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Influence of various super disintegrating agents on the aceclofenac fast dissolving tablets

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ABSTRACT

Fast-dissolving tablets (FDT) of Aceclofenac were prepared by direct-compression method after incorporating superdisintegrants Sodium Starch Glycolate (SSG), and Crospovidone and yellow starch potato in different concentrations. Six formulations having superdisintegrants at different concentration levels were prepared to assess their efficiency and critical concentration level. Yellow starch could be an effective tablet disintegrates. Yellow starch appeared to be yellowish-white fine powder after the alkaline extraction process. Different types of evaluation parameters for tablets were used. Tablets containing yellow starch potato showed superior organoleptic properties, along with excellent *in vitro* and *in vivo* dispersion time and drug release, as compared to other formulations.

Keywords: Direct compression, Aceclofenac, superdisintegrants, Sodium Starch Glycolate, Crospovidone and Yellow Sweet Potato Starch.

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INTRODUCTION

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. Aceclofenac is rapidly and efficiently absorbed after oral administration but has a short half-life of 3-4 h and requires multiple dosing for maintaining therapeutic effect throughout the day [1]. Its biological half-life on the other hand is very short. Out of all the orally administered dosage forms; tablet is most preferred because of ease of administration, compactness and flexibility in manufacturing. Because of change of various physiological functions associated with aging including difficulty in swallowing, administration of intact tablet may lead to poor patient compliance and ineffective therapy. The pediatric and geriatric patients are of particular concern. To overcome this, dispersible tablets [2] and fast-disintegrating tablets [3] have been developed. Molded tablets dissolve completely and rapidly. However lack of strength and taste masking are of great concern [3]. Main advantages of direct compression are low manufacturing cost and high mechanical integrity of the tablets [4]. Therefore, direct compression appears to be a better option for manufacturing of tablets.

The fast disintegrating tablets prepared by direct compression method, in general, are based on the action established by super disintegrates such as sodium starch glycolate, crospovidone and yellow sweet potato starch. The objective of the present work is to develop fast dispersible aceclofenac tablets and to study the effect of functionality differences of superdisintegrants on the tablet properties [5]. Fast-disintegrating tablets are gaining prominence as new drug-delivery systems. These dosage forms dissolve or disintegrate in the oral cavity within a minute without the need of water or chewing [6]. The objective of this study was to enhance safety and efficacy of drug molecule, achieve better compliance, solve the problem of difficulty in swallowing, enhance onset of action, and provide stable dosage form.

MATERIALS AND METHODS

Aceclofenac was received as a gift sample from Mehta Chemicals (Mumbai, India). Crospovidone, sodium starch glycolate, and Micro crystalline cellulose were gifted by Alembic Ltd. All reagents and solvents used were of analytical grade.

Starch Extraction

Yellow starch was extracted from yellow sweet potato (*ipomoea batatas*) yellow sweet potato starch were sliced and dried at 45°C for 24h. Dried yellow sweet potato powder was subsequently dispersed in 0.05% NaOH. After 12h, the supernatant was removed. The solvent was rinsed off with purified water and let stand for 12h. The suspension was filtered, and the powder was dried at 45°C for 24h. This alkaline extraction was modified from the method of Jane et al.

Preparation of mixing blend of drug and excipients

Table-1 Formulation of Aceclofenac FDTs by Direct compression method

| Ingredients | F1 | F2 | F3 | F4 | F5 | F6 |
|-----------------------------|-----|-----|-----|-----|-----|-----|
| Aceclofenac | 100 | 100 | 100 | 100 | 100 | 100 |
| Sodium starch glycolate | 5 | 10 | -- | -- | -- | -- |
| Yellow Sweet Potato Starch | -- | -- | 5 | 10 | -- | -- |
| Crospovidone | -- | -- | -- | -- | 5 | 10 |
| Micro crystalline cellulose | 40 | 35 | 40 | 35 | 40 | 35 |
| Talc | 2 | 2 | 2 | 2 | 2 | 2 |
| Magnesium Stearate | 3 | 3 | 3 | 3 | 3 | 3 |
| Total | 150 | 150 | 150 | 150 | 150 | 150 |

The superdisintegrants (Crospovidone, sodium starch glycolate and yellow sweet potato starch) in varying concentration (05-10%) were used to develop the tablets. All the ingredients shown in [Table 1]) were passed through mesh no. 60. All the ingredients were co-ground in a pestle motor for 5 minutes. The mixed blend of excipients was compressed using a single-punch machine to produce convex-faced tablets weighing 150 mg each, with diameter of 8 mm. A minimum of 50 tablets were prepared for every batch [7,8].

