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Formulation and evaluation of fast dispersible tablets of aceclofenac

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ABSTRACT

Aceclofenac a non-steroidal anti-inflammatory drug, used in posttraumatic pain and rheumatoid arthritis. Aceclofenac fast-dispersible tablet have been prepared by direct compression method using microcrystalline cellulose as a direct compressible vehicle. Croscarmellose sodium and polyplasdone xl-10 were used as a superdisintegrants for the formulation. The disintegration time and dissolution parameter ($t_{50\%}$ and $t_{80\%}$) decreased with increasing the concentration of polyplasdone. Those tablets were evaluated for weight variation, hardness, disintegration time, friability and dissolution.

Keywords: Aceclofenac, fast-dispersible tablet

INTRODUCTION

Fast Dissolving drug delivery is rapidly gaining acceptance as an important new drug delivery technology.[1] These dosage form dissolve or disintegrate in oral cavity within a minute even without need of water or chewing, usually superdisintegrants are added in formulation to facilitate break-up and disintegrate rapidly in to smaller particals.[2] superdisintegrants like croscarmellose, crosspovidone, sodium starch glycolate which represent example of a cross linked cellulose, cross linked polymer and a cross linked starch respectively. And these superdisintegrants act by swelling and due to swelling pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration.[3,4]

Orodispersible tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people.[5] Their growing importance was underlined recently when European Pharmacopoeia adopted the term "Orodispersible tablet" as a tablet that to be placed in the mouth where it disperses rapidly before swallowing and which disintegrates in less than 3 min.[6]

Several platform technologies based on fast disintegrating dosage forms have been developed, such as freeze-dried tablets (Zydis®), compressed fast-disintegrating tablets (Orasolv®, Durasolv®,Wowtab®, Flash Dose®) and fast-dissolving films (Listerine® Pocketpacks).The ZydisTM dosage form was developed by Scherer; it dissolves within 3–5 s in the oral cavity.[7,8,9] Products on the market include Zyprexa® Zydis®, Maxalt-MLT® and Romeron® SolTabs®. This dosage form is produced by freeze-drying aqueous drug/ excipient suspension/solutions within blister packs.[10] The final product is a dried, sponge-like tablet in a special peeloff blister pack.[11].Major disadvantages of the Zydis® technology is the time-consuming freeze-drying process, the limitation to low dose drugs, the poor mechanical properties and moisture sensitivity. Other marketed fast-disintegrating dosage form technologies are based on conventional tabletting method. The OrasolvTM technology is based on an effervescent mixture and taste-masked coated or microencapsulated drugs.[12]. The ShearformTM technology is based on a floss-like matrix.[13]. The floss is a fibrous material similar to cotton-candy fibers, commonly made of saccharides such as sucrose, dextrose, lactose and fructose.[14]. The compression force used for such tablets is relatively low. The resulting tablets are soft, friable and highly moisture sensitive.[15]

Aceclofenac an inflammation site specific a non steroidal anti-inflammatory drug (NSAID) has been indicated for various painful indications.[16] has been used as model drug for the formulation. Present study deals with formulation and evaluation of fast dispersible Aceclofenac tablets, by direct compression method by using superdisintegrants such as croscarmellose sodium and polyplasdone xl-10.

MATERIAL AND METHOD:

Aceclofenac(Mac D, Indore), croscarmellose sodium and polyplasdone xl-10(Concept Pharma.Ltd. Aurangabad,India), Dextrose,microcrystallinecellulose,magnesium,stearate,vanillin, menthol and sodium saccharine from S.D Fine Chem. Mumbai.

Blending and tableting

Tablets containing 100 mg of Aceclofenac are prepared by direct compression method and the various formulae used in the study are shown in Table 1. The drug, diluents, superdisintegrants and sweetener are passed through sieve # 60.All the above ingredients were properly mixed together (in a poly-bag).Talc and magnesium stearate were passed through sieve # 30,mixed and blended with initial mixture in a poly-bag. The powder blend was compressed in to tablets on twelve-station rotary punch-tableting machine (Karnavati, Rimek Mini Press-2) using 10.3 mm concave punch set.

