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# FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF DICLOFENAC SODIUM USING DIFFERENT SUPERDISINTEGRANTS BY DIRECT COMPRESSION METHOD

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**Abstract**

The aim of the present work is to formulate a tablet which disintegrate and dissolve rapidly and give its rapid onset of action: analgesic, antipyretic and anti inflammatory action. Diclofenac sodium is among the most extensively used NSAIDs; employed in musculo skeletal complaints, especially arthritis. Conventional diclofinac sodium tablet available in market are not suitable where quick onset of action is required. Besides, the conventional tablets also show poor patient compliance particularly by geriatric and pediatric patients and those who are suffering from dysphegia, nausea and vomiting. In present study, an attempt had been made to formulate for FDT of diclofenac sodium by using various superdisintegrants like sodium starch glycolate, croscarmellose sodium and crosspovidone (polyplasdone XL) followed by direct compression technique. The tablets were evaluated for weight variation, hardness, friability, disintegration time, wetting time, in vitro dissolution studies and drug content. It was concluded that the batch which was prepared by using combination of crosspovidone and sodium starch glycolate as a superdisintegrant shows excellent disintegration time, enhance dissolution rate, taste masking and hence lead to improve efficacy and bioavaibility of drug.

**Keywords:** *Diclofenac Sodium, Fast dissolving tablet (FDT), Superdisintegrant.*

## Introduction

Conventional dosage form is very popular because of ease of self administration, compact in nature, easy to manufacture and it can be delivered in accurate dose [1]. One important drawback of conventional dosage form (tablet and capsule) is that it possesses higher disintegration time and pharmacological action is achieved after 30-45 min. of dosage form administration [2]. To overcome this problem tablets that can rapidly disintegrate or dissolve (within one minute) in oral cavity have attracted a great deal of attention.[1]

A fast dissolving drug delivery system can be defined as a dosage form for oral administration, which when placed in mouth, rapidly disintegrates or dissolves and can be swallowed in the form of liquid. Conventional dosage form is very popular in pharmaceutical industries because of its low manufacturing cost.

FDT disintegrate and/or dissolve rapidly in the saliva without the need of water. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. The target populations for these new fast-dissolving/disintegrating dosage forms have generally been pediatric, geriatric, and bedridden or developmentally disabled patients. Patients with persistent nausea, who are traveling, or who have little or no access to water are also good candidates for FDT.[3] The ease of administration of a fast-dissolving/disintegrating tablet, along with its pleasant taste, may encourage a patient to adhere to a daily medication regimen. Although a FDT may not solve all compliance issues, it may be enough of an advance to be of therapeutic significance.[4]

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Diclofenac sodium is synthetic, nonsteroidal anti-inflammatory & analgesic compound. The mechanism responsible for its anti-inflammatory / antipyretic / analgesic action is inhibition of prostaglandin synthesis by inhibition of cyclooxygenase (COX). Diclofenac may also be a unique member of the NSAIDs. There is some evidence that diclofenac inhibits the lipoxygenase pathways, thus reducing formation of the leukotrienes (also pro-inflammatory autacoids). It is well absorbed orally and shows 100% bioavailability, more than 99% Protein bound, metabolized and excreted both in urine and biles, and plasma $t_{1/2}$ is 1.2-2 hr. [5,6]

Diclofenac is used for musculoskeletal complaints, especially arthritis (rheumatoid arthritis, osteoarthritis, spondylarthritis, ankylosing spondylitis), gout attacks, and pain management in case of kidney stones and gallstones. An additional indication is the treatment of acute migraines. Diclofenac is used commonly to treat mild to moderate post-operative or post-traumatic pain, particularly when inflammation is also present, and is effective against menstrual pain. [7]

## Material and Methods

Diclofenac sodium, Crosspovidone (PPXL), Sodium Starch Glycolate, Croscarmellose Sodium (Ac-Di-Sol), Mannitol, Microcrystalline cellulose (PH102), Magnesium stearate, Talc, Aspartame, Peppermint flavour were obtained from Ranbaxy Laboratories Ltd. Dewas. All reagents are of analytical grade.

*2.1 Preformulation studies:*

*2.1.1 Drug - Excipients compatibility study*

The study was designed to determine compatibility of drug with different excipients. These studies were carried out in glass vials stoppers with LDPE (Low density polyethylene) plugs. API was mixed with different excipients & kept at different condition like $4^0$C, $40^0$C and $40^0$C at 75% RH for time interval of 1week, 2weeks, and 3weeks.

