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Formulation and Evaluation of Fast Dissolving Tablets of Aceclofenac

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ABSTRACT

Aceclofenac, a nonsteroidal anti-inflammatory drug, is widely used in the treatment of rheumatoid arthritis and other inflammatory conditions. However, its oral bioavailability is limited due to its poor solubility and slow dissolution rate. To overcome these limitations, we have developed fast-dissolving tablets of aceclofenac using novel excipients and formulations.In this study, we designed and evaluated fast-dissolving tablets of aceclofenac using a combination of superdisintegrants, such as croscarmellose sodium and sodium starch glycolate, and a disintegrant, such as cross-linked sodium carboxymethyl cellulose. The tablets were prepared using a wet granulation process and evaluated for their dissolution profile, hardness, and friability.The results showed that the fast-dissolving tablets of aceclofenac exhibited a rapid dissolution profile, with more than 90% of the drug dissolved within 30 seconds. The dissolution rate was significantly faster than that of commercial aceclofenac tablets. The tablets also exhibited good hardness and friability, indicating their suitability for oral administration.The findings of this study suggest that the fast-dissolving tablets of aceclofenac may offer improved bioavailability and faster absorption compared to commercial aceclofenac tablets. The novel formulation and excipients used in this study may have potential applications in the development of fast-dissolving tablets for other poorly soluble drugs. Further studies are needed to evaluate the long-term safety and efficacy of these novel tablets in patients with inflammatory conditions.

Keywords: Aceclofanac,Fats dissolving tablets,Super disintegrants.

Introduction

Oral route of administration is highly agreeable by the patients because of their administration, non-invasiveness and cost effectiveness. Butoral dosage forms are limited by first pass metabolism and gulping of tablets especially incase of paediatric and geriatrics. Fast dissolvingtablets ororaldispersible tablets are novel form of oral dosage systems. These are advantageous because these are rapidly dissolute within couple of seconds in saliva thus enhancing bioavailability in addition also avoids enterohepatic cycling.

Aceclofenac is NSAID analogue of Diclofenac. It is used as pain reliever and inflammation resulted from the Arthritis. Its how sits mode of action by inhibiting the cyclo-oxygen as which is used in synthesis of prostaglandins which causes pain and inflammation.

As Aceclofenac has poor aqueous solubility, it would be beneficial when it is formulated in the form of oral dispersible tablets so that its solubility can be enhanced leading to better absorption of medicament. This research focuses on the formulation of FDT's of dispersible tablets and comparative evaluation of all the techniques.

Formulation development

Preparation of different formulation series of Aceclofenac by Direct compression method

Different batches of tablets were prepared by direct pressure strategy. Drug, diluent, superdisintegrants, surfactant and sweetener were passed however sieve # 40 and magnesium stearate and talc were gone through # 80sieve. Obliged amount of medication, and surfactant was blended first than different excipients were blended completely. The powder was compacted utilizing direct compression process. The formula of different batches is indicated in table.

Table 1 Formula used for Formulations of Aceclofenac by direct compression

Ingredients	Batches coded Quantity (mg)		
	F1	F2	F3
Aceclofenac	100	100	100
Sodium starch glycolate	55	66	77
Microcrystalline cellulose	50	50	50
Talc	10	10	10
Magnesium stearate	5	5	5
Sodium lauryl sulphate	5	5	5
Lactose monohydrate	325	314	303
Total	550	550	550

Preparation of different formulation series of Aceclofenac by Solid dispersion method

Preparation of solid dispersion with carrier by melting solvent method:

It has discovered that 5-10 % w/w of fluid compound could be consolidated in PEG 6000 without huge loss of its strong properties. Thus it is conceivable to plan solid dispersion by first dissolving drug in a suitable solvent and after that the arrangement is consolidated straightforwardly into the melt of PEG (70 ^{0} C) without evacuating the fluid solvent. To this solid dispersion accurately weighed remaining ingredients was added and mixed thoroughly and passed by sieve # 40 and compressed for tablets.[6]

Table 2 Formula used for Formulations of Aceclofenac by Solid dispersion technique

Ingredients	Batches coded Quantity (mg)		
	F1	F2	F3
Aceclofenac	100	100	100
Poly ethylene glycol-6000	0	100	200
Sodium starch glycolate	52	54	56
Microcrystalline cellulose	50	50	50
Talc	10	10	10
Magnesium stearate	5	5	5
Sodium lauryl sulphate	5	5	5
Lactose monohydrate	328	226	124
Total	550	550	550

