].

Table 1: Describe Formulation Design of Diclofenac sodium directly compressible tablet.

TABLET INGREDIENTS (mg) /FORMULATION CODE	F ₁	F ₂	F ₃	F ₄	F ₅	F ₆
Diclofenac sodium	25.0	25.0	25.0	25.0	25.0	25.0
Mannitol	30.0	30.0	30.0	30.0	30.0	30.0
MCC PH 101	122.7	120.2	120.9	118.3	113.1	110.5
Lactose DCL 11	58.0	58.0	58.0	58.0	58.0	58.0
Crospovidone	7.0	-	3.1	4.4	7.0	8.3
Citric acid	1.7	1.7	1.7	1.7	1.7	1.7
Saccharin sodium	6.0	6.0	6.0	6.0	6.0	6.0

Croscarmellose sodium	-	9.5	5.72	7.0	9.5	10.9
Aerosil	3.4	3.4	3.4	3.4	3.4	3.4
Talc	1.7	1.7	1.7	1.7	1.7	1.7
Magnesium Stearate	2.4	2.4	2.4	2.4	2.4	2.4
Menthol	2.0	2.0	2.0	2.0	2.0	2.0
Total	260.0	260.0	260.0	260.0	260.0	260.0

Standard Calibration Curve of Diclofenac sodium

Take 100 mg powder of Diclofenac Sodium and dissolve in 100 ml of pH 6.8 phosphate buffer. This is stock solution. Pipette out 10 ml from this and dilute up to 100 ml using pH 6.8 phosphate buffer. Now pipette out

1, 2, 3, 4 and 5 ml from above solution and dilute up to 10 ml. Measure the absorbance at 283 nm using UV/Visible spectrophotometer and plot the graph of concentration ($\mu\text{g/ml}$) versus absorbance. Table 2

Table 2: Describe Observation of absorbance at different concentration of Diclofenac sodium ($\mu\text{g/ml}$).

CONCENTRATION ($\mu\text{g/ml}$)	ABSORBANCE
10	0.339
20	0.595
30	1.104
40	1.546
50	1.900

illustrates observation of absorbance at different concentration of Diclofenac sodium ($\mu\text{g/ml}$). Figure 1

illustrates Standard Calibration Curve of Diclofenac sodium in pH 6.8 phosphate buffer^[8].

Evaluation of Tablets (Refer Table 3)

Table 3: Describe Evaluation Parameters of tablets.

TESTS	FORMULATION CODE					
	F ₁	F ₂	F ₃	F ₄	F ₅	F ₆
Weight Variation (\pm %)	3.0	3.5	3.5	2.0	2.5	2.5
Hardness (Kg/cm^2)	3.5	3.7	3.6	3.4	3.7	3.9
Friability (%)	0.88	0.76	0.82	0.79	0.86	0.91
Water Absorption Ratio (%)	76.8	75.8	74.6	77.1	77.9	77.6
Average Thickness (mm)	2.68	2.66	2.64	2.61	2.63	2.67
In-vitro Disintegration Time (sec)	102	85	57	48	30	29

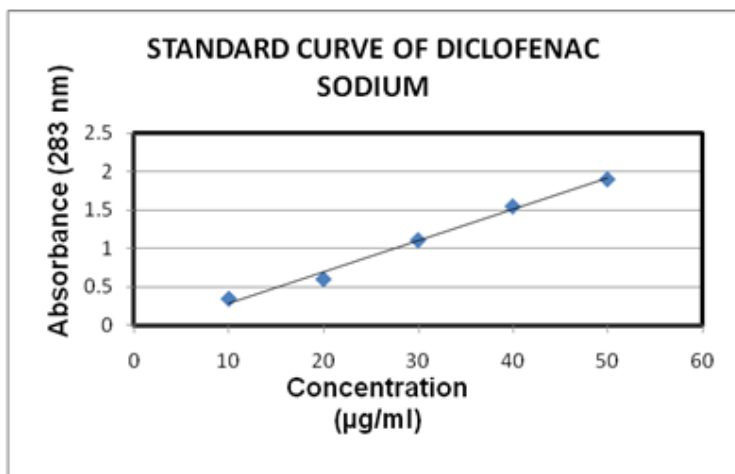


Figure 1: Describe Standard Calibration Curve of Diclofenac sodium in pH 6.8 phosphate buffer.

