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Original Article

Formulation and Characterization of Fast Dissolving Films Containing Aceclofenac

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ABSTRACT

The present work was aimed with the objective of formulating fast dissolving films of aceclofenac to enhance the convenience and compliance by the elderly and pediatric patients. The films were prepared by incorporating the prepared aceclofenac physical mixtures so as to achieve the aimed percent drug release (using cyclodextrins, sucrose and polaxomer 188) in different film forming agents (hydroxyl propyl methyl cellulose E5 &E15). Particular attention was given to the selection of the suitable taste masking agents. The large dose of the drug offered the greatest challenge in optimization of film formula leading to the thickness of the film and further altering the drug release from the film. The films were characterized in term of aceclofenac content, mechanical properties, and disintegration time and dissolution test. The promising film F2 having the optimal formula showing the greatest dissolution and satisfactory in in-vitro disintegration time and physico-mechanical properties compared with a reference marketed product (aceclan tablets). FT-IR studies revealed that there is no interaction between the drug and the polymers used in the study. Statistical analysis revealed significant difference between the test films and the reference product, indicated that the test formulations F1, F3, F4, andF5 exhibited enhanced percentage T90 profiles, F2 and F6 showed comparable profiles with reference.

Key words: Aceclofenac, physical mixtures, cyclodextrins, polaxomer, fast dissolving films

1. INTRODUCTION

Among the delivery routes, the oral route is the most acceptable from patient compliance aspects. Many pharmaceutical firms have directed their research activity in reformulating existing drugs into new dosage forms [1]. One such relatively new dosage form is the oral fast dissolving Films (OFDFs) is prepared using hydrophilic polymers that rapidly dissolves on the tongue or buccal cavity. Fast disintegrating films are the most advanced form of oral solid dosage forms due to more flexibility and comfort. OFDFs

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are useful in patients such as pediatric, geriatrics, bedridden, emetic patients, diarrhea, sudden episode of allergic attacks, or coughing for those who have an active life style. It is also useful whether local action desired such as local anesthetic for toothaches, oral ulcers, cold sores or teething. Most of the existing fast dissolving drug delivery systems are in the form of tablets or in other dosage forms are design to dissolve or disintegrate in the patient's mouth within a few seconds to minutes without need of water or chew [2].

Ideal characteristics of OFDF [3,4, 6]

- Do not require water to swallow and should dissolve or disintegrate in the mouth within a few seconds.
- Compatible with taste masking and other excipients.
- They possess pleasant mouth feel.
- Leave minimal or no residue in the mouth after oral administration.
- Resistant to environmental conditions such as humidity and temperature

In the present research work Aceclofenac, an analgesic drug used in the treatment of acute pain is selected. Aceclofenac is a poorly water-soluble. It chemical name is [(2-{2, 6-dichlorophenyl) amino} phenylacetooxyacetic acid] [5]. It reduce prostaglandin production by inhibiting COX (Cycloxygenase) action that involved n the production of prostaglandins. Aceclofenac is selected in order to improve its dissolution properties and also to develop Flash-disintegrating buccal film formulation. Administration of Aceclofenac by the buccal route (absorption via the gums and cheek) as an alternative to rectally administered is becoming increasingly popular for the treatment of pain in children [7-10]. Hence, the present research work was aimed to enhance the solubility and dissolution rate of poorly water soluble drug (Aceclofenac) using Solid Dispersion technique [11-14].

2. MATERIAL AND METHOD

MATERIALS

Aceclofenac gift sample obtained from Diwis pharma pvt ltd., Hyderabad. β- Cyclodextrin was purchased from Ottokemi pharma Inc., Mumbai. Poloxomer, Hydroxy propyl methyl cellulose E5 & E15 was obtained Loba chemic pvt., Limited. Sodium starch glycolate was purchased from Capricon pharma Inc., Cross carmellose sodium and Poly ethylene glycol 400 obtained from Merck pharma.

METHOD

Estimation of aceclofenac

A number of methods are reported in the literature for the estimation of Aceclofenac. Spectrophotometric method (I.P) [15] was used for the estimation of Aceclofenac at 269 nm in pH 5.8 phosphate buffer.

Construction of calibration curve

Calibration curve of aceclofenac was constructed in pH5.8 artificial saliva. Aceclofenac was accurately weighed and dissolved in sufficient amount of methanol to prepare 1mg/ml solution. From this subsequent dilutions were made with pH5.8 artificial saliva to prepare a series of standard solutions containing 4, 8, 12, 16, and 20 µg of aceclofenac per ml. The solutions were scanned in the region 200 - 400 nm using ELICO-SL 159 UV spectrophotometer and the absorbance of the solutions were measured at 269 nm using pH 5.8 phosphate buffers as a blank. The calibration curve of aceclofenac was shown in Figure 1.

