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Formulation and evaluation of Fast dissolving tablets of Aceclofenac by using Ispagula husk and Fenugreek seed mucilage

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Abstract: -The solubility behaviour of drug remains one of the most challenging aspects in formulation development. The drug therapeutic efficacy mainly depend upon the bioavailability and ultimately upon the solubility. The objective of present study is to formulate and evaluate fast dissolving tablets of aceclofenac by using natural super disintegrants - ispagula husk and fenugreek seed mucilage. Tablets were prepared by direct compression method and the formulation of tablets was optimized to get minimum disintegration time and maximum drug release. The prepared FDT's were evaluated for weight variation, hardness, and friability, disintegration and dissolution studies. The results were found to be in acceptable range according to standard limits.

Key Words: Ispagula husk, Fenugreek seed mucilage, Super disintegrant, *plantago ovate,* FDT"s etc,.

Introduction: The concept of Fast Dissolving Drug Delivery System emerged from the desire to provide patient with conventional means of taking their medication. Because of physiological changes associated with, especially, elderly and pediatrics are quite unable to swallow (Dysphagia); rather, this is a common problem of all age group patients. Solid dosage forms that can be disintegrated, dissolved, or suspended by saliva in the mouth resulting in easy swallowing can provide significant benefits to the pediatric and geriatric population, as well as other patients who prefer the convenience of easily swallowable dosage forms. This tablet disintegrates instantaneously when placed on tongue, releasing the drug that dissolves or disperses in the saliva[1].

Many elderly patients have difficulty swallowing tablets, capsules, or powders. To alleviate this problem, these tablets are expected to dissolve or disintegrate in the oral cavity without drinking water. The disintegrated mass can slide down smoothly along the esophagus with the help of saliva, so even people who have swallowing or chewing difficulties can take it with ease[2].There are two different types of dispersible tablets which have to be distinguished: One dosage form disintegrates instantaneously in the mouth, to be swallowed without the need for drinking water, while the other tablet formulation can readily be dispersed in water, to form dispersion, easy to ingest by the patient[3].

Techniques for Preparing Fast dissolving Tablets:

Many techniques have been reported for the formulation of Fast dissolving tablets or Orodispersible tablets.

1. Freeze drying / lyophilization
2. Tablet Molding
3. Spray drying
4. Sublimation
5. Direct compression
6. Mass extrusion

MATERIALS AND METHODS:

Table No.1: List of materials used in the study

S.No.	Ingredient Name	Supplier
1.	Aceclofenac	Yarrow Chem Products
2.	Ispagula husk powder	Apex International scheme
3.	Fenugreek seed mucilage	Apex International scheme
4.	Microcrystalline cellulose	Leisha Pharma Solutions
5.	Lactose	Antanes Chem Pvt ltd
6.	Megnesium stearate	Remedy Labs
7.	Sodium starch glycolate	Oxford laboratories

METHODOLOGY:

The aim of the present study was to improve the dissolution rate of aceclofenac by using fast dissolving tablet technique and to compare with tablets prepared with Cross povidine &sodium starch glycolate.

Aceclofenac is a non-steroidal anti-inflammatory drug mainly absorbed from the gastrointestinal tract. It is poorly soluble in water. Based on the Biopharmaceutics Classification System (BCS), it can be classified as a Class II drug with high permeability and low solubility. The solubility of aceclofenac in distilled water at 25°C is 0.015 ± 0.002 mg/ml. This is not sufficient for the whole dose to be dissolved in the gastrointestinal tract. Dissolution is therefore the rate-limiting step to absorption of aceclofenac[4].

The main objective of this study was to utilize Ispagula husk powder (IHP) and Fenugreek seed mucilage (FSM) as pharmaceutical excipients and evaluate their disintegration properties. Both are naturally occurring and available plenty in India also cheap and have many nutritional values. Hence an attempt was made to prepare orally disintegrating tablet of a model drug, Aceclofenac using IHP & FSM as natural superdisintegrants.

IHP and FSM are used as natural super disintegrants, lactose as diluent and magnesium stearate as lubricant respectively. The prepared fast dissolving tablets were evaluated for drug release and the obtained dissolution profile was compared with that of pure drug. The optimized formulation was tested for absence of incompatibility by FTIR studies.

