



Formulation and Characterization of Fast Disintegrating Tablet of Aceclofenac by using Sublimation Method

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ABSTRACT

In the present work, fast disintegrating tablets of Aceclofenac were prepared by subliming method with a view to enhance patient compliance. In this paper, two super-disintegrants, viz., croscopovidone and sodium starch glycolate were used in different ratio (2-8 % w/w) with camphor (30 % w/w) as subliming agent. The prepared batches of tablets were evaluated for thickness, weigh variation, hardness, friability, drug content uniformity, wetting time, water absorption ratio, *in-vitro* disintegration time and *in-vitro* drug release. Based on disintegration time (approximately 21 second), three formulations were tested for the *in-vitro* drug release pattern (in pH 7.4 phosphate buffer). Among the three promising formulations, the formulation prepared by using 8% w/w of croscopovidone and emerged as the overall best formulation based on the *in-vitro* drug release characteristics.

Keywords: Fast disintegrating tablets, *in vitro* disintegration time, Croscopovidone, sodium starch glycolate, Aceclofenac.

INTRODUCTION

Many patients express difficulty in swallowing tablets and hard gelatin capsules, resulting in non-compliance and ineffective therapy. [1] Recent advances in novel drug delivery systems (NDDS) aim to formulating a dosage form of drug molecules for convenient administration and to achieve better patient compliance. One such approach leads to development of fast dissolving/disintegrating tablets. [2-4] Advantages of this drug delivery system include convenience of administration and accurate dosing as compared to liquids, easy portability, ability to provide advantages of liquid medication in the form of solid preparation, ideal for pediatric and geriatric patients and rapid dissolution/absorption of the drug, which may produce rapid onset of action. Some drugs are absorbed from mouth, pharynx and esophagus as the saliva passes down into the stomach and in such cases bioavailability of the drug is increased: pre-gastric absorption can result in improved bioavailability and as result of reduced dosage, improved clinical performance through a reduction of unwanted effects. Aceclofenac is a newer non-steroidal anti-inflammatory drug (NSAID). Aceclofenac is a phenyl acetic acid derivative showing effective anti-inflammatory and analgesic properties

mainly used in osteoarthritis, rheumatoid arthritis and ankylosing spondylitis. Because of changes in various physiological functions associated with aging including difficulty in swallowing, administration of intact tablet may lead to poor patient compliance and ineffective therapy. The paediatric and geriatrics patients are of particular concern. To overcome this, fast dissolving/disintegrating tablets has been developed. Fast disintegrating tablets are gaining prominence as new drug delivery system. These dosage forms dissolve or disintegrate in the oral cavity within a minute without the need of water or chewing. [5-6] The objective of this study was to achieve better patient compliance, solve the problem of difficulty in swallowing and enhance onset of action by developing fast disintegrating tablets of Aceclofenac. The effect of concentration of different super-disintegrants such as croscopovidone and sodium starch glycolate on the tablet properties, disintegration time and *in-vitro* drug release was also considered.

MATERIALS AND METHODS

Aceclofenac was obtained from Laborate Pharma, Paonta Sahib, India. Croscopovidone and sodium starch glycolate were obtained from Zydus Cadila Healthcare Ltd., Ahmedabad, India. All other chemicals of analytical grade were purchased from commercial sources.

Preparation of Aceclofenac fast disintegrating tablet

Various formulations of fast disintegrating tablets of Aceclofenac were prepared by using sublimation method. [7-8] The two super-disintegrating agents such as croscopovidone

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and sodium starch glycolate were used in varying concentration as shown in Table 1. Accurately weighed quantity of Aceclofenac, subliming agent (camphor), super-disintegrating agent, aspartame and mannitol were mixed and passed through the sieve # 44. Finally, magnesium stearate and talc were added as lubricating agent. The powder mixture was subjected to compression into tablet using a single-punch tablet machine. After compression tablets were heated in a hot air oven at 60°C until constant weight was obtained to ensure the complete removal of volatilizable component.

Evaluation parameters of Aceclofenac fast disintegrating tablet

Evaluation of pre-compression parameters of powder

Prior to compression, granules were evaluated for their flow and compressibility parameters. Flow properties of granules were determined by angle of repose method. Compressibility index of granules were determined by Carr's index and Hausner ratio.^[9-10]

Evaluation of post-compression parameters of Tablets

Post compression, the tablets were evaluated for their characteristics such as thickness, weight variation, hardness, friability, drug content uniformity, disintegration test, wetting time, water absorption ratio and *in-vitro* dissolution study.