Preparation of different formulation series of Aceclofenac by Wet granulation method

Tablets containing 100mg of API are prepared by wet granulation technique by using 10%w/v PVP as a binder. The accurately weighed all ingredients were mixed and triturated gentle by adding binder solution. The obtained granules were dried at 60^0 C for complete drying and the dried powder was mixed with magnesium stearate and talc and blended. Then the powder compressed in to tablets.[7]

Table 3 Formula used for Formulations of Aceclofenac by Wet granulation method

Ingredients	Batches coded Quantity (mg)		
	F1	F2	F3
Aceclofenac	100	100	100
Sodium starch glycolate	52	54	56
Microcrystalline cellulose	50	50	50
Talc	10	10	10
Magnesium stearate	5	5	5
Sodium lauryl sulphate	5	5	5
Lactose monohydrate	328	326	324
Total	550	550	550

Evaluation of Aceclofenac FDT's

The prepared FDT's are evaluated for various official specifications

Hardness

The crushing strength of tablets (hardness) was measured using Monsanto hardness tester. The force required to crush the tablet was measured in Kg/cm^2.

Friability

The friability of a sample of 10 tablets was measured using a Roche Friabilator. 10 pre-weighed tablets were rotated at 25rpm for 4minutes. The tablets then reweighed after removal of fines and the %of weight loss was calculated using formula:
$\%Friability=(W_i-W_f)\times100\div W_i$ Where W_i= initial weight of tablets
W_f= final weight of tablets

Weight variation

10 tablets of each batch were selected at a random and average weight was calculated.
The individual tablets were weighed and the weight was compared with an average weight.

Wetting time

The wetting time of tablets was evaluated by the use of a piece of double folded tissue paper placed in a petri dish containing 6ml of water. A pre-weighed tablet was placed on this paper and the time for complete wetting of tablet was noted as wetting time.

In vitro dispersion time

The tablet was added to 10ml of water and time required for complete dispersion was measured. Two tablets from each formulation batches were randomly selected and in vitro dispersion time was performed.

In vitro dissolution study of tablets

The in-vitro study of tablets was carried out using USP II dissolution apparatus (paddle method). The in-vitro dissolution Medias used was phosphate buffers 6.8pH and 7.5pH. The FDT of formulation batch was dropped in to 900ml of dissolution media maintained at a temperature of 37 ± 0.5^0 C and stirred at a specified rpm i.e. 50rpm. 5ml of aliquots of dissolution medium were withdrawn at a time interval of 5, 10, 15, 20, 25,

30 minutes which was replaced with 10ml of fresh dissolution medium. The samples withdrawn were filtered and diluted and assayed at 275nm using UV- visible double beam spectrophotometer.

RESULT AND DISCUSSION

Pre formulation study (identification and characterization of Aceclofenac)

Appearance:

A white, crystalline powder.

Melting point:

The temperature at which the drug melts was found to be 149-153^{0}C which is as per the specifications in the certificate of analysis issued by the manufacturer.

IR Spectra of Aceclofenac:

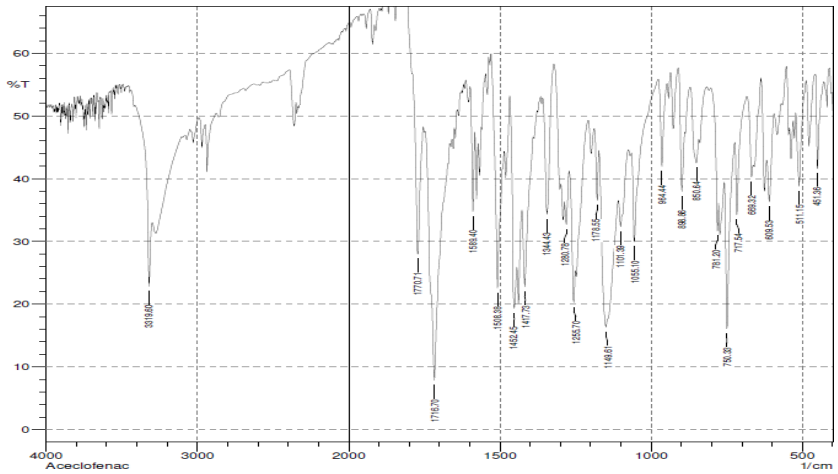


Figure 1 IR spectra of Aceclofenac

Concentration and absorbance values for standard calibration curve of Aceclofenac in methanol at λ_{max}= 275nm.