Standard solutions:

Standard solutions of different concentrations of aceclofenac were prepared by diluting suitable quantities (2, 4, 6, 8, 10 ml) of stock solution with pH 0.1N HCl buffer to get 2, 4, 6, 8 and 10 µg/ml solutions. The absorbance of the above concentrations was measured at 275 nm using UV spectrophotometer against the respective blanks[5].

Solubility Studies:

For the selection of best non-volatile solvents, solubility studies were performed. In this procedure, pure drug was dissolved in two different non-volatile solvents (propylene glycol and polyethylene glycol 400) and distilled water. Excess amount of pure drug was added to the above solvents. Obtained saturation solutions were mixed with magnetic stirrer. After that the saturated solutions were centrifuged at 3000 rpm for about 15 minutes and the supernatant was collected and analyzed by UV spectrophotometer[6].

Table No.2: Solubility terminology

Solubility	Parts of solvent required for 1 part of solute
Very soluble	<1
Freely soluble	1-10
Soluble	10-30
Sparingly soluble	30-100
Slightly soluble	100-1000
Very slightly soluble	1000-10000
Practically insoluble	>10000

Pre-compression properties:

All the fast dissolving tablet formulations were evaluated for angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio[7].

Formulation of fast dissolving tablets:

Preparation of fast dissolving tablets of Aceclofenac:

The critical parameters to formulate a fast dissolving tablet are choice of superdisintegrant and optimization of concentration of superdisintegrant. The main criteria for fast dissolving tablet is to disintegrate and dissolve rapidly in oral Cavity in 15-60 seconds, without need of water. All the ingredients were co-ground in a pestle and motor and then talc and magnesium stearate were added and mixed for 10 minutes. The mixed blend of drug-excipient was compressed to produce tablets of strength 350mg.

Table No.3: Formulae for fast disintegrating tablets of aceclofenac

FORMULATION CODE	DRUG (mg)	Cross povidine (mg)	IHP (mg)	SSG (mg)	FSM (mg)	MCC (mg)	LACTOSE (mg)	MAGNESIUM STEARTE (mg)
F_1	100	7	-	-	-	100	136	7
F_2	100	14	-	-	-	100	129	7
F_3	100	21	-	-	-	100	122	7
F_4	100	-	7	-	-	100	136	7
F_5	100	-	14	-	-	100	129	7
F_6	100	-	21	-	-	100	122	7
F7	100	-	-	7	-	100	136	7
F8	100	-	-	14	-	100	129	7
F9	100	-	-	21	-	100	122	7
F10	100	-	-	-	7	100	136	7
F11	100	-	-	-	14	100	129	7
F12	100	-	-	-	21	100	122	7

IN-VITRO EVALUATION TESTS

Weight variation test:

The weight variation test was performed as per USP. Twenty tablets were randomly selected from each formulation and individually weighed. The average weight and weight variation were calculated as described in I.P.

$$\% \text{ Weight variation} = \frac{\text{(Individual weight – Average weight)}}{\text{[Average weight] x 100}}$$

Table No.4: Limits for weight variation test as per I.P.

Tablet weight	% deviation allowed
< 80	± 10%
80 – 250	± 7.5%
> 250	± 5%

Drug content:

Randomly 5 tablets were collected, crushed and weighed the amount equivalent to 100 mg of drug. Transferred to 100 ml volumetric flask, dissolved in small volume of methanol and volume made up to mark with 0.1N HCl buffer. Appropriate dilution was done and the sample was analyzed for drug content at 275 nm spectrophotometrically[8].

Hardness:

The hardness of formulated fast dissolving tablets was assessed using a Monsanto hardness tester and the mean hardness of three tablets was determined.

Limit: 4 – 7 kg/cm^2

Friability:

The Roche friability test apparatus was used to determine the friability of the tablets. 20 tablets were weighed and placed in the apparatus, and allowed to operate for 100 revolutions at a rate of 25 rpm. The tablets were collected, dedusted and reweighed. The percentage of the friability was calculated.