*2.1.2 Physical Characterization of Blend*

Physical Characterization of Blend was done for Particle size distribution, Bulk Density, Tapped density and compressibility index.

### Particle size distribution

Particle size distribution of the blend was done in electronic sifter, Hosokawa Alpine 200 LS-N. About 20 g of the blend was weigh and added to sieve # 150, # 85, # 60, and # 36, with subsequent weighing of the blend in between. Time of sifting with each mentioned sieve was 2 min. / sieve.

### Determination of Bulk Density, Tapped density and compressibility index

Firstly, the graduated cylinder was tare to zero, certain quantity of powder (W) was carefully poured into the graduated cylinder and the same was weighed. Also, the volume ($V_0$) was noted. The graduated cylinder was then closed with lid and set into the density determination apparatus (Bulk density apparatus, Campbell electronics). The density apparatus was set for 350 taps and after that the volume ($V_f$) was determined. The Bulk Density, Tapped density was calculated using the following formulas:

$$\text{Bulk Density} = W/V_0$$

$$\text{Tapped density} = W/V_f$$

Where W = Weight of powder, $V_0$ = Initial volume, $V_f$ = Final volume

### Compressibility Index

The compressibility index is determined by measuring both bulk density and the tapped density of a powder. [8]

$$\text{Compressibility Index (\%)} = \frac{\text{Tapped density} - \text{Bulk density} \times 100}{\text{Tapped density}}$$

*2.2 Formulation of tablets by direct compression method:*

Weigh all the ingredients accurately and pass through sieve # 36. Mix all the ingredients geometrically except Magnesium stearate. Then lubricate the blend with Magnesium stearate. Tablets were compressed using tooling of 9.0mm; circular punches with break line on one side and plain on the other side and dies were fixed to the 16 station single rotary tablet compression machine (Cadmach, Ahmadabad, India). Table 1 illustrate the formulation design of tablet.

*2.3 Evaluation of tablets:*

*2.3.1 Weight variation*

Twenty tablets were randomly selected from each formulation and average was determined. Then individual tablet were weighed and individual was compared with average weight.[8]

*2.3.2 Friability*

The friability of tablets was determined using friability test apparatus (Campbell Electronics, India). About 6.5 g tablets ($W_{initial}$) were transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or 100 revolutions. The tablets were dedusted and weighed again ($W_{final}$)[8]. The percentage friability was calculated by,

$$F = \frac{W_{initial} - W_{final}}{W_{final}} \times 100$$

*2.3.3 Hardness*

The hardness of the tablets was determined using Dr. Schleuniger hardness tester. It was expressed in kilo Pascal (kp). Ten tablets were randomly selected from each formulation and hardness of the same was determined .The results are expressed in average value [8].

*2.3.4 Thickness*

Twenty tablets were randomly selected from formulations and thickness was measured individually by vernier caliper. It was expressed in millimeter and average was calculated [8].

*2.3.5 Disintegration test*

The disintegration time of the fast dissolving tablets was determined using Disintegration test apparatus. The operation was performed on 6 tablets.[9,10]

*2.3.6 Wetting time*

Five circular tissue papers of 10 cm diameter are placed in a Petri dish with a 10 cm diameter. Ten millimeters of water-containing Eosin, a water-soluble dye, is added to Petri dish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time [11].

*2.3.7 In-vitro dissolution rate study*

In-vitro dissolution rate study was done by using USP Type II apparatus which was rotated at 75 rpm. Phosphate buffer pH 6.8 (900 ml) was taken as dissolution medium. Temperature of the dissolution medium was maintained at 37±0.5°c. Aliquots of dissolution medium were withdrawn at specific time interval and it was filtered. Absorbance of filtered solution was determined by Spectrophotometer (SYSTRONICS-UV Double beam spectrophotometer-2101) at 283 nm and drug concentration was determined from standard calibration curve [12]. The dissolution rate studies for all designed formulations were done as presented in table 2 and shown in fig.1

*2.3. 8 Determination of drug content*

20 tablets was taken and powdered accurately. Powdered containing about 50mg of Diclofenac sodium was taken and shake it with 60ml methanol in 200ml volumetric flask and dilute to volume with methanol. 5ml of this solution was taken and diluted up to 100ml with methanol and absorbance was noted at 285 nm [13].