Table 4. Absorbance data for UV identification of Aceclofenac in methanol

Concentration(mg/ml)	**Absorbance(nm)**
2	**0.097**
4	**0.247**
6	**0.366**
8	**0.506**
10	**0.622**
12	**0.771**
14	**0.892**

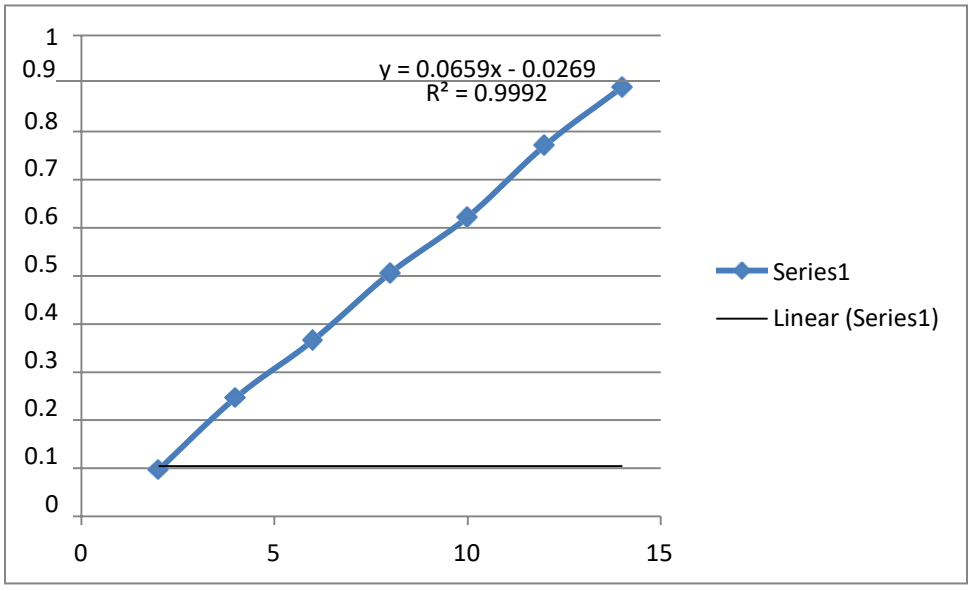


Figure 2 Calibration curve of Aceclofenac in methanol

Concentration and absorbance values for standard calibration curve of Aceclofenac in Acid Buffer (pH 1.2):at λ_{max}= 272.4nm.

Table 5 Absorbance data for UV identification of Aceclofenac in Acid Buffer (pH 1.2)

Concentration(mg/ml)	**Absorbance(nm)**
2	**0.052**
4	**0.107**
6	**0.146**
8	**0.180**
10	**0.224**

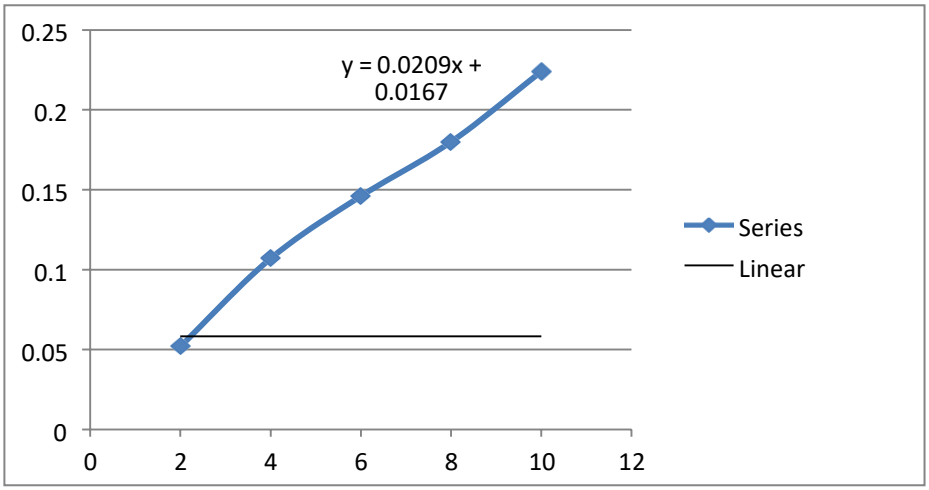


Figure 3 Calibration curve of Aceclofenac in Acid Buffer (pH 1.2)