Percentage friability = [(Initial weight – Final weight)/Initial weight)] x 100

Disintegration test:

The disintegration test was carried out using disintegration test apparatus as specified in the Indian Pharmacopoeiawhich consists of a basket rack holding 6 plastic tubes, opened at the top and covered at the bottom by a 10-mesh screen. Tablets were placed in the tubes of basket rack assembly and were immersed in 900 ml of water kept in 1 liter beaker held at 35˚ C. The apparatus was operated at a rate of 30±2 oscillations per minute and the time taken by the tablets to disintegrate was noted[9].

Table No.5: Limits for disintegration test as per I.P.

Type of tablet	Time (min)
Uncoated	< 15
Film coated	< 30
Sugar coated	< 60

***In-vitro* dissolution studies:**

The *in-vitro* drug release profiles of aceclofenac from directly compressed fast dissolving tablets were obtained using a dissolution rate test apparatus USP type-II (paddle type).

Dissolution apparatus: Electro lab ETC 11L

Dissolution medium : 900 ml of 0.1N HCl buffer

Apparatus type : Paddle

Speed : 50 rpm

Temperature : 37 ± 2˚C

The dissolution study of tablets was carried out in 900 ml of 0.1N HCl buffer as the dissolution medium maintained at 37 ± 2˚C and 50 rpm. Then 5 ml samples were collected up to 60 min at intervals of 5, 10, 15, 20, 30, 40, 50 and 60 min. The dissolution medium was replaced with 5 ml fresh dissolution fluid to maintain sink condition. The withdrawn samples were filtered and analyzed spectrophotometrically at 275 nm. The mean of three determinations was used to calculate the drug release from each of the formulations[10].

Comparative dissolution studies were done for prepared fast dissolving tablet formulations (F1-F3) using crosspovidone and formulations (F4-F6) using ispaghula powder.

Calibration curve of Aceclofenac:

Table No.6: Calibration curve of Aceclofenac

S.No.	Concentration (µg/ml)	Absorbance at 275 nm
1	0.0	0.0
2	2.0	0.048
3	4.0	0.100
4	6.0	0.152
5	8.0	0.210
6	10	0.260

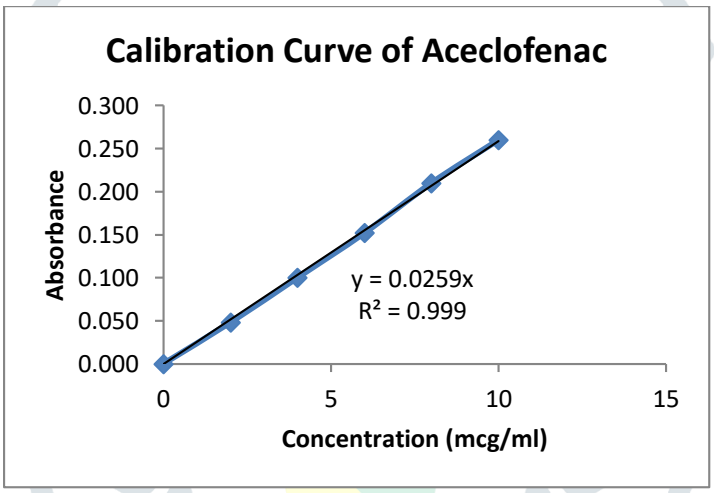


Fig.1: Calibration Curve of Aceclofenac in 0.1 N HCl

Solubility studies

The solubility of aceclofenac was studied in various solvents propylene glycol (PG), polyethylene glycol 400 (PEG) and distilled water.

Table No.7: Solubility studies of Aceclofenac in various solvents

Solvent	Solubility (mg/ml)
Poly ethylene glycol- 400	14.62
Propylene glycol	22.4
HCl	21.93
Distilled water	0.015

Evaluation of Pre-compression parameters:

Table No.8: The results of pre-compression studies

Formulation code	Angle of repose	Hausner's ratio	Carr's index	Bulk density	Tapped density
F1	17.21±0.05	1.17	16.26	0.40±0.10	0.46±0.01
F2	14.27±0.04	1.12	11.45	0.38±0.10	0.41±0.03
F3	19.03±0.03	1.15	13.22	0.39±0.07	0.44±0.12
F4	23.90±0.07	1.18	14.59	0.41±0.11	0.46±0.08
F5	25.18±0.06	1.16	11.27	0.36±0.09	0.58±0.11
F6	27.11±0.01	1.11	12.85	0.41±0.05	0.46±0.06
F7	22.79±0.07	1.14	13.33	0.39±0.11	0.45±0.08
F8	23.23±0.06	1.19	14.29	0.31±0.09	0.53±0.11
F9	26.16±0.01	1.17	16.01	0.47±0.05	0.49±0.06
F10	16.21±0.05	1.15	11.29	0.42±0.10	0.43±0.01
F11	13.27±0.04	1.12	11.87	0.37±0.10	0.41±0.03
F12	17.03±0.03	1.11	11.12	0.33±0.07	0.42±0.12

***In- vitro* evaluation tests of fast dissolving tablets of Aceclofenac:**

Table No.9: *In- vitro* evaluation tests of fast dissolving tablets

Formulation code	Weight variation	Hardness (kg/cm^2)	Friability (%)	Disintegration Time (sec)
F1	349±1.07	3.4±1.2	0.53±0.02	36
F2	348±1.13	3.3±1.1	0.21±0.08	45
F3	351±0.98	3.3±0.6	0.28±0.03	39
F4	348±1.01	3.1±1.4	0.19±0.04	43
F5	351±0.81	3.0±0.8	0.20±0.03	49
F6	349±0.79	3.4±0.5	0.23±0.08	44
F7	104.34	3.4±1.4	0.21±0.04	43
F8	110.14	3.2±0.8	0.19±0.03	38
F9	95.65	3.4±0.5	0.22±0.08	31
F10	98.55	3.3±1.2	0.29±0.02	35
F11	95.65	3.2±1.1	0.25±0.08	32
F12	95.65	3.3±0.6	0.22±0.03	29

Table No.10: Dissolution Profile of Formulations (% drug released vs time)

Time (min)	CP F1	CP F2	CP F3	IHP F4	IHP F5	IHP F6	SSG F7	SSG F8	SSG F9	FSM F10	FSM F11	FSM F12
0	0	0	0	0	0	0	0	0	0	0	0	0
5	3.64	4.86	10.08	4.32	5.44	10.87	3.6	4.71	9.72	5.4	5.83	11.23
10	5.9	8.96	14.44	6.52	10.3	15.77	5.79	8.56	14.36	8.74	10.4	16.12
15	7.6	14.65	24.3	8.5	14.36	25.16	7.23	14.36	23.11	13.86	14.4	25.23
20	13.1	23.18	31.43	14.22	23.58	35.28	12.6	22.32	30.63	19.76	24.66	35.64
25	17.93	30.1	37.44	19.15	30.6	49.68	15.91	29.23	36.36	28.33	32.07	56.16
30	18.65	42.48	59.76	20.74	47.16	68.76	17.71	40.68	57.6	29.44	54.36	71.64
40	25.52	54.72	69.84	27.68	62.28	81.36	24.94	53.64	69.12	32.11	65.16	86.76
50	30.78	70.56	78.84	36.36	79.2	97.56	30.45	68.04	77.4	34.45	84.6	98.28
60	41.04	80.64	93.24	44.28	86.04	99.72	40.32	79.2	92.16	55.44	90.36	99.75

Release kinetics of formulations:

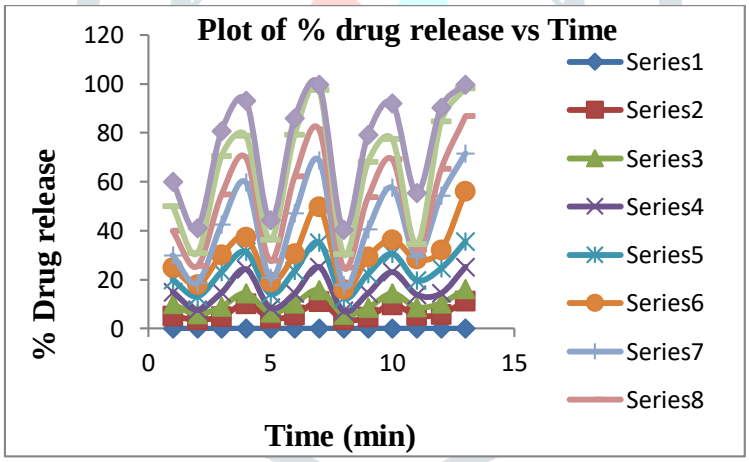


Fig.2: Dissolution Profiles of Aceclofenac formulations prepared with Crosspovidone (F1-F3), IHP (F4-F6), SSG (F7-F9) and FSM (F10-F12)

