

Novel approach of aceclofenac fast dissolving tablet

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Abstract: Fast disintegrating tablets (FDTs) have received ever increasing demand during the last decade, and the field has become a hastily growing area in the pharmaceutical industry. Upon introduction into the mouth, these tablets dissolve or disintegrate in the mouth in the absence of additional water for easy administration of active pharmaceutical ingredients. Aceclofenac, an NSAID, has been recommended orally for the treatment of bone and connective tissue disorder and thus the formulation of the same resulted in development of several FDT technologies. The present aim is to formulate a tablet which disintegrate and dissolve rapidly and give its rapid onset of action: analgesic, antipyretic and anti-inflammatory action. Besides, the conventional tablets also show poor patient compliance an attempt had been made to formulate for FDT of aceclofenac by using various super disintegrants like sodium starch glycolate, croscarmellose sodium and crosspovidone (polyplasdone XL) and PEG 6000 followed by novel technique. The tablets were evaluated for friability, hardness, weight variation, disintegration time, wetting time, *in vitro* dissolution studies and drug content studies. It was concluded that the batch which was prepared by using combination of crosspovidone and sodium starch glycolate as a super disintegrant shows excellent disintegration time, enhance dissolution rate, taste masking and hence lead to improve efficacy and bioavailability of drug.

Keywords: Aceclofenac, Fast disintegrating tablets (FDTs), croscarmellose sodium, crosspovidone, SSG.

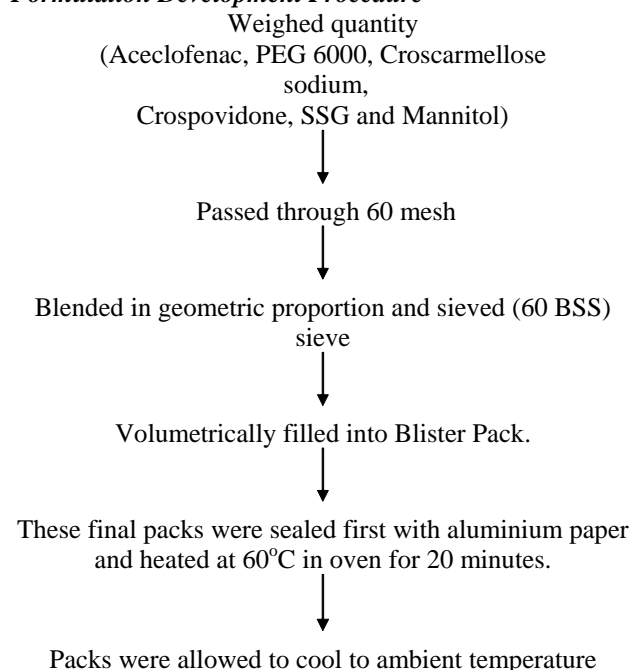
INTRODUCTION

Fast disintegrating tablets are dosage form, which disintegrate and dissolve in patient's mouth within quickly without requiring water, or chewing, providing best alternative for the patient suffering from difficulty in swallowing (Gedamand Ghuge, 2010). Fast disintegrating tablets have an edge over conventional dosage form because of greater bioavailability. Mouth dissolving dosage forms are increasingly being recognized in both industry and academia (Khurana and Bedi, 2009). Uniqueness and majority of orally administered dosage form especially fast dissolving drug delivery systems have started gaining popularity and acceptance because of rapid disintegration, dissolution, self-administration that without water or chewing (Sharma and Yadav, 2010). Recent advances in technology and novel drug delivery systems (NDDS) have presented viable dosage alternatives for patients who have difficulty in swallowing tablets or capsules and further, the aim to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance; one such approach is fast dissolving tablets (Lieberman and Karnig, 1987; Lohitnavy *et al.*, 2003). Higher incidences of gastrointestinal complications are associated with conventional dosage forms, when administered through oral route. Further, topical administration offers the advantage of local, enhanced drug delivery to affected tissues with reduced bioavailability and least systemic adverse effects, seen in

condition as that of gastrointestinal ulcer and hemorrhage. Thus, a well formulated topical preparation that can effectively deliver aceclofenac to the site of action in rheumatic diseases will go a long way in reducing the gastrointestinal side-effects of the drug.

MATERIAL AND METHODS

Formulation Development Procedure



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Fig. 1: Aceclofenac fast dissolving tablet the Blister pack is heated in an oven for 20 minutes at 60°C.



Fig. 2: Aceclofenac fast dissolving tablet

Characterization of tablets

Drug - Excipients compatibility study

Differential scanning calorimetry (DSC) scans of pure drug, placebo formulations and drug loaded selected fast dissolving tablets (F2) were performed using DSC-PYRIS-1 (Perkin-Elmer, USA). The analysis was performed with a heating range of 50-480°C and at a rate of 10°C/min.

