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Formulation and Evaluation of Fast Dissolving Tablet of Aceclofenac by Sublimation Method

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ABSTRACT

This investigation is based on the treatment and diagnosis which is caused by pain and swelling. Swelling can be caused by the leakage of fluids into the tissues due to some chemicals. Aceclofenac is a derivative of the diclofenac group of the non-steroidal anti-inflammatory drug (NSAID). Aceclofenac exhibits analgesic and anti-inflammatory effects. This study aims to formulate, prepare and evaluate fast dissolving tablets of Aceclofenac drug using the sublimation method. Camphor is used as sublimating agent. The fast dissolving tablet is the way that improves patient compliance by taste masking. The fast dissolving tablet raises the bioavailability of insoluble and hydrophobic drugs due to the rapid disintegration and dissolution of the drugs. According to this study, the Aceclofenac tablet was prepared using sodium starch glycolate as a disintegrant, magnesium stearate and talc as a lubricant, mannitol as sweetener, and diluents, crospovidone as superdisintegrant and microcrystalline cellulose as a dispersing agent. The preformulation studies have been done for thickness, uniformity of weight, friability, wetting time, *in-vitro* disintegration time, and *in-vitro* dissolution time. Phosphate buffer (pH 6.8) was used as media for dissolution. 27 - 30 sec is the disintegration time of Aceclofenac tablet whereas 90 % of the drug was released within 30 min. Stability studies of the tablet taken at 40 ± 2°C/75% ± 8% RH for 1 month displayed nonsignificant drug loss. The different parameters like *in-vitro* disintegration, wetting time, and *in-vitro* dissolution were carried out during the research work. 8 % of crospovidone showed the best results. This study demonstrated that the Aceclofenac tablet exhibits a higher rate of release.

INTRODUCTION

The oral route of drug administration is the most preferred route for solid dosage forms because of ease of administration, precise dosage, self-medication, and patient compliance. [1] Non-steroidal anti-inflammatory drugs (NSAIDs) are generally prescribed due to their analgesic, anti-inflammatory, and antipyretic activity. [2] NSAIDs are commonly recommended for the treatment of rheumatoid arthritis, osteoarthritis, and dysmenorrhoea. [3] The chemical name of Aceclofenac is (2-[(2,6-dichlorophenyl) amine] phenylacetoxyacetic acid). Aceclofenac is commonly based on the inhibition of prostaglandin synthesis. It inhibits the *cyclo-oxygenase* enzyme, which is responsible for the production of prostaglandin. [4]. The synthesis of Cytokines, interleukin (IL-1), tumour necrosis factor, and prostaglandin E2 (PGE2) can also be inhibited by Aceclofenac drug. [5] Many patients like geriatric, pediatric have difficulty in swallowing conventional tablets, which results in poor patient compliance. This difficulty can be overcome by an innovative drug delivery system called a fast-dissolving tablet. Scientists have developed this kind of innovative drug delivery system. Saliva is responsible for the disintegration/ dissolution/ dispersion of tablets in the mouth. The tablet can be administered without the use of water. [6]. The absorption of the drug in the oral cavity and the pregastric absorption of saliva containing dispersed drugs that pass down into the stomach is the main reason for the increased bioavailability of FDTs. [7]

OBJECTIVE

The objective of this investigation is to formulate and evaluate fast dissolving tablets of Aceclofenac by sublimation method as well as to increase profile in a short duration of time. Pre-formulation studies of tablets were done using several quality parameters like weight variation, hardness, friability, wetting time and water absorption ratio, *in-vitro* dispersion time, *in-vitro* disintegration time, and *in-vitro* dissolution time. Stability studies were performed.

MATERIALS AND METHODS

Table No. 1: Materials used in the formulation of fast dissolving tablet of Aceclofenac tablet

Sr. No.	Material	Manufacturer
1.	Aceclofenac	Ipeca Pharmaceutical Pvt. Ltd.
2.	Magnesium stearate	S.D Fine Chem. Ltd, Mumbai
3.	Mannitol	S.D Fine Chem. Ltd, Mumbai
4.	Microcrystalline cellulose	S.D Fine Chem. Ltd, Mumbai
5.	Crospovidone	S.D Fine Chem. Ltd, Mumbai
6.	Sodium starch glycolate	S.D Fine Chem. Ltd, Mumbai
7.	Potassium dihydrogen phosphate	S.D Fine Chem. Ltd, Mumbai
8.	Talcum powder	National Chemicals
9.	Camphor	

Drug – excipient compatibility studies

The compatibility of superdisintegrant that is Crospovidone and individual excipients was established by FTIR and the spectrum was recorded in the wavelength region of 4000 – 400 cm^{-1}. Any changes in the composition after combining with the excipients were investigated with IR spectral analysis.