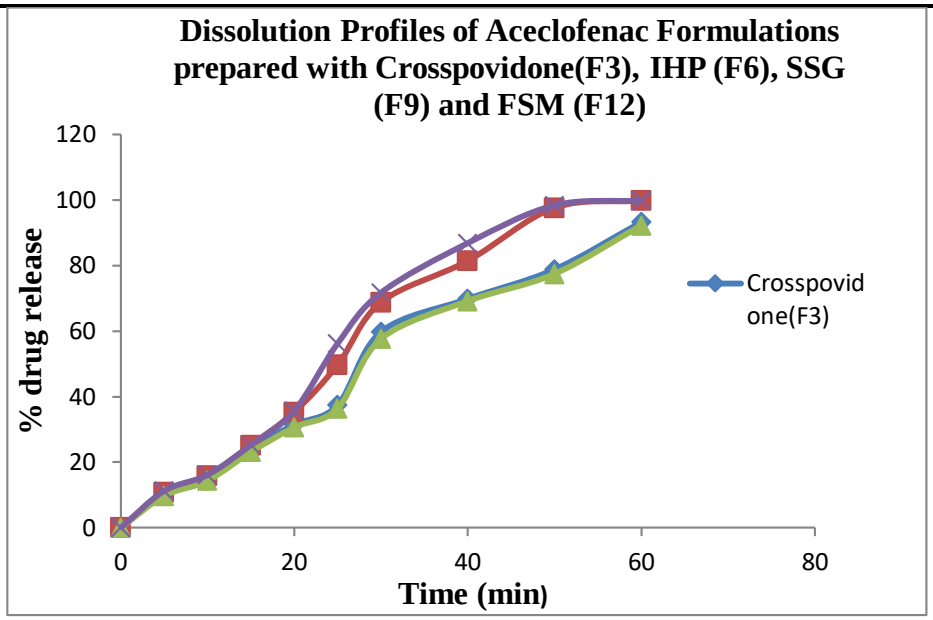


Fig.3: Comparitive Dissolution Profiles of Aceclofenac Formulations prepared with Crosspovidone (F3), IHP (F6), SSG (F9) and FSM (F12)

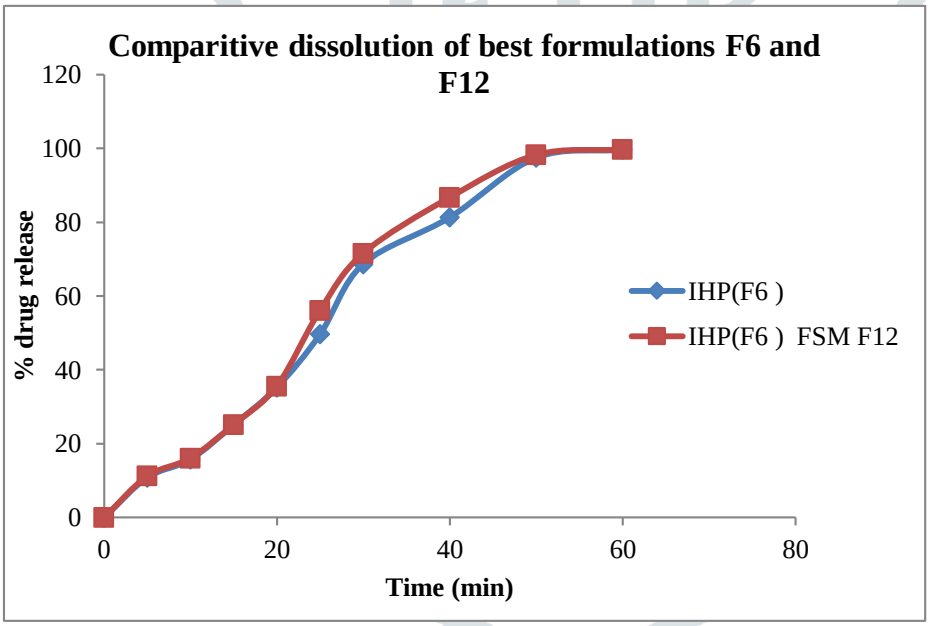
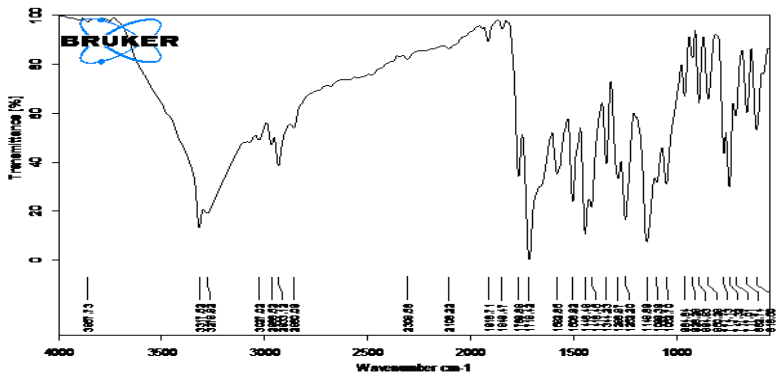