Fourier Transform Infrared Spectroscopy

The spectroscopic technique was conducted using a Shimadzu FTIR 8300 Spectrophotometer and the spectrum of the same was recorded in the region of 4000 to 400 cm^{-1} . The method consisted of dispersing a sample (drug and drug-excipient mixture, 1: 1 ratio) in KBr (200-400 mg) and compressing into discs by applying a pressure of 5 tons for 5 min in a hydraulic press. The pellet was placed and the spectrum was obtained. Spectra were recorded in duplicate for each of the samples. (Siddiqui *et al.*, 2011).

Physical Characterization of Blend

Was done for Particle size distribution, Bulk Density, Tapped density and compressibility index.

Particle size distribution

Was done in electronic sifter, Hosokawa Alpine 200 LS-N. About 20 g of the blend was weighed and added to sieve #150, #85, #60 and #36, with subsequent weighing of the blend in between. Time of sifting with each mentioned sieve was 2 min. / sieve (Chang *et al.*, 2000).

Determination of Bulk density, angle of repose and compressibility index

Firstly, the graduated cylinder was tare to zero, certain quantity of powder (W) was carefully poured into the

graduated cylinder and the same was weighed. Also, the volume (V) was noted. The graduated cylinder was then closed with lid and set into the density determination apparatus (Bulk density apparatus, Campbell electronics). The density apparatus was set for 350 taps and after that the volume (V) was determined. The Bulk Density, Tapped density was calculated using the following formulas:

$$\text{Bulk Density} = W/V_0$$

Where W= Weight of powder, V_0 = Initial volume, V_f =Final volume

Compressibility Index The compressibility index is determined by measuring both bulk density and the tapped density of a powder. (Lieberman and Karnig, 1987).

$$\text{Compressibility Index (\%)} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Angle of repose: $\tan \alpha = H/R$

H is the height of the pile, and R is the radius of the base of the conical pile.

Hardness

Was determined using Schleuniger hardness tester. It was expressed in kilo Pascal (kp). Ten tablets were randomly selected from each formulation and hardness of the same was determined. The results are expressed in average value.

Friability

Was determined using friability test apparatus (Campbell Electronics, India). About 6.5 g tablets (W) were transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or 100 initial revolutions. The tablets were dedusted and weighed again (W). The percentage friability was calculated by

$$F = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

Weight variation

Twenty tablets were randomly selected from each formulation and average was determined. Then individual tablet were weighed and individual was compared with average weight.

Disintegration test

Was determined using Disintegration test apparatus. The operation was performed on 6 tablets.

Determination of drug content

20 tablets was taken and powdered accurately. Powdered containing about 50mg of Aceclofenac was taken and shake it with 60ml methanol in 200ml volumetric flask and dilute to volume with methanol. 5ml of this solution was taken and diluted up to 100ml with methanol and absorbance was noted at 276nm.

In vitro dissolution rate study

Was done by using USP Type II apparatus which was rotated at 75 rpm in Sorenson's buffer (pH 6.2) was taken as dissolution medium. Temperature of the dissolution medium was maintained at $37 \pm 0.5^\circ\text{C}$. Aliquots of dissolution medium were withdrawn at specific time interval and it was filtered. Drug concentration was determined from standard calibration curve (Allen *et al.*, 2000; Makino *et al.*, 1998; Koizumi *et al.*, 1997).

Stability Studies

The best formulation was charged for stability studies at temperature and relative humidity of $40^\circ\text{C}/75\%$ RH for period of one month. The parameter used to assess the effect of stress condition on tablets include: Weight variation, Avg. Thickness, Friability, Disintegration Time, Avg. Hardness, Wetting time, Drug content and % Drug released.

RESULTS

Drug-Excipient Compatibility Studies

The DSC thermograms of pure aceclofenac and its mixture with different excipient (1: 1). A sharp endotherm at 154.49°C corresponding to its melting point/transition temperature was showed by pure aceclofenac. No appreciable changes were seen in the melting endotherms of the physical mixture (aceclofenac+ superdisintegrants) as compared to pure drug. Interactions between drug and additives used in the preparation were absent as showed in fig. 3.

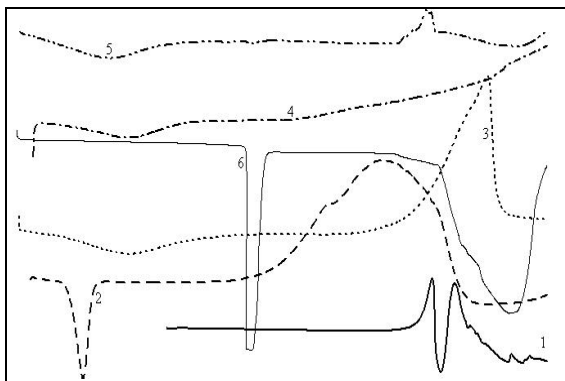


Fig. 3: DSC thermograms of pure aceclofenac and its mixture with different excipient (1:1).