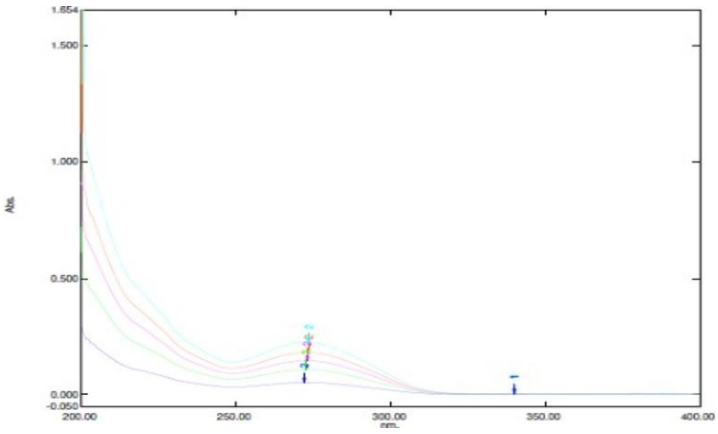


Figure 4 UV spectrum of Aceclofenac in Acid Buffer (pH 1.2)

Concentration and absorbance values for standard calibration curve of Aceclofenac in Phosphate Buffer (pH 7.5) at λ_{max}= 274nm.

Table 6 Absorbance data for UV identification of Aceclofenac in Phosphate Buffer (pH 7.5)

Concentration(mg/ml)	**Absorbance(nm)**
2	**0.187**
4	**0.312**
6	**0.478**
8	**0.627**
10	**0.767**

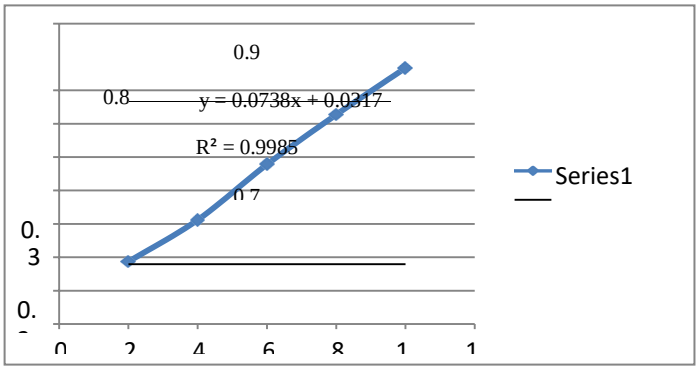


Figure 5 Calibration curve of Aceclofenac in Phosphate Buffer (pH 7.5)

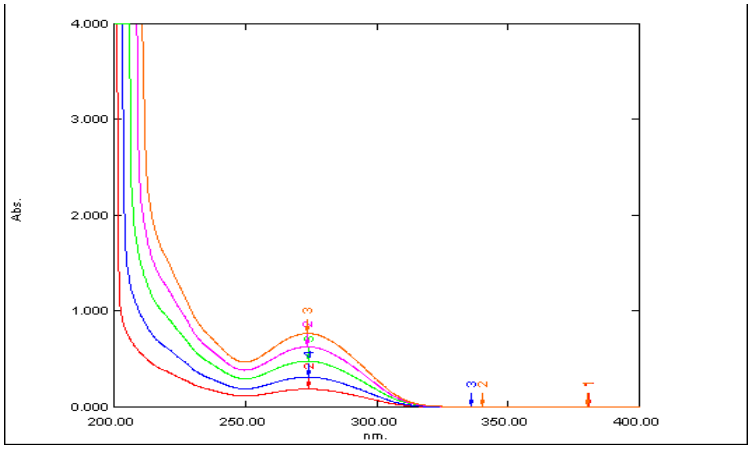


Figure 6 UV spectrum of Aceclofenac in Phosphate Buffer (pH 7.5)

Concentration and absorbance values for standard calibration curve of Aceclofenac in Phosphate Buffer (pH 6.8) at λ_{max}= 274nm.