Preparation of Fast Dissolving Tablet of Aceclofenac

The weighed quantity of superdisintegrant (Crospovidone) was taken. Aceclofenac was taken and mixed with the superdisintegrant. Then sieved by the sieve No. 44. After that magnesium stearate and talc and microcrystalline cellulose were mixed with the prepared mixture and sieved by sieve No. 85. A volatile ingredient (camphor) was added in the above formulation. The volatile material was then removed by sublimation leaving behind a highly porous matrix. Mannitol and camphor were used, respectively, as tablet matrix and subliming material. Camphor was vaporized by subliming in a vacuum at 80 ˚C for 30 minutes to develop pores in the tablets. The composition of various batches are described in Table No. 2.

Evaluation of Fast Dissolving Tablet of Aceclofenac

Weight variation

A composite sample of tables (usually 20) was taken and weighed throughout the compression process. The composite weight is divided by 20. However, provide an average weight but contained the usual problem of average weight. [8]

Hardness

The lower plunger was placed in contact with the tablet, and a zero reading was taken. The upper plunger was then forced again a spring by turning a threaded bolt until the tablet fractures. As spring is compressed, a pointer rides along a gauge in the barrel to indicate the force. The force of fracture was recorded and the zero recordings were deducted from it. [9]

Friability

Roche friabilator is used to measure the friability of the drug. Weighed 6 tablets and placed in the friabilator revolves at 25 rpm, 100 revolutions, dropping those tablets at a distance of 6 inches with each revolution. The tablet is rotated for at least 4 minutes. After a given period, test tablets were dusted and reweighed. The loss in the weight of the tablet is the measure of friability. [10]

$$\% \text{ Friability} = \text{loss in weight} * 100 / \text{initial weight}$$

Wetting time and water absorption ratio

A piece of tissue paper folded twice was placed in a small petri dish (ID = 6.5cm) containing 6 ml of phosphate buffer pH 6.8, a tablet was put on the paper, and the time for complete wetting was noted down. The wetted table was then weighed. Water absorption ratio R was calculated by the following equation. [11]

$$R = 100 * Wb / Wa$$

Where,

Wb = water before absorption

Wa = water after absorption

In-vitro dispersion time

The tablet was added to 10 ml of phosphate buffer solution (6.8) at 37 ± 0.5 ˚C and the time required for complete dispersion of tablet is measured. [12]

In-vitro disintegration time

Disintegration test apparatus is used for measuring *in-vitro* disintegration time. One tablet was kept in each tube of the basket. The basket was immersed in the water bath at 37 ± 2 °C. A stopwatch was used for determining the time required for complete disintegration. [13]

In-vitro dissolution studies

In-vitro dissolution studies for Aceclofenac fast dissolving tablets was evaluated using the USP paddle method at 50 rpm in 900 ml of phosphate buffer pH 6.8 as dissolution media, controlled at 37 ± 0.5 °C. 5 ml aliquot of the solution was withdrawn from the dissolution apparatus after a definite time interval, and the samples were replaced with fresh dissolution medium. The absorbance of these solutions was observed at 274 nm using a UV spectrophotometer. [14]

Accelerated stability studies

The stability studies of formulated tablets were carried out at 40/75 (˚C/RH) and room temperature for one month. The effect of temperature, humidity, and time on the physical characteristics of the tablet was evaluated for assessing the stability of the prepared formulation. [15]

ACKNOWLEDGMENT:

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Conflict of interest

There are no conflicts of interest.

RESULT AND CONCLUSION

Fast dissolving tablet of Aceclofenac was prepared by the sublimation method. The formulation was carried out using superdisintegrant and other excipients and optimized the

concentration and hardness of the tablet to give the least disintegration time and get greater drug release. The taste and odour were acceptable for geriatric and paediatric patients. The hardness of the tablet was found to be 3.5 kg/sq cm and have good mechanical strength. The friability of the formulation S3, S6 was found to be 0.89 and 0.93 %. That was below 1 %. All the tablets from each formulation passed the weight variation test, as the % weight variation was within the Pharmacopoeial limits of ± 7.5 % of the weight.

The composition of the batch S1 was in the ratio of 2:4 crospovidone: sodium starch glycolate. The water absorption ratio was 68.9 ± 2.5 % and the 87 % drug was released within 30 min. The composition of the batch S2, S4, and S6 was in the ratio 4:8, 0:8, and 8:0. Hardness was good but more than 100 % drug was released within 30 min. The composition of the batch S3 and S5 was in the ratio 0:4 and 4:0. The hardness was less than 4 but the % drug released was 90 % within 30 min.