Fourier Transform Infrared Spectroscopy

The FTIR spectra of pure drug aceclofenac, placebo formulations (without drug) and drug loaded fast dissolving tablet (FDT) were recorded. The results are showed in fig. 4 to 7. C=O stretching of COOH and CH bending of CH₃ group respectively indicates the presence of drug in the polymer without any interaction and the peaks at 1857.95 nm , 2553.01 nm , 3027.69 nm and 963.53 nm confirms the presence of drug. All the above peaks were also present in drug loaded fast dissolving tablet

(FDT). From the result it is evident that peaks alone and in combination are coinciding which indicate that the drug do not seems to have interaction with the excipients of ocular insert in physical mixture.

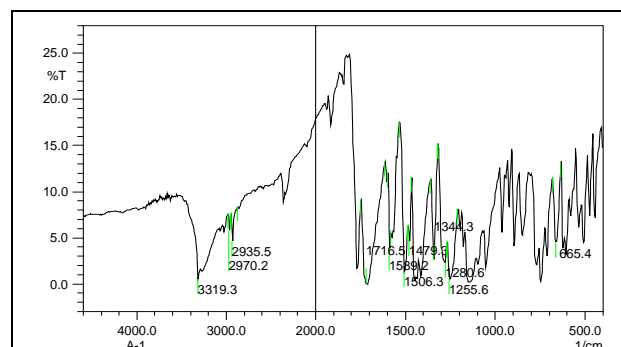


Fig. 4: IR spectra of pure aceclofenac

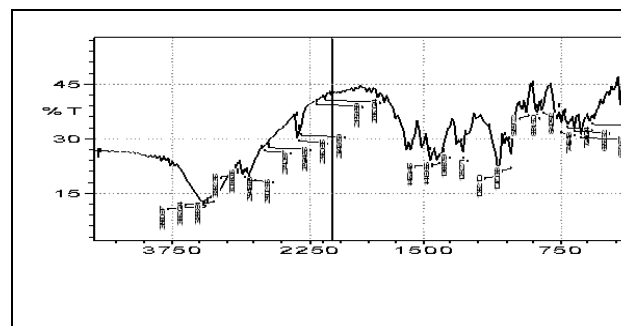


Fig. 5: Aceclofenac + Croscarmellose sodium + PEG 6000 + Mannitol

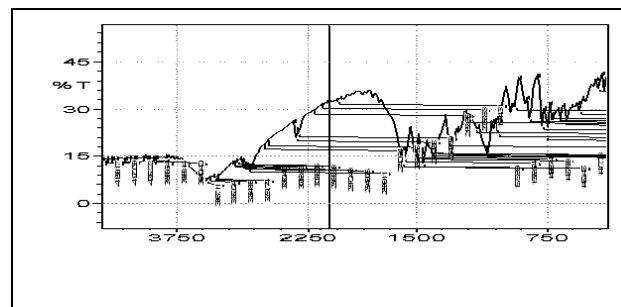


Fig. 6: Aceclofenac + Crospovidone + PEG 6000 + Mannitol

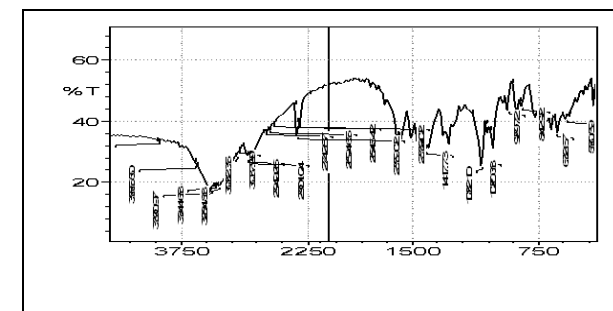


Fig. 7: Aceclofenac + SSG + PEG 6000 + Mannitol

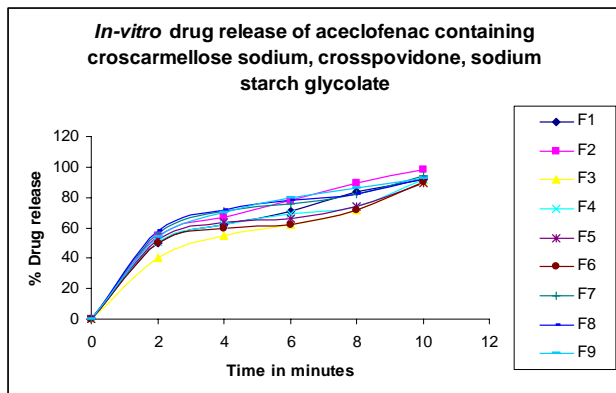


Fig. 8: In-vitro drug release of aceclofenac fast dissolving tablet

The compositions of different formulations and preformulation studies and evaluation parameters like friability, hardness, weight variation, thickness, disintegration time, dissolution rate and assay for drug content were found to be satisfactory and the results were presented in table 1. The formulation containing Croscarmellose sodium shows sufficiently decrease in disintegration time was less than 20 sec and the formulation F2 show disintegration time 14 sec. where as in case of Crospovidone (PPXL) disintegration time was less than 22 sec and Sodium Starch Glycolate disintegration time was less than 25 sec. The bulk density was ranged from 0.51 ± 0.01 to 0.54 ± 0.01 gms/cc. The angle of repose values was ranged from 25.76 ± 0.06 to 33.52 ± 2.47 . Formulation F2 shows a good flow property whereas the rest are in the range of fair to passable flow property. For compressibility Index the value is ranged from 15.26 ± 0.83 to 19.69 ± 0.83 . Formulation F2 shows a value 15.26 ± 0.83 which means the flow property is good.

Table 1: Composition and characterization of FTD

Ingredient	Formulation								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Aceclofenac	25	25	25	25	25	25	25	25	25
Croscarmellose sodium	6	12	15	-	-	-	-	-	-
Crospovidone	-	-	-	6	12	15	-	-	-
SSG	-	-	-	-	-	-	6	12	15
PEG 6000	75	75	75	75	75	75	75	75	75
Mannitol	195	188	185	195	188	185	195	188	185
Characterization									