Table 7 Absorbance data for UV identification of Aceclofenac in Phosphate Buffer (pH 6.8)

concentration(µg/ml)	Absorbance(nm)
5	0.141
10	0.235
15	0.359
20	0.469
25	0.641
30	0.691

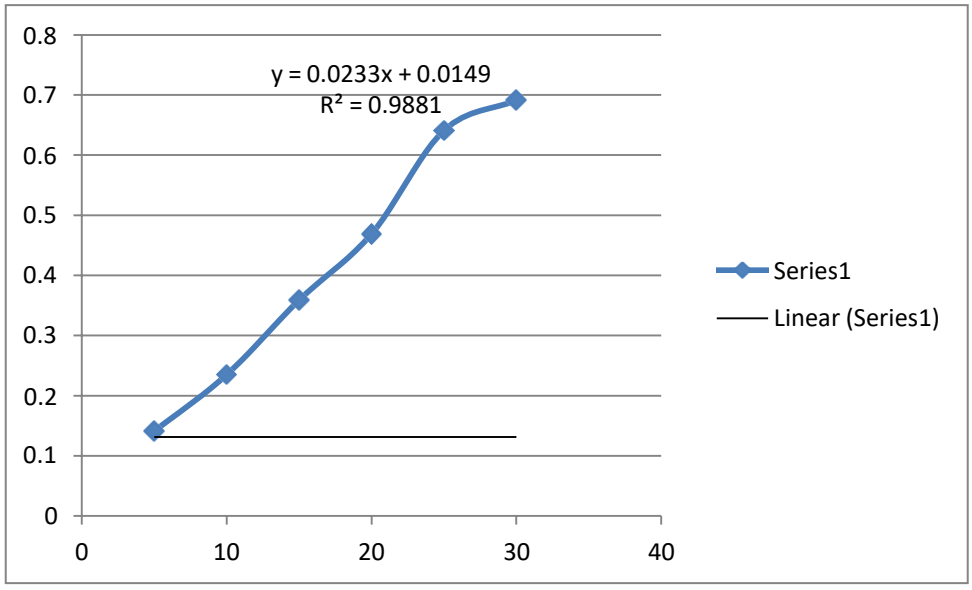


Figure 7 Calibration curve of Aceclofenac in Phosphate Buffer (pH 6.8)

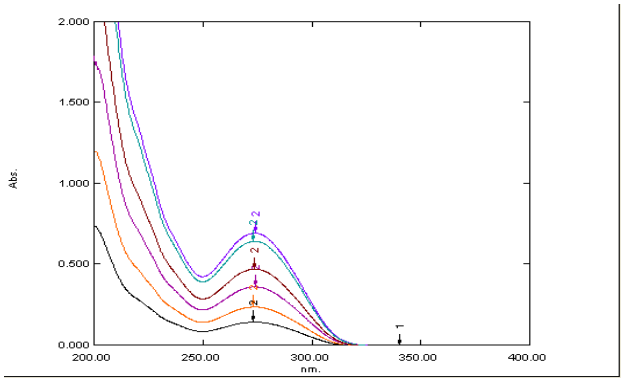


Figure 8 UV spectrum of Aceclofenac in Phosphate Buffer (pH 6.8)

Physical compatibility study of theAceclofenac with different excipients

The physical compatibility study was designed to determine the interaction of Aceclofenac with various excipients proposed to be used in the formulation. Aceclofenac along with the physical mixture of Aceclofenac with various excipients were kept at different environmental conditions for physical compatibility studies as shown in table. A comparison of the initial sample, control sample and samples kept at different environmental conditions for physical change was made periodically at different time. The Aceclofenac was found to be physical compatible with all the excipients has no colour changes or lump formation occurred in samples kept at different environmental conditions with respect to initial and control samples.

Table 8 Physical compatibility study of theAceclofenac with different excipients

S.NO	Composition	Ratio (w/w)	Final weight (mg)	Initial	Control(weeks)			40^0C,75%RH open(weeks)				
					1	2	3	4	1	2	3	4
1	Drug(Aceclofenac)	-	100mg	White colour	√	√	√	√	√	√	√	√
2	Drug: Microcrystalline cellulose	1:1	100mg	White colour	√	√	√	√	√	√	√	√
3	Drug: Sodium starch glycolate	1:1	100mg	White colour	√	√	√	√	√	√	√	√
4	Drug: Sodium laryl sulphate	1:1	100mg	White colour	√	√	√	√	√	√	√	√
5	Drug: Magnesium stearate	1:1	100mg	White colour	√	√	√	√	√	√	√	√
6	Drug: Talc√√	1:1	100mg	White colour	√	√	√	√	√	√	√	√