The wetting time, *in-vitro* dispersion time, *in-vitro* disintegration, and *in-vitro* dissolution time were within the acceptable limit.

Table No. 2: Composition of fast dissolving tablet of Aceclofenac by sublimation method

Formulation code	Aceclofenac (mg)	Camphor (mg)	MCC (%)	Mannitol (%)	Crospovidone: SSG (%)	Magnesium stearate (%)	Talc (%)
S1	100	60	70	10	2:4	2	4
S2	100	60	70	10	4:8	2	4
S3	100	60	70	10	0:4	2	4
S4	100	60	70	10	0:8	2	4
S5	100	60	70	10	4:0	2	4
S6	100	60	70	10	8:0	2	4

Table No. 3: Preformulation parameters of fast dissolving tablet of Aceclofenac

Formulation code	Bulk density (gm/cm^3) Avg ± SD	Tapped (gm/cm^3) Avg ± SD	Compressibility (%) Avg ± SD	Hausner's ratio (%) Avg ± SD	Angle of repose (%) Avg ± SD
S1	0.369 ± 0.12	0.445 ± 0.12	17.0 ± 0.37	1.20 ± 0.08	25 ± 0.78
S2	0.321 ± 0.07	0.389 ± 0.16	21.1± 0.24	1.21 ± 0.07	30 ± 0.53
S3	0.312 ± 0.08	0.467 ± 0.11	31.2 ± 0.27	1.4 ± 0.04	34 ± 0.33
S4	0.35 ± 0.06	0.448 ± 0.12	19.8 ± 0.27	1.25 ± 0.07	29 ± 0.58
S5	0.420 ± 0.06	0.507 ± 0.8	17.15 ± 0.37	1.20 ± 0.08	35 ± 0.32
S6	0.432 ± 0.03	0.550 ± 0.00	21.4 ± 0.25	1.27 ± 0.07	33 ± 0.40

Each data represents Mean ± SD (n=3)

Table No. 4: Post-compression parameters of fast dissolving tablet of Aceclofenac

Formulation code	Hardness Kg/cm^2 Avg ± SD	Friability (%) Avg ± SD	Wetting time (sec) Avg ± SD	Water absorption ratio (%) Avg ± SD	In-vitro dispersion time (sec) Avg ± SD	In-vitro disintegration time (sec) Avg ± SD
S1	4 ± 0.05	0.89 ± 0.3	25.3 ± 0.2	68.9 ± 2.5	27.7 ± 0.4	26.5 ± 0.3
S2	4 ± 0.05	0.79 ± 0.2	23 ± 0.3	69.1 ± 2.4	25.8 ± 0.4	24 ± 0.4
S3	3.5 ± 0.08	0.74 ± 0.4	24.3 ± 0.3	66.2 ± 2.7	30.2 ± 0.3	29.1 ± 0.2
S4	3.5 ± 0.08	0.82 ± 0.3	25.5 ± 0.2	70.1 ± 2.3	29.7 ± 0.3	29.2 ± 0.2
S5	4 ± 0.05	0.88 ± 0.2	26.1 ± 0.2	72.1 ± 2.1	28.3 ± 0.3	27.1 ± 0.3
S6	3.5 ± 0.08	0.79 ± 0.3	25.9 ± 0.2	71.1 ± 2.9	29.1 ± 0.3	26.4 ± 0.3

Each data represents Mean ±SD (n=3).

Table No. 5: *In-vitro* drug release profile of fast dissolving tablet of Aceclofenac

Formulation code	Dissolution media	Time (min)	Absorbance	% drug release
S1	Phosphate buffer	0	0.002	3
		5	0.006	15
		10	0.012	33
		15	0.017	48
		20	0.024	69
		25	0.029	84
		30	**0.031**	**90**
S2	Phosphate buffer	0	0.002	3
		5	0.007	18
		10	0.009	24
		15	0.015	42
		20	0.023	66
		25	0.027	78
		30	**0.030**	**87**
S3	Phosphate buffer	0	0.002	3
		5	0.006	15
		10	0.012	33
		15	0.017	48
		20	0.024	69
		25	0.029	84
		30	**0.031**	**90**
S4	Phosphate buffer	0	0.004	0
		5	0.009	15
		10	0.013	27
		15	0.02	48
		20	0.026	66
		25	0.029	75
		30	**0.034**	**90**
S5	Phosphate buffer	0	0.003	3
		5	0.007	15
		10	0.012	30
		15	0.017	45
		20	0.021	57
		25	0.024	66
		30	**0.03**	**84**
S6	Phosphate buffer	0	0.004	3
		5	0.010	15
		10	0.013	30
		15	0.02	45
		20	0.025	57
		25	0.027	66
		30	**0.037**	**90**