Preformulation studies

Organoleptic Properties:

The drug sample was viewed visually and viewed under the compound microscope for the determination of its color using the black and white backgrounds and nature of the drug sample. Then the results were compared with the official books and Indian Pharmacopoeia.

Solubility:

The solubility of the drug sample was carried out in different solvents (aqueous and organic) according to the Indian Pharmacopoeia. The results are then compared with those given in the official books.

FT-IR studies

Compatibility between the drug and excipients was important during the formulation. These studies were carried out using FTIR studies. Drug and excipients were prepared in differ ratios for the analysis. The freshly prepared drug and excipient mixtures spectra were recorded by using FT-IR. Then the mixtures were examined for their compatibility was analysed by comparing the recorded spectra [16].

Preparation of Physical Mixture:

- The physical mixtures were prepared by geometric dilution method.
- 100 mg of aceclofenac was taken in a mortar to it 100 mg of Cyclodextrin (CD)/ Sucrose/Poloxamer was added to the mortar in geometric dilution with intermittent mixing.
- The product was collected and triturated thoroughly for uniform mixing. 100 mg equivalent of aceclofenac was accurately weighed and stored until further use.

Table 1: Composition of Aceclofenac Solid Dispersions

S.No	Ingredients (mg)	A	B	C	D	E
1	Aceclofenac	100	100	100	100	100
2	Sucrose	--	125	--	--	--
3	Cyclodextrin	--	--	125	--	--
4	Polaxomer	--	--	--	125	--
5	Marketed product	--	--	--	--	---

EVALUTION OF PHYSICAL MIXTURES [17]:

The physical mixtures prepared were evaluated for the following:

- Drug content
- Dissolution rate
- Drug and Excipient interactions by IR spectra

Drug content:

The physical mixture was taken in a 100ml volumetric flask, 20ml ethanol and 20 ml of pH 5.8 Phosphate buffer was added and the contents were sonicated for 10min and made up to the mark with pH 5.8 phosphate buffer. This solution was suitably diluted with pH 5.8 phosphate buffer and was assayed at 257nm for Aceclofenac.

Dissolution study:

The dissolution rate testing of aceclofenac fast dissolving film

was studied using USP XXII dissolution rate testing apparatus, (paddle type) (LAB INDIA DISSO 2000) at 50 rpm. pH 5.8 phosphate buffer 900ml is used as dissolution medium which maintained at 37± 0.5°C. At definite time intervals, 5 mL of the fluid was withdrawn. Filtered through 0.45 µm membrane filter and again 5 ml of the fluid was replaced. Suitable dilutions were done with the dissolution fluid and the samples were analyzed spectrophotometrically at 257 nm.

Method of Preparation of Fast Dissolving Films of Aceclofenac [18-20]:

The oral fast dissolving films were prepared by solvent casting method using HPMC E5, HPMC E 15, as film base with different concentrations. PEG-400 was used as plasticizer, Mannitol, Aspartame were used as sweetening agent, and citric acid was used as saliva stimulating agent, CCS and SSG were used as disintegrating agents. Polymers are dissolved in water by using magnetic stirrer. Mannitol, Aspertame, Citric acid, CCS, SSG and PEG 400 were added to the polymer solution and stirred for 2 minutes on a magnetic stirrer. Solid dispersion of drug solution was added to the above solution under continuous stirring for 2 minutes and sonicated for 5 minutes to remove air bubbles. This solution was casted on a Petri dish and dried in hot air oven at 40º C for 12 hours. The films were carefully removed from Petri dish, checked for any imperfections and cut into required size. The samples were stored in a desiccator for further analysis.

Table 2: Formula for Preparation of Fast Dissolving Films

INGREDIENTS	F_1	F_2	F_3	F_4	F_5	F_6	Purpose
DRUG SD(gm)	1	1	1	1	1	1	API
HPMC E 5 (mg)	300	400	500	-----	----	----	Film forming agent
HPMC E15LV(mg)	----	-----	----	300	400	500	Film forming agent
PEG-400(ml)	0.1	0.1	0.1	0.1	0.1	0.1	Plasticizer
MANNITOL(mg)	10	10	10	10	10	10	Sweetening agent
ASPERTAME (mg)	10	10	10	10	10	10	Sweetening agent
CITRIC ACID(mg)	1	1	1	1	1	21	Saliva stimulating agent
CCS (mg)	25	25	25	25	25	25	Disintegrating agents
SSG (mg)	10	10	10	10	10	10	Disintegrating agents
WATER(ml)	4	4	4	4	4	4	Solvent

EVALUATION OF BUCCAL FAST DISSOLVING FILMS [21-25]:

Morphological properties:

A visual inspection for physical appearance of films and evaluation of texture was done by feel or touch.