Evaluation of dispersible tablet

Tablets were evaluated for hardness, weight variation, friability, thickness, wetting time and disintegration time. In weight variation test,

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Table 1: Formulae used in the preparation of tablets

Ingredients (mg)	A1	A2	A3	A4	A5
Aceclofenac	100	100	100	100	100
Dextrose	126	101	101	76	76
Croscarmellose sodium	25	50	25	50	25
Polyplasdone xl-10	- -	25	25	50	
Microcrystalline cellulose	25	25	25	25	25
Magnesium stearate	1.5	1.5	1.5	1.5	1.5
Sodium saccharine	10	10	10	10	10
Vanillin	5 5	5	5	5	
Menthol	6 6	6	6	6	
Talc	1.5	1.5	1.5	1.5	1.5

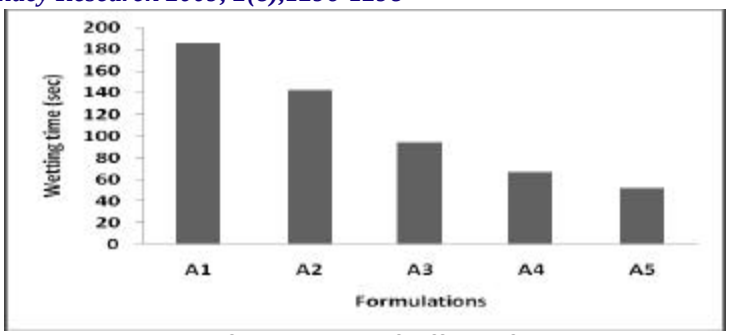

Fig.3: Comparison of wetting time of different formulations.

Table 2. Physical characteristics of dispersible tablet formulation*

Formulation	Hardness	Friability	Wt.variation (%)	Wetting time	Disintegration time (sec)	% drug content
A1	3.4 ± 0.24	0.74 ± 0.02	2.4	186	140 ± 2	99.84 ± 0.8
A2	3.5 ± 0.12	0.67 ± 0.12	2.1	142	92 ± 1	101.2 ± 0.3
A3	3.3 ± 0.46	0.84 ± 0.15	1.8	94	73 ± 3	98.89 ± 0.7
A4	3.6 ± 0.74	0.32 ± 0.09	2.8	67	59 ± 2	99.87 ± 0.9
A5	3.4 ± 0.23	0.49 ± 0.08	2.6	52	36 ± 4	99.34 ± 1.2

*Values are expressed as mean ± SD. n=3

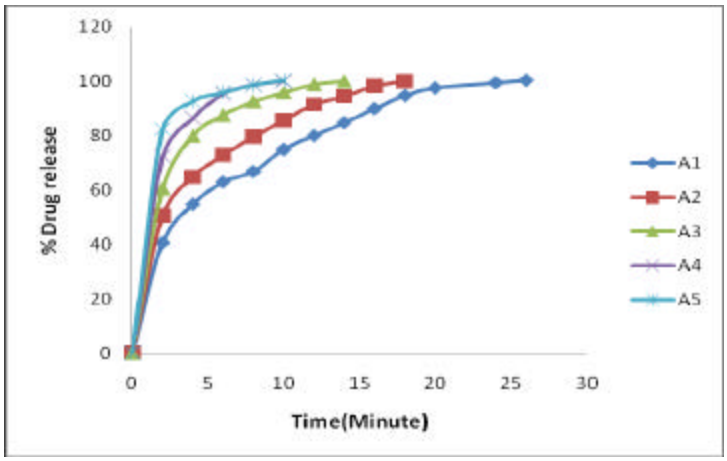

Fig.1: Comparison of dissolution profile of different formulations

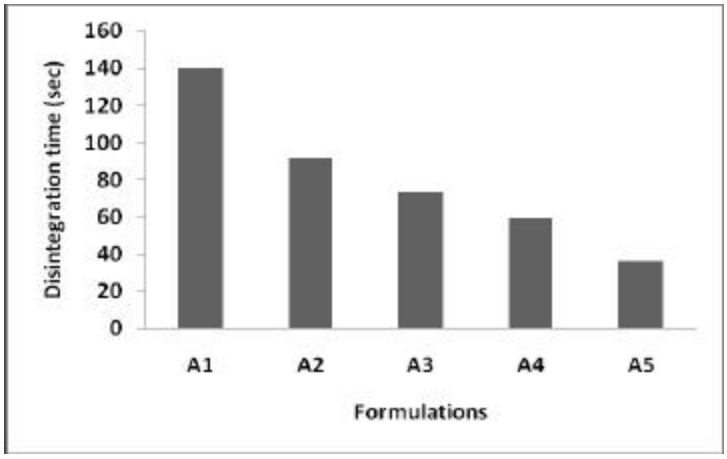

Fig.2: Comparison of disintegration time of different formulations.