Weight Variation

Twenty tablets were selected at a random and average weight was determined. Then individual tablets were weighed and the individual weight was compared with a average weight^[9].

Hardness and Friability

Friability of tablets was checked by using Roche Friabilator. The device subjects a number of tablets to the combined effect of abrasions and shock by utilizing a plastic chamber that revolves at 25 rpm, dropping the tablets at distance of 6 inches with each revolution. Prewighed sample of tablets was placed in the friabilator, which was then operated for 100 revolutions. Tablets were dusted and reweighed. Tablet requires certain amount of hardness to withstand mechanical shock. Tablet hardness has been defined as “the force required to break a tablet in a diametric compression test.” The Pfizer tester and Monsanto tester are mainly used to measure tablet hardness^[9].

Water Absorption Ratio

A piece of tissue paper folded twice was placed in a small petri dish containing 6 ml of water. A tablet was put on the tissue paper and allowed to completely wet. The wetted tablet is then weighed^[10].

It can be calculated by following formula:

$$\text{Water absorption ratio} = \frac{W_a - W_b}{W_b} \times 100$$

Where,

W_a = Weight of tablet after water absorption

W_b = Weight of tablet before water absorption

Thickness

Thickness is measured by sliding calliper scale (Vernier callipers). Tablet thickness should be controlled within 5% variation of a standard value^[10].

In-vitro Disintegration Time

Tablet was added to 20 ml of water containing beaker, at 37 ± 0.5 °C. Time required for complete disintegration of a tablet was measured. Table 3 illustrates disintegration time of various formulations^[10, 11].

Dissolution Study

Dissolution rate was studied by using USP type II apparatus, rotated at 75 rpm; 900 ml of Phosphate buffer pH 6.8 was used as dissolution medium. Temperature of dissolution medium was maintained at 37 ± 0.5 °C. Aliquot of dissolution medium was withdrawn at specific time interval and it was filtered. Absorption of filtered solution was checked by UV spectroscopy at 283 nm and drug content was determined from standard calibration curve. Dissolution rate was studied for all designed formulations. Table 4 illustrates dissolution data of tablets. Figure 2 and 3 illustrate the graph of cumulative % drug release versus Time and % Dissolution efficiency versus Formulation batches respectively^[12].

Table 4: Describe Dissolution profiles of formulations.

TIME (min.)	CUMULATIVE % DRUG RELEASE					
	F ₁	F ₂	F ₃	F ₄	F ₅	F ₆
0	0	0	0	0	0	0
5	29.2	32.8	36.7	39.9	41.1	42.8
10	49.3	53.4	61.9	64.3	67.4	68.9
15	65.8	71.2	75.8	78.7	84.7	85.9

20	78.2	79.8	86.5	87.2	92.3	93.2
25	85.9	87.1	90.2	92.3	95.9	96.1
30	92.3	93.5	94.8	95.6	97.8	97.9