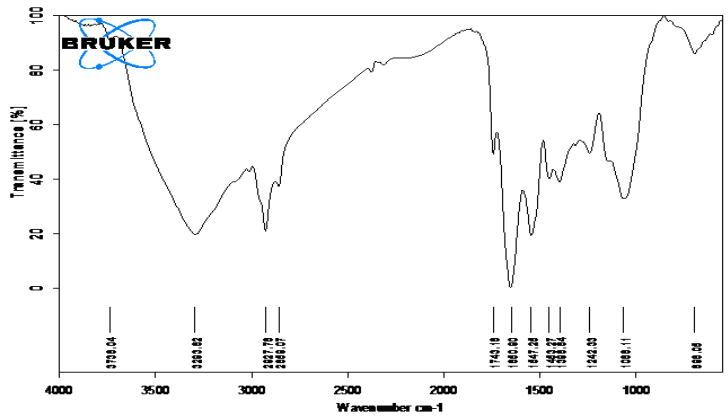
Fig.4: Comparative Dissolution Profiles of Aceclofenac formulations, F6 (IHP) and F12 (FSM)

Incompatibility studies by FTIR spectra

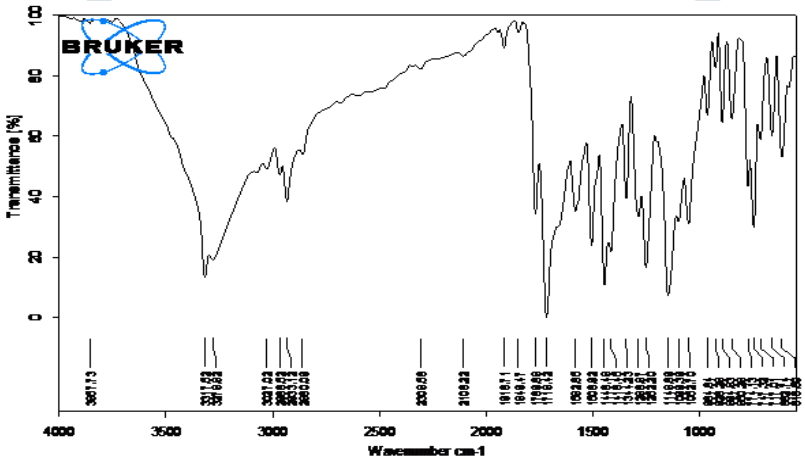
FTIR spectra of Aceclofenac:



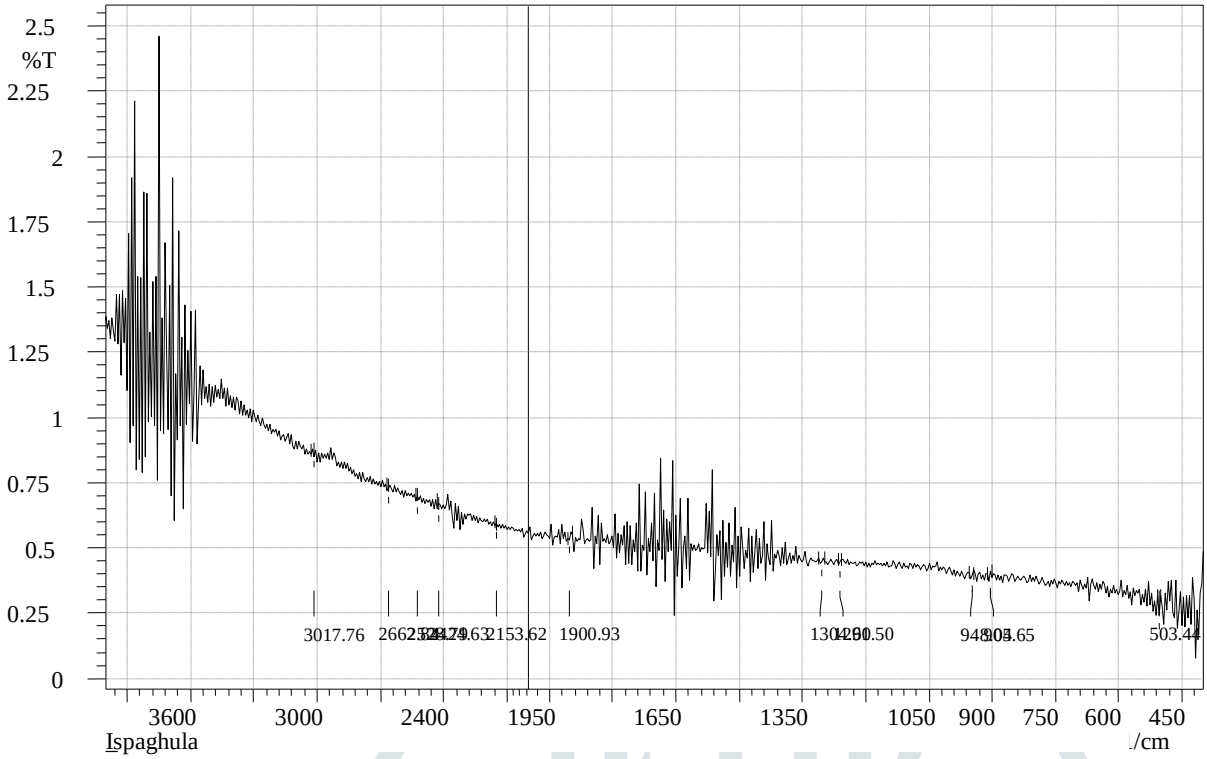
FTIR spectra of Fenugreek seeds mucilage:



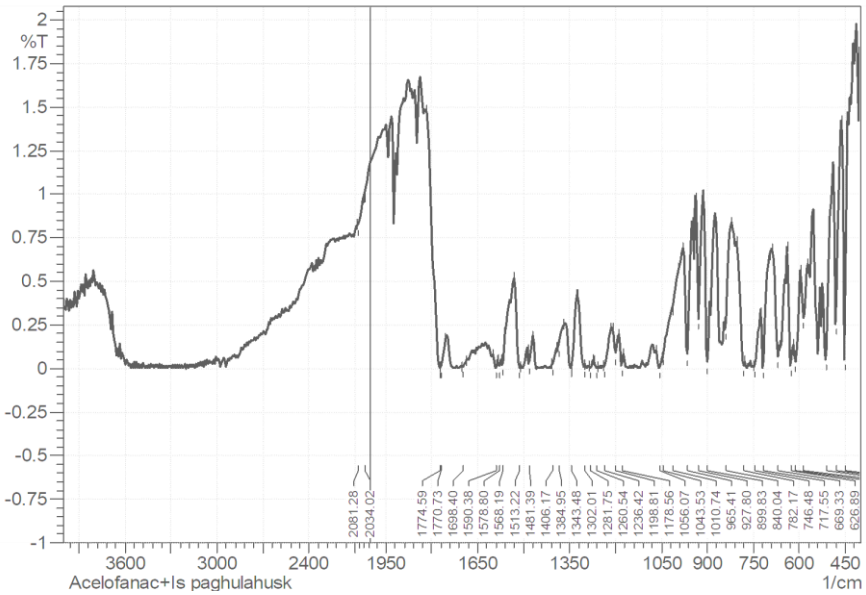
FTIR spectra of mixture of Aceclofenac and Fenugreek seed mucilage:



FTIR spectra of Ispaghula



FTIR spectra of mixture of Aceclofenac and Ispaghula husk powder



DISCUSSION:

All the formulations have shown pre-formulation tests results within the limits indicating good flow properties.

All the formulations have also passed the post-compression parameters within the limits. Disintegration was found to be rapid with a range of 29-49 sec.

FTIR studies revealed that there are no incompatibilities among the ingredients used in formulation.

Based on the *in-vitro* dissolution studies, the following interpretation was done:

- Formulations, F1 to F3 containing crosspovidone as disintegrant shown 41.04, 80.64 and 93.24% drug release respectively in 60 min.
- Formulations, F4 to F6 containing isphagula husk powder shown 44.28, 86.04 and 99.72% drug release respectively in 60 min.
- Formulations, F7 to F9 containing sodium starch glycolate as disintegrant shown 40.32, 79.2 and 92.16% drug release respectively in 60 min.
- Formulations, F10 to F12 containing Fenugreek seed mucilage shown 55.44, 90.36 and 99.75% drug release respectively in 60 min.

Among all the formulations (F1-F3) containing crosspovidone as disintegrating agent, formulation F3 has shown high drug release of 93.24% in 60 min.

Among all the formulations (F4-F6) containing isphagula husk powder, formulation F6 has shown high drug release of 99.72% in 60 min.

Among all the formulations (F7-F9) containing sodium starch glycolate as disintegrating agent, formulation F3 has shown high drug release of 92.16% in 60 min.

Among all the formulations (F10-F12) containing Fenugreek seed mucilage, formulation F6 has shown high drug release of 99.75% in 60 min.

Results of *in-vitro* drug release also revealed that, as the concentration of super disintegrates increases cumulative percent of drug release was also significantly increases. Formulations F1-F3 & F7-F9 containing synthetic super disintegrates showed less drug release when compared to formulations containing natural super disintegrates i.e. formulations F4-F6 & F10-F12 this might be due to swelling effect of natural super disintegrates. Based upon the results of *in-vitro* drug release results formulation F6 & F12 were considered as optimized formulations.

SUMMARY AND CONCLUSION

Aceclofenac is a non-steroidal anti-inflammatory drug whose solubility is low and hence dissolution rate enhancement is required to be done for better bioavailability. In the present investigation, fast dissolving tablet technique was applied to enhance the dissolution rate of poorly soluble drug, aceclofenac.

Calibration curve for pure drug, Aceclofenac was constructed using pH 0.1N HCl buffer at λ_{max} 275 nm.

Various formulations were designed using synthetic and natural super disintegrants. Various pre-compression studies and post compression parameters were evaluated. *In-vitro* drug release studies were conducted for 60 min for all the formulations. The *in-vitro* drug release profile has revealed that formulations F6& F12 are the optimized formulations. FTIR studies were conducted to check the compatibility of drug with ingredients used in the formulation.

All the formulations have shown the results of pre-compression and post-compression parameters within the acceptable limits. FTIR studies revealed that there are no incompatibilities among the ingredients used in formulation.

CONCLUSION:

Fast dissolving tablets of Aceclofenac with isphagula powder and fenugreek seed mucilage could be considered as safe and useful oral delivery system to increase the drug bioavailability and to improve patient compliance. From this study, it can be concluded that natural super disintegrants could be applied effectively in preparation of FDTs with better water absorption, disintegration and drug released properties. The prepared FDTs disintegrate within a minute; thereby enhance the absorption leading to increased bioavailability of Aceclofenac. The study leads us to conclude that *plantago ovata* and *Trigonella foenum-graecum*can be successfully used as natural super disintegrants. Thus natural super disintegrants exhibits faster drug dissolution and improved bioavailability, thereby helping in effective therapy and improved patient compliance.

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