Bulk density (g/ml)	0.51 ± 0.01	0.54 ± 0.01	0.52 ± 0.01	0.53 ± 0.01	0.52 ± 0.01	0.51 ± 0.01	0.53 ± 0.01	0.53 ± 0.01	0.52 ± 0.01
Angle of repose (g/ml)	30.2	25.76	31.56	33.56	32.48	31.25	32.56	33.46	33.2
Compressibility index %	18.6	15.26	19.63	17.53	18.65	18.32	18.36	18.02	18.23
Hardness (kg/cm^2)	1.62	1.63	1.45	1.62	1.58	1.57	1.60	1.61	1.59
Friability (%)	0.62	0.45	0.63	0.74	0.83	0.63	0.72	0.75	0.78
Thickness (mm)	2.74	2.7	2.71	2.68	2.77	2.71	2.74	2.73	2.77
Disintegration Time (sec.)	20	14	16	22	21	18	25	23	20
Drug content	-	98.9	-	94.6	-	-	96.2	-	-

The hardness of the tablets of all batches was ranged from 1.23 ± 0.15 to 1.63 ± 0.11 kg/cm^2 . The hardness reported is enough to maintain the integrity of the tablet as well as not to affect the disintegration of the tablet in the mouth. The percentage friability was ranged from 0.45 ± 0.005 to $0.83 \pm 0.04\%$. Drug content studies were done on selected batches and a result was presented in table 1 which showed that the drug content is within limit. As fast dissolution formulation F2 shows satisfactory % drug release and disintegrating time.

DISCUSSION

Dissolution studies were performed for all prepared batches % cumulative drug release was calculated for all batches prepared with different super disintegrants. In vitro dissolution rate study shows that after 10 min formulation F1 to F3 % drug release is 90%, 98%, 93% respectively containing croscarmellose sodium and for crospovidone formulation F4 to F6 the % drug release was found to be 92%, 89%, and 90% respectively for sodium starch glycolate formulation F7 to F9 drug release was found to be 94%, 93%, 93%. Stability Studiesthe stability testing was done as per the ICH guidelines. Drug content of the formulations on storage for 3 months at 40°C and 96.5% RH. Concentration of the super disintegrants was increased the stability decreased.

CONCLUSION

The present study it may be concluded that fast dissolving tablet of aceclofenac can be formulated by novel technique by using suitable super disintegrant (Croscarmellose sodium, Crospovidone (PPXL), Sodium Starch Glycolate). The IR and DSC studies revealed that

there was no interaction between aceclofenac and excipients used in the preparation of tablets. The tablets prepared were found to be within the official limits with respect to hardness, weight variation, drug content, friability. The formulation F2 with the concentration of (4%) of Croscarmellose sodium gave the least disintegration time of 11seconds. Formulation F2 showed the maximum cumulative percentage drug release (98%).

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