Thickness uniformity:

All the films were evaluated for thickness by using thickness gauge with a least count of 0.01mm. The thickness was measured at three different spots of the films and the average was taken.

Folding endurance:

The folding endurance was measured manually for the prepared films. The flexibility of films can be measured quantitatively in terms of folding endurance. A strip of film was cut (approximately 3x2cm^2) and repeatedly folded at the same place till it breaks. The number of times the film could be folded at the same place without breaking gave the value of folding endurance.

Surface pH:

An acidic or alkaline pH may cause irritation to the oral mucosa, it is determined to keep the surface pH of fast dissolving film as close to neutral as possible. A combined pH electrode is used for this purpose. Film was slightly wetted with water and pH was measured by bringing the electrode in contact with the surface of oral film. This study is performed on three films of each formulation and mean ± SD was calculated.

Drug content uniformity test:

3x2 cm^2 film was kept in 25 ml of pH 6.8 phosphate buffer. This solution was sonicated for 5 minutes and filtered. Drug content was determined spectroscopically after appropriate dilution at 257 nm using UV visible spectrophotometer.

***In vitro* disintegration test:**

This test was performed by placing the film in a glass Petri dish containing 10 mL of pH 5.8phosphate buffer. The time required for the film to break and disintegrate was noted as *in vitro* disintegration time.

***In vitro* dissolution studies:**

The *in vitro* drug dissolution was carried out in 900 ml of pH 5.8 phosphate buffer at 37±0.5ºC, using USP Apparatus-II at a stirring speed of 50 rpm. The samples were withdrawn at a time interval of one minute. Fresh buffer solution was replaced immediately after each sampling. The absorbance was measured using spectrophotometer at λ max of 257 nm.

ANOVA:

In our present research work, one way ANOVA has been used to find out whether there is statistically significant difference between the time taken for 90 % of the drug to dissolve from various aceclofenac formulations.

The null hypothesis is that all the T_{90} values are equal and there is no significant difference between them. The ANOVA separates the total sum of squares in to between sum of the squares (BSS) and within the sum of squares

(WSS). The BSS represents difference among the treatments, large values indicating large treatment differences. The WSS represents difference within the treatments or error. The difference within the treatment is a measure of variability of the observation [26].

If the F test is significant and more than two treatments are included in the experiment, it may not be obvious immediately which treatments are different, some (or) all of the treatments are different. Least significant difference procedure is used for multiple comparisons. One way ANOVA and least significant procedure were applied to the T_{90} values obtained from the formulations. From this the best / similar formulations were identified [27].

3. RESULTS AND DISCUSSIONS

FT-IR studies:

The FT-IR spectra of the pure Aceclofenac, pure β-Cyclodextrin, pure Poloxamer, pure Sucrose, pure HPMC-E5,pure HPMC -E15,pure Mannitol, pure Aspartame, pure Croscarmellosesodium, pure Citric acid, pure Sodium starch glycolate, pure PEG400 and the mixtures of drug and excipients were given as figures 2-11.

Assay of the drug content:

All the solvent deposited systems and the physical mixture prepared by the geometric dilution method were found to contain 95% to 105% of the amount that should contain.

The assay results of various formulations are given in the Table 3.

Dissolution Rate Studies:

The percent of aceclofenac dissolved at the various time intervals were calculated and plotted against time. The results were given in the table 4-5, graphical plots of percentage of aceclofenac dissolved versus time,Ln of percentage of aceclofenac undissolved versus time are shown in figures 12-13 and also calculated the half life(t_{50}),first order rate constant(k_1) percentage of Dissolution efficiency (%DE).

EVALUTION OF FAST DISSOLVING ACECLOFENAC FILMS

Prepared Aceclofenac fast dissolving films were white in colour, glossy in appearance and smooth in texture without any imperfections.

Thickness measurement:

Thickness was measured by thickness gauge. Prepared films with this thickness are suitable to place on tongue without any discomfort. Results are summarized in below Table 6.

Determination of folding endurance:

It is an indication of brittleness of a film. The results showed that folding endurances was decreased with an increase in the polymer concentration. Folding endurance was found between the 8-22.thesevalues indicated that all the developed films were not brittle during handling and packing. . Results are summarized in below Table 6.

Surface pH:

Surface pH of all mouth dissolving films prepared by using different polymers, were found to be in the range of 5.4-5.67pH, which was close to neutral pH. It indicated that the films may have less potential to irritate the oral mucosa. . Results are summarized in below Table 6.

Drug content uniformity:

Drug content in the films was evaluated and values were found in between 97.2-103.9. . Results are summarized in below Table 6.

***In vitro* disintegration time:**

When compared to other formulations, films prepared with HPMC E5 are less disintegration time in the mouth. Among all, F_1 has less disintegration time (45 seconds). Results are summarized in below Table 6.