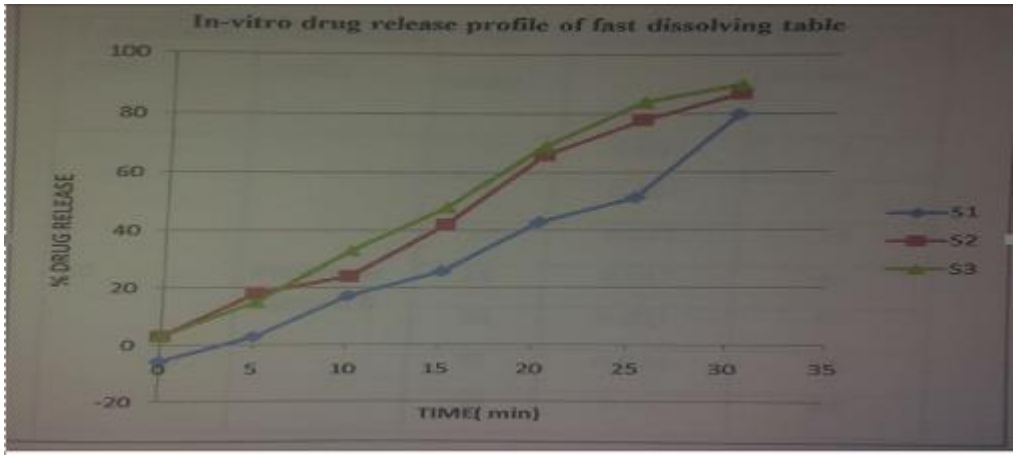

Figure No. 1: Graph showing three formulations S1, S2, S3

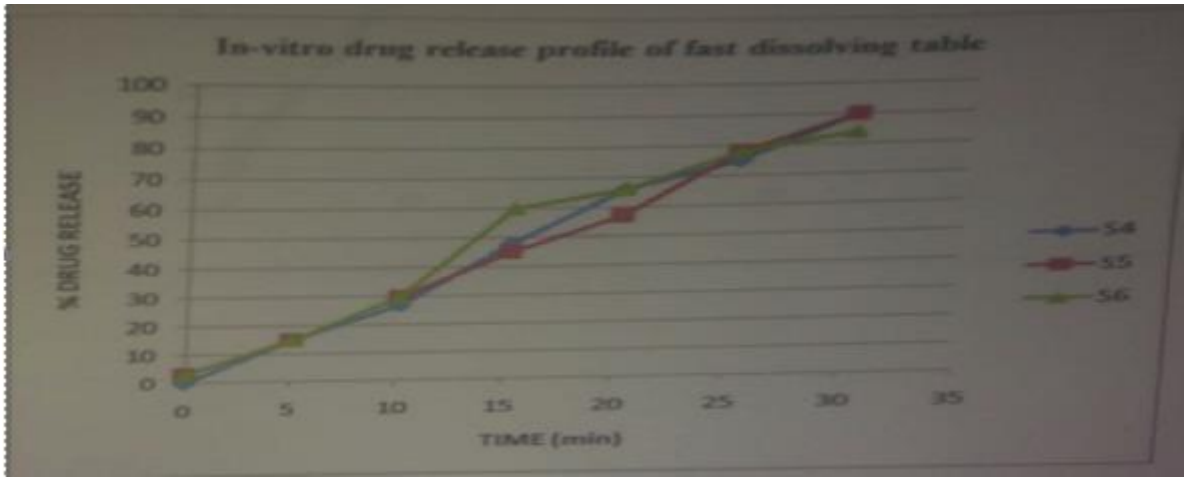

Figure No. 2: Graph showing three formulations S4, S5, S6

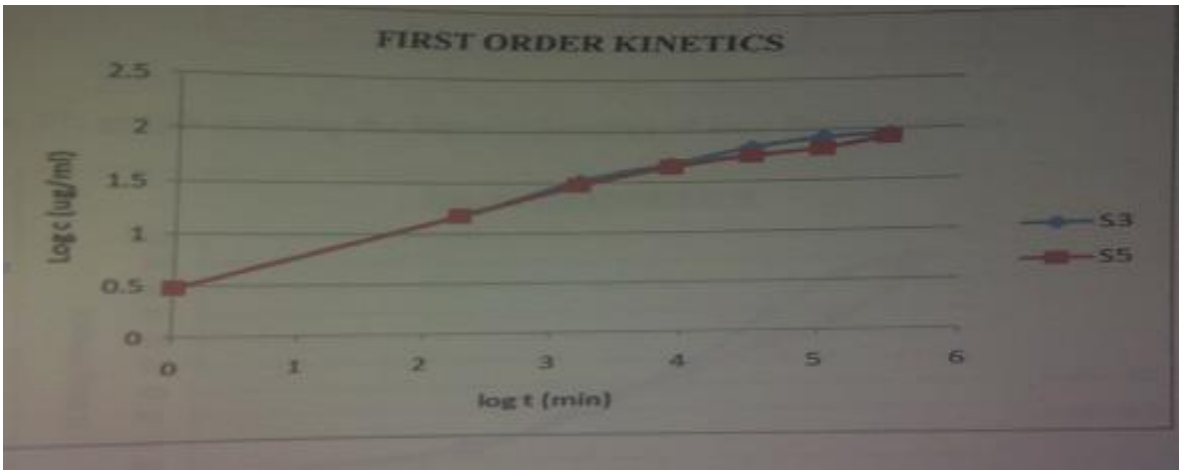

Figure No. 3: Graph showing first-order kinetics of best formulation