Thickness: Dimension of the tablets was measured by using a calibrated dial caliper. Five tablets of each formulation were picked out randomly and its thickness was measured individually.^[11-12]

Weight variation: The procedure described in Indian Pharmacopoeia (IP, 1996)^[13] was employed to determine the weight variation of the tablets. Ten tablets were randomly selected from each batch and weighed on an electronic balance and mean weight was taken. Each tablet was then weighed individually and standard deviation in weight was calculated for each batch.^[14]

Hardness: Five tablets were randomly selected from each batch and hardness of tablets was determined by using Monsanto hardness tester. The mean values and standard deviation for each batch were calculated.^[12]

Friability: Friability indicates the ability of a tablet to withstand mechanical shocks while handling. Friability of the tablets were determined using Roche Friabilator and is expressed in percentage (%). Ten tablets were initially weighed (W_{initial}) and placed into the friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions and then the tablets were weight again (W_{final}). The loss in tablet weight due to abrasion or fracture was the measure of tablet friability. Percent friability (f) was calculated by using the following formula.^[12]

$$f = \frac{W_{\text{initial}} - (W_{\text{final}})}{(W_{\text{initial}})} \times 100$$

% friability of less than 1 % is considered acceptable.

Drug content uniformity: Three tablets were powdered and weigh accurately equivalent to 100 mg of Aceclofenac and transferred into a 100 ml volumetric flask. Initially, 10 ml of methanol was added and shaken for 10 minutes. Then, the volume was made up to 100 ml with methanol. Subsequently, the solution in the volumetric flask was filtered, and 1 ml of the filtrate was suitably diluted and analyzed for drug content at 273 nm using UV-spectrophotometer (Shimadzu 1700, Japan).

Disintegration test: The disintegration time was determined by using USP Tablet disintegration test apparatus using 900

ml of distilled water without disk. The time in seconds taken for complete disintegration of the tablets until no mass remaining in the apparatus was measured.^[11-12]

Wetting time: The wetting time and capillarity of the oral dispersible tablets were measured by a conventional method. The tablet was placed in a petridish of 6.5 cm diameter containing 10 ml water at room temperature and the times for complete wetting of tablets were recorded.^[12]

Water absorption ratio: A piece of tissue paper folded twice was placed in a small petridish containing 6 ml of distilled water. A tablet was put on the paper and the time required for complete wetting of the tablet was measured. The wetting tablet was then weighed. Water absorption ratio "R" was determined using the equation as follows^[14]:

$$R = \frac{W_a - W_b}{W_b} \times 100$$

Where, W_a is Weight of tablet after water absorption and W_b is Weight of tablet before water absorption.

In-vitro drug release studies

The *in-vitro* drug release studies of Aceclofenac from the tablets were carried out using USP dissolution test apparatus type-II (Paddle type) in 900 ml of dissolution medium (Phosphate buffer pH 7.4) at 37±0.5°C temperature and rotated at 50 rpm. In this test, single tablet from each formulation was used for the studies. At specified time intervals, 5 ml samples were collected and immediately replaced with an equal volume of fresh medium. Samples were suitably diluted and analyzed by using UV-spectrophotometer (Shimadzu 1700, Japan) at 273 nm. All the tests were carried out in triplicate.^[15]

Table 1: Composition of fast disintegrating tablet of Aceclofenac

Formulation ingredients (mg/tablet)	F ₀	F ₁	F ₂	F ₃	F ₄	F ₅	F ₆
Aceclofenac	100	100	100	100	100	100	100
Camphor	60	60	60	60	60	60	60
Crospovidone	-	4	8	16	-	-	-
Sodium starch glycolate	-	-	-	-	4	8	16
Aspartame	2	2	2	2	2	2	2
Mannitol	32	28	24	16	28	24	16
Magnesium Stearate	2	2	2	2	2	2	2
Talc	4	4	4	4	4	4	4
Total	200	200	200	200	200	200	200

