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FORMULATION AND DEVELOPMENT OF ACECLOFENAC FAST DISSOLVING TABLETS: SUBLIMING AGENTS

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ABSTRACT
Attempts were made to prepare fast dissolving tablets of Aceclofenac by employing sublimation method to study the effect of different subliming agents and fillers. Formulations were evaluated for precompressional parameter such as angle of repose, % compressibility and Hausner's ratio. Tablets were subjected to post compressional analysis for the parameters such as hardness, friability, in-vitro disintegration time, wetting time and dissolution. Drug compatibility with excipients was checked by FT-IR studies. The results revealed that quantity of camphor, menthol, urea and type of filler significantly affect the response variables.

Key words *Fast Dissolving Tablets, Aceclofenac, Sublimation.*

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INTRODUCTION

Mouth dissolving tablets disintegrate or dissolve in saliva and are swallowed without the need for water. They are beneficial to swallowing tablets and capsules. Thus difficulty is particularly experienced by pediatric and geriatric patients. Various techniques such as freeze
drying, sublimation, spray drying, moulding, massextrussion and direct compression method have been reported for preparation of mouth dissolving tablets. most popular solid dosage forms are being tablets and capsules; one
important drawback of these dosage forms for some patients, is the difficulty to swallow. Drinking water plays an important role in the swallowing of oral dosage forms. Often times people experience inconvenience in swallowing conventional dosage forms such as tablets when water is not available,in the case of motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic conditions and bronchitis. For these reasons, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted great deal of attention. Aceclofenac,(2-{2-{2(2,6-dichlorophenyl) amino phenyl} acetyl} oxyacetic acid), a non steroidal anti-inflammatory drug (NSAID) has been indicated for various painful indicationsand proved as effective as other NSAIDs with lower indications of gastro-intestinal adverse effects and thus, resulted in a greater compliance

with treatment Hence in the present work Aceclofenac fast dissolving tablets were prepared by vacuum drying technique by using different sublimating agents and to study the effect functionality differences of subliming agents on the tablet properties.

MATERIALS AND METHODS

Aceclofenac was obtained as gift sample from KAIRAV Chemicals Ltd, MUMBAI MCC;Ac-di-sol (croscarmellose sodium) was obtained from Maple biotech pvt ltd, Pune, India. Crosspovidon, Camphor, Menthol, Urea, Mannitol, Talc and Magnesium stearate, Sodium Saccharin, Vanillin, Menthol, Talc was purchased from ReachemLab. Chemicals Pvt. Ltd. Chennai. All other materials were of analytical reagent grade.

Preparation of tablets:

Tablets containing 100mg of Aceclofenac were taken and then it was mixed with mannitol, directly compressible microcrystallinecellulose, superdisintegrants,Ac-di-sol (croscarmellose sodium),crosspovidon and different subliming agents in different concentrations in a plastic container.

Magnesium stearate and talc were passed through sieve no. 60 mixed and blended with initial mixture in the plastic container followed by compression of the blend. After compression the tablets were collected and vacuum dried at 60°C until a constant weight was obtained to ensure the complete removal of sublimable components to make the tablet porous. (Table 1)

EVALUATION OF POWDER MIXED BLEND:

The powder blend was evaluated for flow properties as follows.

1) Angle of Repose

Angel of repose was determined using cylinder method. The blend was poured through a cylinder that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and the angle of repose (q) was calculated using the formula.

$$\theta = \tan^{-1} (h/r)$$

Where,

θ = angle of repose

h = height of the pile r = average radius of the powder cone.

Table 1: Composition of fast disintegrating tablets

Ingredients (mg)	A1	A2	A3	B1	B2	B3	C1	C2
ACECLOFENAC	100	100	100	100	100	100	100	100
Crosspovidon	-	-	-	4	6	8	-	-
MCC	30	32	34	-	-	-	-	-
Mannitol	24	17	10	50	43	36	54	49
Camphor	30	35	40	-	-	-	-	-
Menthol	-	-	-	30	35	40	-	-
Urea	-	-	-	-	-	-	30	35
Aspartame	10	10	10	10	10	10	10	10
Magnesium Stearate	3	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3	3
Total weight	200	200	200	200	200	200	200	200

2)Bulk density: Bulk density was determined by pouring gently 25 gm of sample through
a glass funnel in to a 100 ml graduated cylinder. The volume occupied by the sample was recorded. Bulk density was calculated.

3)Tapped density: 25 gms sample (tablet blend) was poured gently through a glass funnel in to a 100ml graduated cylinder. The cylinder was tapped from height of 2 inches until a constant volume was obtained. Volume occupied by the sample after tapping were recorded and tapped density was calculated.