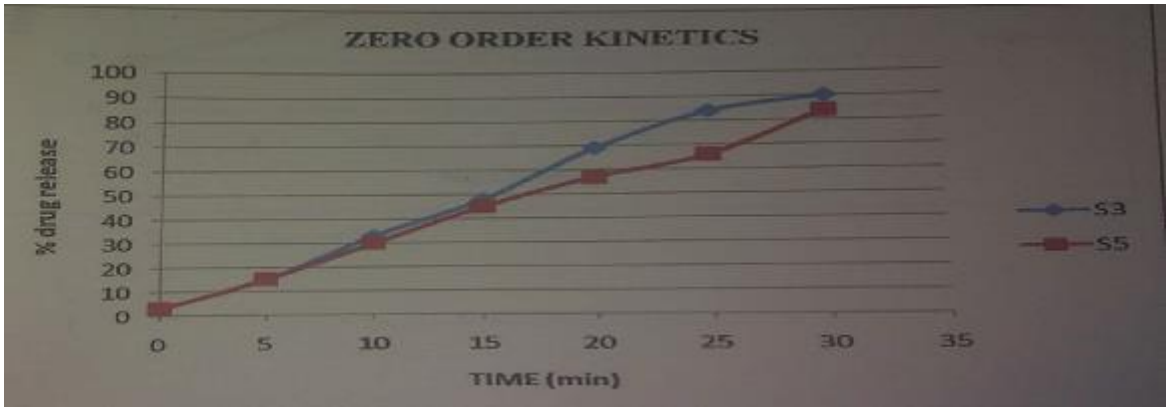

Figure No. 4: Graph showing zero-order kinetics of best formulation

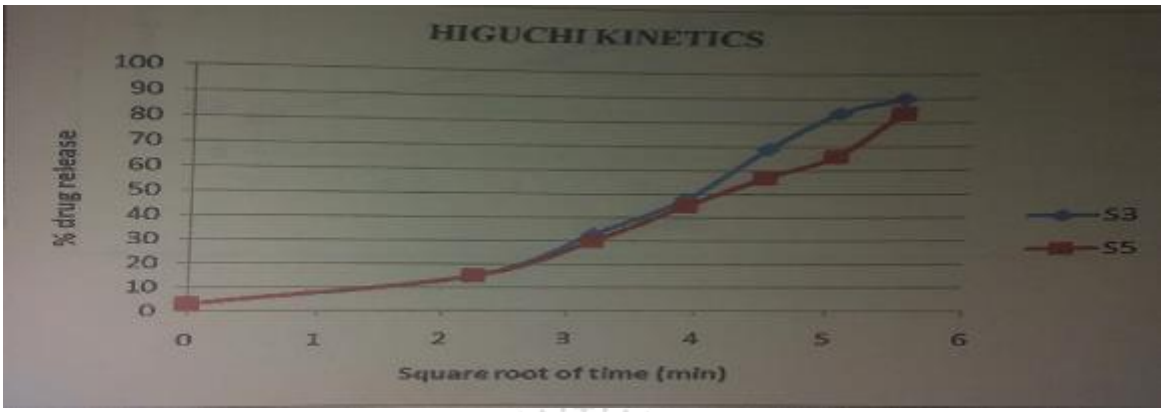

Figure. No. 5: Graph showing Higuchi kinetics of best formulation

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