*2.3.9 Stability Studies*

The best formulation was charged for stability studies at temperature and relative humidity of $40^0$C / 75%RH for period of one month. The parameter used to assess the effect of stress condition on tablets include: Weight variation, Avg. Thickness, Friability, Disintegration Time, Avg. Hardness, Wetting time, Drug content and % Drug released [8].

## 3. Results and discussion

The compositions of different formulations are presented in table 1. The preformulation studies and evaluation parameters like weight variation, friability, hardness, thickness, disintegration time, wetting time, dissolution rate and assay for drug content were found to be satisfactory and the results were presented in table 2 and 3.

**Table 1: Formulation design of fast dissolving tablet of diclofenac sodium**

| Tablet Ingredients(mg) | $B_1$ | $B_2$ | $B_3$ | $B_4$ | $B_5$ | $B_6$ |
|---|---|---|---|---|---|---|
| Diclofenac sodium | 50 | 50 | 50 | 50 | 50 | 50 |
| Crospovidone (PPXL) | 6 | - | - | 6 | 6 | - |
| Croscarmellose Sodium (AC-DI-SOL) | - | 5 | - | 5 | - | 5 |
| Sodium Starch Glycolate | - | - | 10 | - | 10 | 10 |
| Mannitol | 120 | 121 | 116 | 115 | 110 | 111 |
| Microcrystaline cellulose (PH102) | 12 | 12 | 12 | 12 | 12 | 12 |
| Magnesium stearate | 3 | 3 | 3 | 3 | 3 | 3 |
| Talc | 4 | 4 | 4 | 4 | 4 | 4 |
| Aspartame | 3 | 3 | 3 | 3 | 3 | 3 |
| peppermint flavour | 2 | 2 | 2 | 2 | 2 | 2 |
| Total | 200 | 200 | 200 | 200 | 200 | 200 |

**Table 2 : Preformulation studies of Blends**

| Tablet Ingredients(mg) | $B_1$ | $B_2$ | $B_3$ | $B_4$ | $B_5$ | $B_6$ |
|---|---|---|---|---|---|---|
| Bulk density(g/ml) | 0.52 | 0.50 | 0.51 | 0.50 | 0.50 | 0.48 |
| Tapped density(g/ml) | 0.62 | 0.62 | 0.61 | 0.63 | 0.62 | 0.58 |
| Compressibility index (%) | 16.1 | 19.4 | 16.4 | 20.6 | 19.4 | 20.5 |

**Table 3 : Evaluation of fast dissolving tablets of Diclofenac Sodium of different batches**

| Parameter | $B_1$ | $B_2$ | $B_3$ | $B_4$ | $B_5$ | $B_6$ |
|---|---|---|---|---|---|---|
| % weight variation | 1.8 | 2.3 | 2.4 | 2.2 | 1.9 | 2.1 |
| Thickness(mm) | 2.71 | 2.68 | 2.7 | 2.75 | 2.77 | 2.84 |
| Friability (%) | 0.54 | 0.26 | 0.58 | 0.47 | 0.62 | 0.65 |
| Disintegration Time(sec.) | 74 | 67 | 72 | 43 | 30 | 47 |
| Hardness (kp) | 4.53 | 4.96 | 4.60 | 4.80 | 4.41 | 4.50 |
| Wetting time (sec.) | 79 | 74 | 75 | 49 | 34 | 52 |

The formulation containing Crospovidone (PPXL) and Sodium Starch Glycolate shows sufficiently decrease in disintegration time (i.e. 30 sec.) among all the formulation. When Crospovidone (PPXL), Sodium Starch Glycolate, Croscarmellose Sodium (Ac-Di-Sol) was used alone in the formulations, disintegration time was

noticed more than 1 min. furthermore. When combination of these superdisintegrant was used, significant decrease in a disintegration time was achieved. In vitro dissolution rate study shows that after 10 min formulation $B_4$ - $B_6$ percentage drug release 94.27%, 99.98%, 95.76% respectively. Drug content studies were done on selected batches and results are presented in table 4 which shows that the drug content are within limit. As fast dissolution formulation $B_5$ shows satisfactory % drug release and disintegrating time as shown in fig. 1 and 2.