4)CompressibilityIndex:

The simplest way for measurement of free flow of powder is compressibility, a indication of the case with which a material can be induced to how is given by compressibility index (I) which is calculated as follows Where Vb is the bulk volume and is tapped volume. The value below 15% indicates a powder with usually give rise to good flow characteristics, whereas above 25% indicate poor Flowability.

5) Hausner ratio: Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following formula

Hausner ratio =Pt/Pb

Where, Pt tapped density and *Pb* is bulk density lower Hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Invitro release studies:

The *in-vitro* dissolution study was carried out in the USP dissolution test apparatus (Electrolab TDT - 08 L Dissolution tester USP) type 2 (paddle). 900 ml of the dissolution medium (Phosphate buffer pH 7.4) was taken in vessel and the temperature was maintained at 37 ± 0.50C. The speed of the paddle was set at 50 rpm. 5ml of the dissolution medium was withdrawn and the same amount of fresh medium was replenished to the dissolution medium. The sample withdrawn was filtered and diluted with Phosphate buffer pH 7.4 prior to analysis in the UV Spectrophotometer at 274 nm.

Table-2: Pre-compressional parameters of powder blend used in this technique:

Formulation	Angle of repose (0)	Bulkdensity (gm/cm3)	Tapped density (gm/cm3)	Compressibility index (%)	Hausner ratio
A1	29.13	0.57	0.68	16.176	1.192
A2	27.32	0.58	0.69	15.942	1.189
A3	29.52	0.56	0.68	17.647	1.214
B1	28.11	0.59	0.68	13.235	1.152
B2	30.01	0.60	0.73	17.808	1.216
B3	29.26	0.60	0.71	15.492	1.183
C1	30.17	0.59	0.69	14.492	1.169
C2	26.63	0.56	0.67	16.417	1.196

Table 3: Results of the post-compression parameters

Formulation	Weight variation (5%)	Thickness (cm)	Hardness (kg/cm2)	Friability (%)	Tensile Strength (Kg/cm2)	Porosity (%)	Content (%)	Disintegration Time (Sec)
A1	Pass	0.4	3.4	0.57	13.10	20	99.38	32
A2	Pass	0.5	3.2	0.25	12.74	12	99.45	34
A3	Pass	0.4	3.3	0.47	12.60	18	99.65	30
B1	Pass	0.5	3.5	0.58	9.92	25	99.78	20
B2	Pass	0.6	3.3	0.66	13.65	22	99.32	28
B3	Pass	0.5	3.6	0.62	12.55	36	99.88	24
C1	Pass	0.6	3.3	0.42	13.42	40	99.72	40
C2	Pass	0.5	3.4	0.45	13.68	42	99.65	38

Table 4: Invitro Drug Release of Batch In 7.4 pH Phosphate Buffer

Time (min)	A1	A2	A3	B1	B2	B3	C1	C2
5	55.20	57.30	58.35	65.78	85.78	83.08	45.36	44.36
10	55.80	57.68	59.48	66.66	86.78	84.32	46.36	45.88
15	56.60	61.25	61.20	68.58	88.88	87.12	46.88	48.85
20	57.25	63.85	63.85	69.98	91.58	89.23	48.58	49.65
25	57.45	65.29	65.98	71.25	93.75	91.02	50.28	52.69
30	59.40	66.15	67.85	73.88	95.88	93.85	51.65	54.23
35	64.38	67.25	69.45	74.98	96.85	94.96	52.36	56.49
40	64.98	68.38	72.22	79.58	97.02	96.90	53.96	58.98
45	68.88	70.58	73.58	84.98	98.38	97.70	58.98	60.85
50	72.72	72.68	74.34	93.58	100	98.99	64.68	68.52
55	78.22	75.83	76.88	98.85		100	72.98	76.22
60	84.56	83.65	87.98	99.99			78.69	77.36

RESULTS AND DISSCUSIONS:

The use of superdisintegrants for preparation of mouth dissolving tablets is highly effective and commercially feasible. The values of the pre-compressional parameters such as angle of repose, bulk density, tapped density, compressibility index and hausner ratio evaluated were with in prescribed limits and indicated a good free flowing property. The results are shown in table-2. The results of post-compressional parameters such as weight variation, hardness, friability, porosity, thickness, tensile strength, assay and disintegration time. The results are shown in table-3. The results of in vitro drug release are shown in table-4. Using the same excipients, the tablets were prepared, without 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 mouth-dissolving tabletgets dispersed in the mouth quickly and releases the drug early as compared to its formulated conventional tablet. The tablets of the batch B2 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 pain.

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