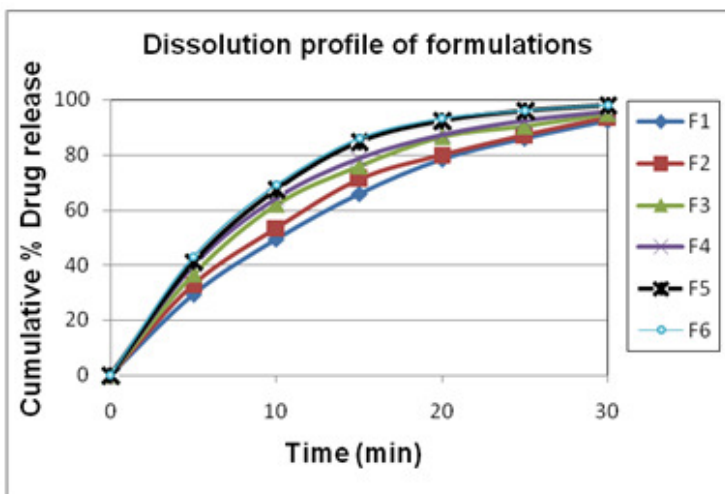


Figure 2: Describe Graph of Cumulative % Drug release Versus Time.

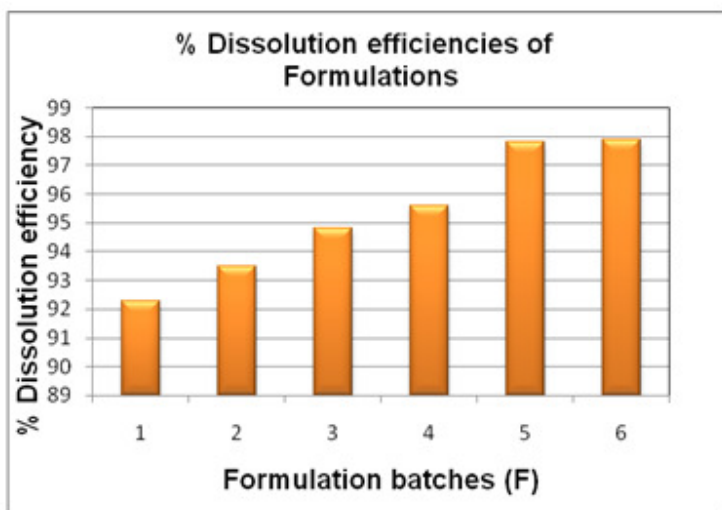


Figure 3: Describe Graph of % Dissolution efficiencies V/s formulation.

RESULT AND DISCUSSION

The compositions of the formulations are shown in the Table 1. The evaluation parameters like weight variation, friability, hardness, thickness and water absorption ratio and disintegration time of the prepared Fast disintegrating tablets were satisfactory (Table 3). The last two formulations (F₅ and F₆) showed sufficiently decrease in disintegration time i.e. 30 sec and 29 sec

respectively. The concept of super disintegrant addition method proved to be beneficial in order to lower the disintegration time. The quicker disintegration time may be attributed to faster water uptake by the tablets. When Crospovidone or Croscarmellose sodium was used alone in the formulations, decrease in the disintegration time was noticed. Furthermore, when both of these two were used in the suitable combination (3.7% and 2.7% respectively), significant decrease in a disintegration time was achieved. However, use of higher amounts of superdisintegrants (4.2% and 3.2% respectively) had not showed much significant decrease in the disintegration time. Dissolution profiles revealed that, after 20 minutes, formulations F₁-F₆ shows % Drug release of 78.2, 79.8, 86.5, 87.3, 92.3 and 93.2 respectively. As Fast disintegrating formulations F₅ and F₆ showed almost similar % Drug release and Disintegration time and there is no rationale behind using higher amount of superdisintegrants; formulation batch F₅ can be said optimized for Fast disintegrating tablets. Friability of all batches was in the range of standard limit (less than 1%).

CONCLUSION

The Fast disintegrating tablets of Diclofenac sodium were formulated by using the superdisintegrants, Croscarmellose sodium and Crospovidone. The combination of superdisintegrants, Croscarmellose sodium and Crospovidone at a concentration of 3.7% and 2.7% respectively of the dosage form was found successful to prepare Fast disintegrating tablets by direct compression method. The proposed Fast disintegrating formulation possessed ideal and reproducible characteristics of disintegration time and drug release profile.

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