**Fig 1: Disintegration time (min.) of various batches containing different superdisintigrant and its combination**

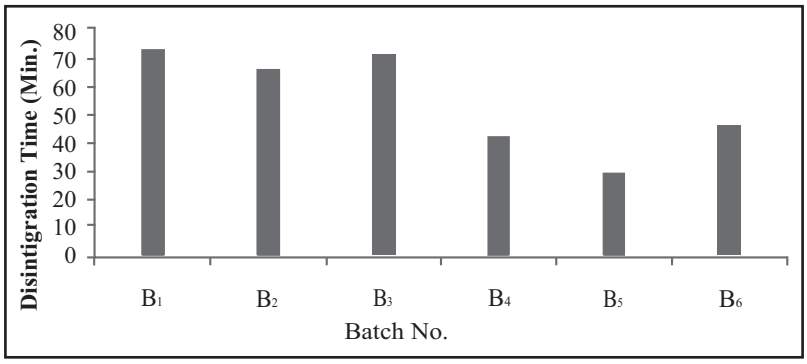
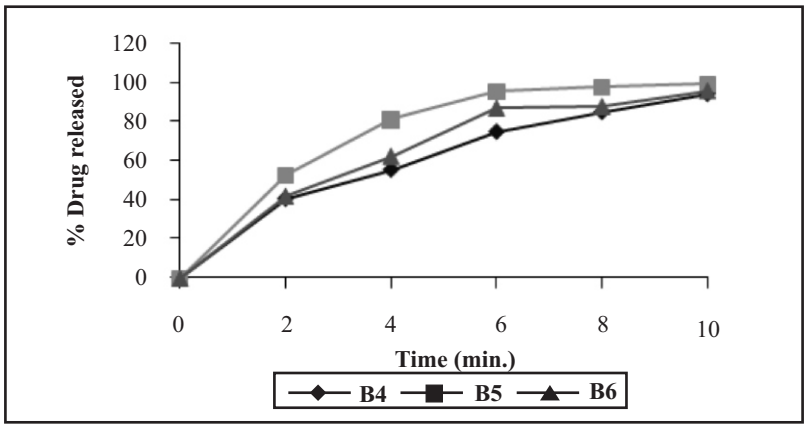



**Fig. 2: Comparative study of % drug release of FDT of diclofinac sodium of different batches**




Thus the formulation batch $B_5$ can be said as best combination of superdisintigrant for fast dissolving tablet of diclofinac sodium. Stability studies were carried out with selected formulation i.e. $B_5$ and the results of studies indicated the formulation was stable at $40^0$C / 75%RH as presented in table 5 and 6.

**Table 4: Drug content studies of fast dissolving tablets of Diclofenac Sodium**

| Batch No. | Assay (%) |
|---|---|
| $B_4$ | 98.35 |
| $B_5$ | 99.21 |
| $B_6$ | 99.07 |

**Table 5: Study of different parameter**

| S. No. | Parameter | Result |
|---|---|---|
| 1. | % weight variation | 2.0 |
| 2. | Avg. Thickness(mm) | 2.76 |
| 3. | Friability (%) | 0.71 |
| 4. | Disintegration Time | 31sec. |
| 5. | Avg. Hardness (kp) | 4.39 |
| 6. | Wetting time (sec.) | 36 |
| 7. | Drug content | 99.09 |

**Table 6: Stability studies (% Drug Released) of fast dissolving tablets of Diclofenac Sodium of batch $B_5$**

| Time in Min. | % Drug released of Batch No. $B_5$ |
|---|---|
| 0 | 0 |
| 2 | 50.98 |
| 4 | 80.42 |
| 6 | 94.84 |
| 8 | 98.29 |
| 10 | 99.53 |

## Conclusion

From the present study it may be concluded that fast dissolving tablet of diclofinac sodium can be formulated by direct compression method by using suitable superdisintegrant (Crosspovidone (PPXL), Sodium Starch Glycolate). The combination of Crosspovidone (PPXL), Sodium Starch Glycolate was found to be best among the different combination of superdisintigrant. The proposed fast dissolving formulations possess ideal and reproducible characteristics of disintegration time and enhanced dissolution and thus give better patient compliance compare to conventional tablet of diclofinac sodium.

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