Evaluation of tablets

Prepared tablets were evaluated for hardness (Monsanto hardness tester), friability (Roche friabilator), weight variation, *in vitro* dispersion time, wetting time and drug content [9], [10]. *In vitro* dissolution studies of fast-dissolving tablets were performed by using type II apparatus as specified in United State Pharmacopoeia at 100 rpm; and Sorenson's buffer (pH, 6.8), 900ml, was used as dissolution medium. Temperature of dissolution medium was maintained at 37°C ± 0.5°C. Aliquot of dissolution medium was withdrawn at a specific time interval and it was filtered. Absorption of filtered solution was checked by UV spectroscopy (Shimadzu, Japan), and drug content was determined from standard calibration curve. Dissolution rate was studied for all designed formulations and conventional tablet.

Hardness

The tablet hardness, which is the force required to break a tablet in a diametric compression force. The hardness tester used in the study was Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring.



Friability

The friability of a sample of 20 tablets was measured using Roche friabilator (Electrolab, Mumbai, India). Twenty tablets were weighed, rotated at 25 rpm for 4 minutes. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss was calculated. Friability below 1% was considered acceptable.

Weight variation test

Weight variation test was done by weighing 20 tablets individually, calculating the average weight and comparing the individual tablet weight to the average weight.

In vitro disintegration time [11]

The disintegration time of the tablet was measured in water ($37\pm 2^{\circ}\text{C}$) according to disintegration test apparatus with disk. The time in seconds taken for the complete disintegration of the tablet with no palpable mass in the apparatus was measured in seconds. Three tablets from each batch (formulation) were tested for the disintegration time calculations.

Wetting time [12]

A piece of tissue paper folded twice was placed in a small petridish (ID= 6.5 cm) containing 6 ml of simulated saliva pH 6.8, a tablet was put on the paper, and the time for complete wetting was measured.

Drug Content

Twenty tablets were weighed and powdered. An amount of the powder equivalent to 20mg of aceclofenac was dissolved in 100ml of pH 7.4 phosphate buffer, filtered, diluted suitably and analyzed for drug content at 274nm using UV-Visible spectrophotometer (UV 1601 Shimadzu, Japan).

In vitro dissolution profile [13]

Dissolution studies were carried out by USP paddle method at $37\pm 0.50^{\circ}\text{C}$, taking 900ml of phosphate buffer pH 7.4 as a dissolution medium. Speed of rotation of paddle was set at 50 rpm. Absorbance of sample was measured at 274 nm by spectrometrically.

RESULTS AND DISCUSSION

The use of superdisintegrants for preparation of fast-dissolving tablets is highly effective and commercially feasible. These superdisintegrants accelerate disintegration of tablets by virtue of their ability to absorb a large amount of water when exposed to an aqueous

environment. The absorption of water results in breaking of tablets and therefore faster disintegration. This disintegration is reported to have an effect on dissolution characteristics as well.

Prepared fast-dissolving tablet gets dispersed in the mouth quickly and releases the drug early as compared to its formulated conventional tablet. Three different superdisintegrants Sodium starch glycolate, Crospovidone, and Yellow Sweet Potato Starch - were tried to achieve fast dispersion of tablets.