Table 2: Evaluation of Pre-Compression parameters of powder

Formulation Code	Angle of repose (degrees)	Compressibility Index (%)	Hausner's Ratio
F ₀	16.42	14.28	1.114
F ₁	19.64	16.53	1.121
F ₂	14.19	12.68	1.103
F ₃	11.98	10.42	1.098
F ₄	18.14	15.85	1.119
F ₅	16.23	13.57	1.113
F ₆	11.15	09.78	1.092

RESULTS AND DISCUSSION

Fast dissolving tablets of Aceclofenac were prepared by sublimation method employing crospovidone and sodium starch glycolate as super-disintegrants in different ratio along with up to 30 % w/w of camphor as a subliming agent. A total of six formulations and a control formulation F₀ (without super-disintegrants) were designed. The flow properties of the powder mixture are important for the

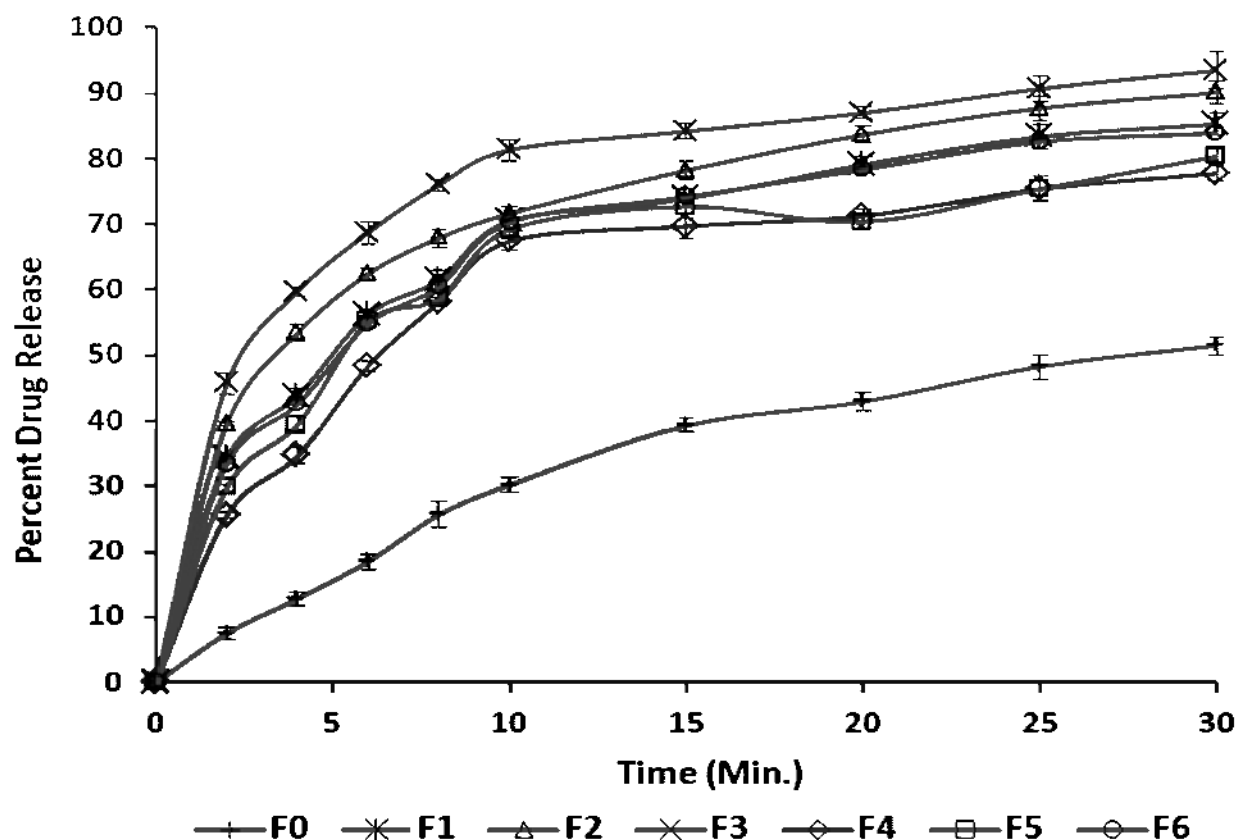
Table 3: Evaluation of Post-Compression parameters of Tablet