7	**Drug: Lactose monohydrate**	**1:1**	**100mg**	**White colour**	√	√	√	√	√	√	√	√
8	**Drug: Poly ethylene glycol-6000**	**1:1**	**100mg**	**White colour**	√	√	√	√	√	√	√	√

√: Refers to the same as original. RH:- stands for relative humidity

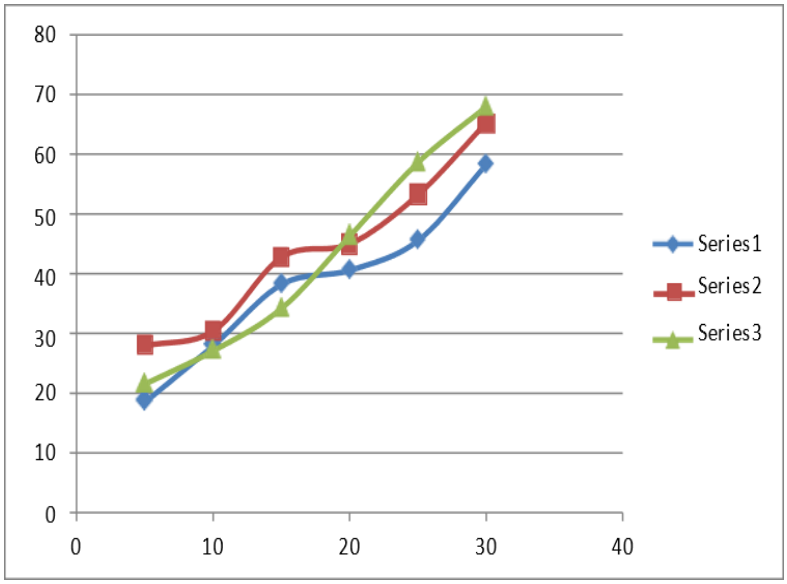
Results of formulation series of Aceclofenac by different methods

Table 9 Results of formulation series of Aceclofenac by direct compression method

Parameters	**Formulations**		
	F1	**F2**	**F3**
Hardness(kg/cm2)	**3.52**	**3.54**	**3.56**
Friability(%)	**0.857**	**0.556**	**0.723**
Weight variation	**Pass**	**Pass**	**Pass**
Wetting time(sec)	**193**	**181**	**165**
In vitro dispersion time(sec)	**137**	**122**	**118**

Table 10 Cumulative percentage of Aceclofenac release from formulated tablets

o	**Time (min)**	**F1**	**F2**	**F3**
1	**5**	**18.82**	**28.14**	**21.68**
2	**10**	**28.21**	**30.65**	**27.24**
3	**15**	**38.35**	**42.97**	**34.36**
4	**20**	**40.66**	**45.11**	**46.51**
5	**25**	**45.61**	**53.35**	**58.81**
6	**30**	**58.27**	**65.34**	**68.14**



Series1- (F1), Series2-(F2), Series3-(F3).
Figure 9 Comparison of cumulative %release of different formulation prepared by direct compression method.

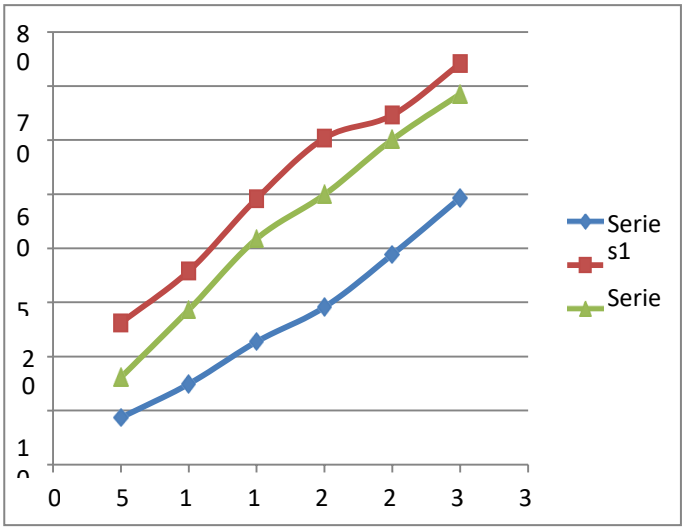
Table 11 Results of formulation series of Aceclofenac by solid dispersion technique

Parameters	**Formulations**		
	F1	**F2**	**F3**
Hardness(kg/cm2)	**3.22**	**3.18**	**3.12**
Friability(%)	**0.551**	**0.632**	**0.618**
Weight variation	**Pass**	**Pass**	**Pass**
Wetting time(sec)	**154**	**93**	**117**
In vitro dispersion time(sec)	**103.7**	**78.9**	**84.4**