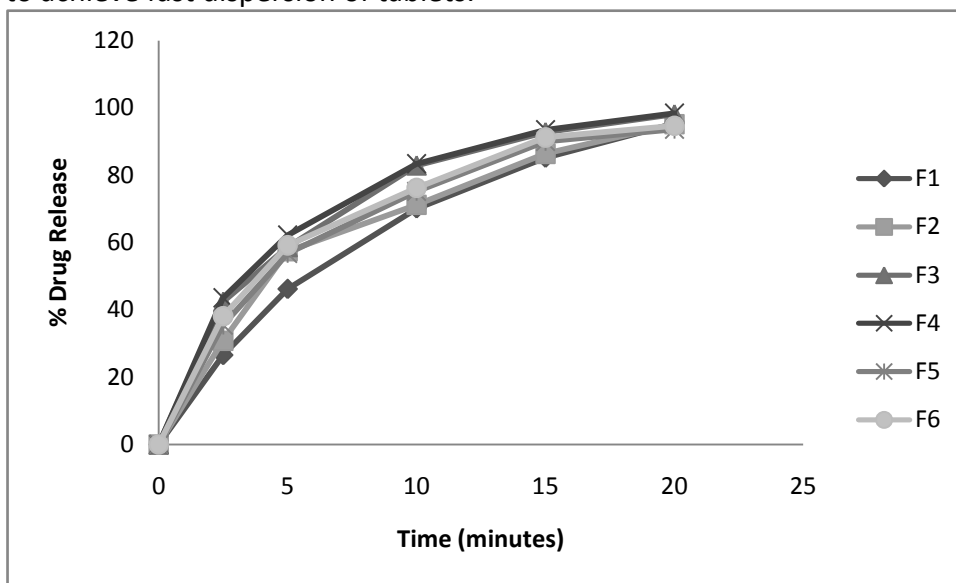


Fig-1 Dissolution Parameters of fast dissolving tablets

Table-2 Formulation parameter

| Formulation | Hardness Kg/cm ² (±SD), n=3 | Friability (%)(±SD) (n=6) | Drug content (mg%) (±SD) (n=10) | Wetting time(sec) (±SD) n=3 | Weight variation (±SD) n=20 |
|-------------|--|---------------------------------|---------------------------------------|-----------------------------------|--------------------------------------|
| F1 | 3.2 ±0.13 | 0.66±0.8 | 99.82±0.4 | 32.14±1.8 | 150.15±1.7 |
| F2 | 3.2±0.11 | 0.66±0.15 | 99.85±0.5 | 65.14±1.7 | 150.16±1.5 |
| F3 | 3.2±0.11 | 0.59±0.11 | 99.56±0.6 | 74.15±1.6 | 150.18±1.9 |
| F4 | 3.2±0.14 | 0.59±0.3 | 99.87±0.8 | 75.82±1.8 | 150.02±1.8 |
| F5 | 3.2±0.15 | 0.64±0.12 | 99.77±0.7 | 48.12±1.5 | 150.06±1.7 |
| F6 | 3.2±0.11 | 0.64±0.12 | 99.63±0.5 | 42.12±1.4 | 150.08±1.6 |

Table 3: Dissolution studies of fast dissolving tablets of aceclofenac.

| Formulation code | after 2.5min % Release | after 5min % Release | after 10min % Release | after 15min % Release | after 20min % Release |
|------------------|------------------------|----------------------|-----------------------|-----------------------|-----------------------|
| F1 | 39.12 | 56.19 | 81.26 | 91.26 | 95.37 |
| F2 | 39.53 | 57.43 | 81.74 | 91.43 | 95.11 |
| F3 | 42.41 | 58.95 | 82.93 | 92.81 | 96.21 |
| F4 | 43.54 | 58.68 | 83.37 | 93.51 | 97.47 |
| F5 | 41.13 | 56.72 | 80.24 | 90.67 | 93.58 |
| F6 | 41.39 | 57.41 | 81.98 | 91.23 | 94.69 |

The prepared tablets in all the formulations possessed good mechanical strength with sufficient hardness in the range of 3.2 kg/sq cm. Friability values below 1% were an indication of good mechanical resistance of the tablets. Formulations prepared by sublimation method were found to be more friable. All the tablets from each formulation passed weight variation test, as the % weight variation was within the pharmacopoeial limits of $\pm 7.5\%$ of the weight. The weight variation in all the six formulations was found to be 150mg, which was in pharmacopoeial limits of $\pm 7.5\%$ of the average weight. The percentage drug content of all the tablets was found to be between 99.87 % of aceclofenac which was within the acceptable limits. The wetting time for all the six formulations was performed in triplicate. In vitro dispersion is a special parameter in which the time taken by the tablet to produce complete dispersion is measured. Tablets were prepared with sodium starch glycolate F-1 to F-2, Yellow Sweet Potato Starch F-3 to F-4 and crospovidone F-4 to F-6. The wetting time, in vitro dispersion time of the tablets were also considerably reduced in tablets containing, Yellow Sweet Potato Starch which may be attributed due to the wicking type of disintegrates (Yellow Sweet Potato Starch) formed thus facilitating the disintegrates to bring about faster disintegration. Formulation parameter evaluated [Table 2]. However, tablets containing yellow sweet potato starch showed the fastest disintegration, as shown in [Figure 1] and drug released studies shown in [Table 3]. *In vitro* dissolution studies F4 tablet showed good dissolution efficiency and rapid dissolution. The study shows that the dissolution rate of aceclofenac can be enhanced to a great extent by direct-compression technique with the addition of superdisintegrants, which gives quick relief from emesis.

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