Formulation Code	Thickness (mm ²)	Hardness* (kg/cm ²)	Weight Variation*** (mg)	Friability (%)	Drug Content* (%)	Disintegration Time** (Seconds)	Wetting Time* (Seconds)	Water Absorption Ratio* (%)
F ₀	2.091	4.78±0.192	196±3.215	0.60	93.74±0.62	142.04±3.21	132.54±3.15	57.78±2.45
F ₁	2.108	4.82±0.184	198±2.051	0.58	96.26±0.25	27.19±1.54	24.69±1.74	64.85±1.26
F ₂	2.021	4.62±0.212	201±1.742	0.30	96.68±0.59	23.78±1.64	20.41±1.52	69.528±1.98
F ₃	2.034	4.65±0.190	199±1.015	0.62	98.03±0.28	21.95±1.61	16.74±1.14	74.48±0.98
F ₄	2.029	4.64±0.121	204±4.357	0.61	93.47±0.35	36.26±1.45	32.45±1.89	67.24±2.15
F ₅	2.029	4.64±0.095	196±3.265	0.59	96.70±0.68	40.85±0.24	38.57±0.98	72.67±0.74
F ₆	2.025	4.63±0.087	202±1.924	0.52	99.04±0.56	44.19±0.16	42.81±0.84	78.35±1.46

*n = 3, values are expressed as a mean ± S D

**n = 6, values are expressed as a mean ± S D

***n = 10, values are expressed as a mean ± S D

**Fig. 1: In-vitro drug release profile of fast disintegrating tablet of Aceclofenac**

uniformity of mass of the tablets; the flow of the powder mixture was analyzed before compression to tablets. Low Hasner's ratio (≤ 1.12), compressibility index (≤ 16.53) and angle of repose (≤ 19.64) values indicated a fairly good flowability of powder mixture (Table 2). As the tablet powder mixture was free flowing, tablets produced were of uniform weight with acceptable weight variation in the range from 196 mg to 204 mg due to uniform die fill. Hardness (4.62 - 4.82 kg/cm²) and friability loss (0.30 - 0.62 %) indicated that tablets had a good mechanical resistance. Drug content was found to be high (≥ 93.47 %) in all the tablet formulations. Water absorption ratio and wetting time, which are important criteria for understanding the capacity of disintegrants to swell in pressure of little amount of water were found to be in the range of 57.78 - 78.35 % and 16.74 - 132.54 seconds respectively (Table 3).

The most important parameter that needs to be optimized in the development of fast disintegrating tablets is the disintegration time of tablets. In the present study, It is

observed that the disintegration time of the tablets had no effect ($P > 0.05$) with increasing level of croscopovidone. However, disintegration time increased ($P < 0.05$) with increase in the level of sodium starch glycolate in the tablets. It indicates that increase in the level of sodium starch glycolate had a positive effect on the disintegration of the tablets. At higher levels, formation of a viscous gel layer by sodium starch glycolate^[16] might have formed a thick barrier to the further penetration of the disintegration medium and hindered the disintegration or leakage of tablet contents. Thus, tablet disintegration is retarded to some extent with tablets containing sodium starch glycolate. The faster disintegration of croscopovidone tablets may be attributed to its rapid capillary activity and pronounced hydration with little tendency to gel formation. Thus, these results suggest that the disintegration times can be decreased by using wicking type of disintegrants (croscopovidone).

Wetting times of the tablets significant decrease ($P < 0.05$) with increase in the level of croscopovidone (2 % to 8 %). It is

interesting to note that wetting times increased ($P<0.05$) with increase in the level of sodium starch glycolate from 2 % to 8 % in the tablets. Thus; wetting times of tablets with crospovidone was found less than sodium starch glycolate. These results are in consistent with disintegration test results. *In vitro* drug release studies were carried out in pH 7.4 phosphate buffer and the dissolution profile depicted in Fig. 1.

It is concluded that the formulation F₃ containing 8 % w/w of crospovidone along 30 % w/w of camphor as a subliming agent was found to be promising and has shown as *in vitro* disintegration time of 21 second, wetting time of 16 second and water absorption ratio of 74.48 % when compared to control formulation (F₀) which shows 142.04 second, 132.54 second and 57.78 % values respectively for the above parameters.

ACKNOWLEDGEMENTS

The authors are grateful to Laborate Pharma, Paonta Sahib, HP, India for providing gift sample of Aceclofenac.

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