twenty tablets were selected at random and their average weight was determined using an electronic balance (Shimadzu Aux200, Japan).The tablets were weighed individually and compared with average weight. The Pfizer hardness tester and Roche friabilator were used for the test of hardness and friability loss respectively. Disintegration time was measured using USP tablet disintegration test apparatus (ED2L, Electrolab, India) using 900 ml of distilled water without disk at room temperature (30^0).Thickness of the tablet was measured by dial caliper (Mitutoya, Model CD-6 CS, Japan).The wetting time was measured with the piece of tissue paper folded twice and placed in a Petry dish containing sufficient water. A tablet was kept on a paper and time for complete wetting of tablet was measured.

Drug content

Six tablets were powdered and weight equivalent to 10 mg of Aceclofenac was accurately weighed and transferred in to 100 ml volumetric flask .Initially 10 ml of phosphate buffer (pH 7.4) was added and shaken for 10 min. Then, volume was made up to 100 ml with phosphate buffer(pH 7.4).This solution was filtered, and 1 ml of filtrate was suitably diluted and analyzed at 275 nm using UV-visible spectrophotometer (Model-Lambda 25, PerkinElmer).The drug content of the sample was estimated from their standard curve.

Dissolution study

Dissolution study was carried out by using by digital tablet dissolution test apparatus (Paddle type, Model TDT-08L, Electrolab,(USP),India) in 900 ml of Phosphate buffer pH 7.4, monitored at 50 rpm and 37^0C.Aliquots were withdrawn at two minute time interval and were immediately replenished with the same volume of fresh buffer medium. Aliquots were filtered, following appropriate dilutions, were analyzed at 275 nm using UV-visible spectrophotometer (Model-Lambda 25, Perkin Elmer).The comparisons of dissolution profiles are shown in Fig.1

RESULTS AND DISCUSSION

Before formulating, preformulation study has been performed, drug-excipients (1:1) mixture of (drug: superdisintegrant) compatibility study by using IR spectrophotometer (Model-Spectrum Rx, Perkin Elmer) has been studied. There are no any changes in functional groups of the drug. The powder mixture shows good flow properties, Low Hausner ratio = (1.34), compressibility index (= 25.33) and angle of repose (= 18.54), these values indicate that the powder is having fairly good flowability properties. All the formulations were prepared under similar conditions to avoid processing variables. Weight variation of the tablets 2.34% which is within the limit (= 5%). Hardness of the

tablets was (3.44 ± 0.35) Kg.cm^2 The friability loss of the tablets was (0.61 ± 0.092%).The drug content of all formulations was found to be in the range of (99.82 ± 0.78%).

The most important parameter that needs to be developed for the fast dispersible tablet is the disintegration time. In present study all the formulations disintegrated within (= 140 sec), which fulfills the official requirement (= 3 min). Fig 2 shows the disintegration behavior of the all formulations. It is observed that disintegration time of formulations A1 to A5 decreased (from 140 to 36 sec), by increasing level of polyplasdone xl-10 because of its rapid capillary activity and pronounced hydration with little tendency to gel formation.[2]

Dissolution process of the tablet depends on wetting followed by disintegration of the tablet. The measurement of wetting time may be useful as another confirmative test for the evaluation of fast dispersible tablet. Fig.3 shows wetting time of various formulations. Significant decrease in wetting time observed by increasing level of polyplasdone from (8.33 to 16.66 %). The $t_{50\%}$ and $t_{80\%}$ values decreased with increasing the concentration of polyplasdone. In-vitro dissolution study was performed for all formulations, shown in Fig 5, It is observed that optimized formulation (A5) revealed that more than 80 % drug was released within 1.94 min.

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