Table 12 Cumulative percentage of Aceclofenac release from formulated tablets

No	**Time (min)**	**F1**	**F2**	**F3**
1	**5**	**8.70**	**26.22**	**16.15**
2	**10**	**14.92**	**35.8**	**28.64**
3	**15**	**22.74**	**49.17**	**41.77**

4	**20**	**29.12**	**60.36**	**49.94**
5	**25**	**38.86**	**64.61**	**60.12**
6	**30**	**49.33**	**74.14**	**68.54**



Series1- (F1), Series2-(F2), Series3-(F3).
Figure 10 Comparison of cumulative %release of different formulation prepared by solid dispersion technique.

Table 12 Results of formulation series of Aceclofenac by Wet granulation method

Parameters	**Formulations**		
	F1	**F2**	**F3**
Hardness((kg/cm2)	**4.1**	**4.5**	**4.7**
Friability(%)	**0.447**	**0.683**	**0.722**
Weight variation	**Pass**	**Pass**	**Pass**
Wetting time(sec)	**145**	**159**	**147**
In vitro dispersion time(sec)	**123**	**138**	**148**

Table 13:Cumulative percentage of Aceclofenac release from formulated tablets

No	**Time (min)**	**F1**	**F2**	**F3**
1	**5**	**16.11**	**13.83**	**11.59**
2	**10**	**27.58**	**23.37**	**20.82**
3	**15**	**33.67**	**30.77**	**25.91**
4	**20**	**49.13**	**34.93**	**31.77**
5	**25**	**52.5**	**46.06**	**45.87**

6	**30**	**63.8**	**59.5**	**57.1**

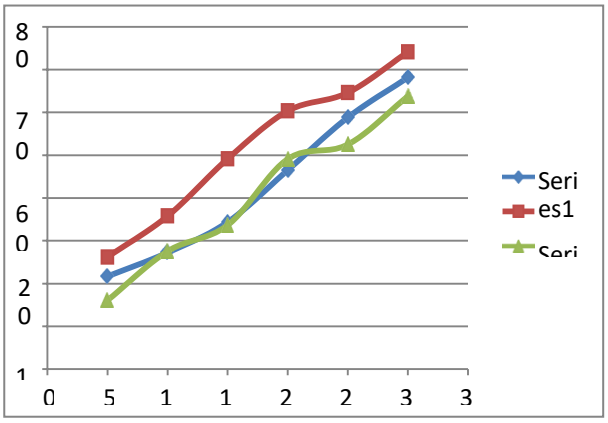


Figure 5.12 Comparison of % release of three preparation techniques

Series1- Direct compression (F3),
Series2 solid dispersion (F2),
Series3-wet granulation (F1)

SUMMARY AND CONCLUSION

Oral dosage forms are limited by first pass metabolism and gulping of tablets especially in case of pediatric and geriatrics. Fast dissolving tablets or oral dispersible tablets are novel form of oral dosage systems which disintegrates in couple of seconds so that the proportion of drug that reaches the systemic circulation is increased. Aceclofenac is poorly aqueous soluble, so it can be formulated as oral dispersible tablets, which enhances its dissolvability and ultimately its bioavailability is increased.

The Main objective of the study was to develop, optimize, evaluate and compare the percentage release of drug Aceclofenac FDT's prepared by different techniques such as direct compression, Solid dispersion and Wet granulation. The sample of pure drug (Aceclofenac) was identified and characterized as per requirements of certificate of analysis (COA) issued by the manufacturer. The identification of Aceclofenac was confirmed by melting point and IR spectra. The solubility of Aceclofenac in various dissolution media and solvent meets the specification as per requirements of certificate of analysis (COA).

The present investigation done to select an optimum formulation which is showing good percentage release of drug than other techniques and comparison of the techniques about their drug release profile.

After compression of powder blend, the tablets were evaluated for various parameters i.e. hardness, friability, wetting time, weight variation, disintegration time and in-vitro dissolution.

The effect of concentration and type of superdisintigrants on in- vitro drug release used in formulations of fast dissolving tablets was also investigated. the higher in-vitro drug release results of FDT's showed that batch formulated containing PEG-6000 (1:1 ratio) formulated by solid dispersion technique and lower % of drug release in found to be in wet granulation technique.

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