Dissolution Rate Studies:

The percent of aceclofenac dissolved at the various time intervals were calculated and plotted against time. The results were given in the table 6-7, graphical plots of percentage of aceclofenac dissolved versus time, Ln of percentage of aceclofenac undissolved versus time. Those are represented in figure 14-15, and also calculated the half life(t_{50}),first order rate constant(k_1),percentage of Dissolution efficiency (%DE).

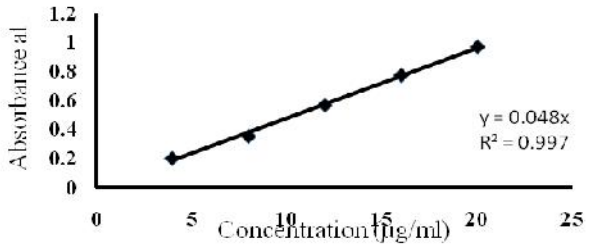

Fig 1: calibration curve of aceclofenac in pH 5.8 phosphate buffer

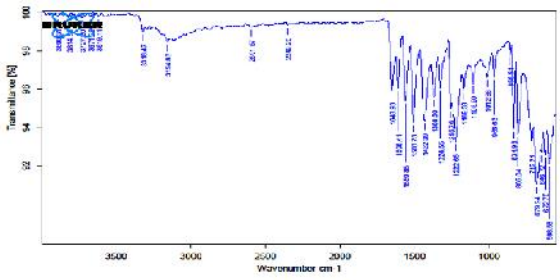

Fig 2: FTIR spectra of aceclofenac API

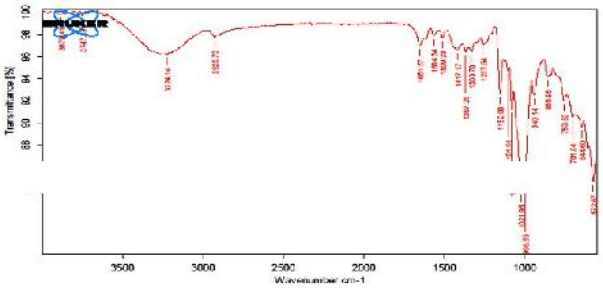

Fig 3: FTIR spectra of β-cyclodextrin

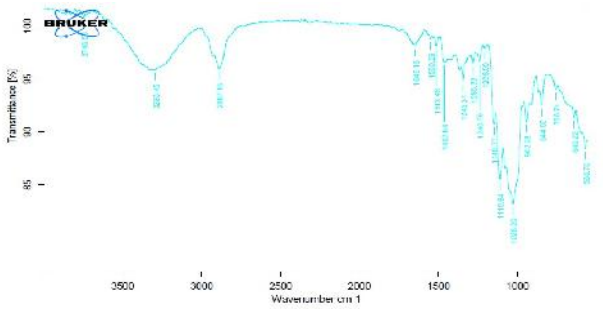

Fig 4: FTIR spectra of polaxomer

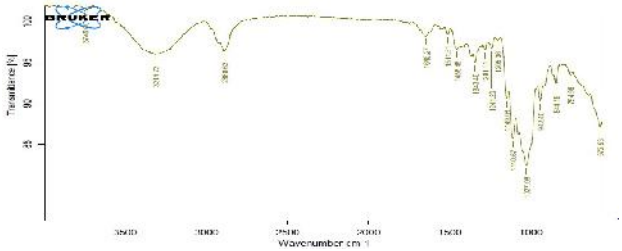

Fig 5: FTIR spectra of HPMC E5

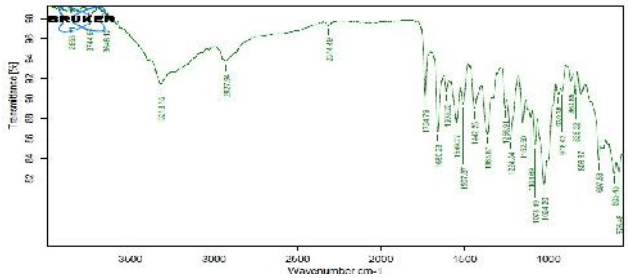

Fig 6: FTIR spectra of HPMC E15

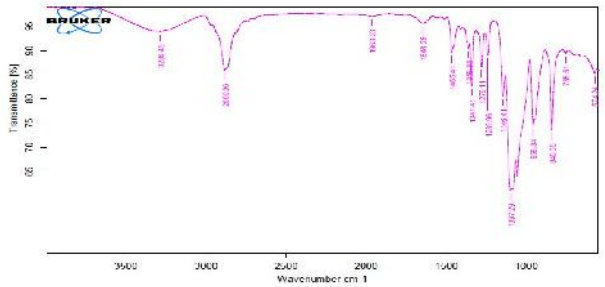

Fig 7: FTIR spectra of aceclofenac + β-cyclodextrin

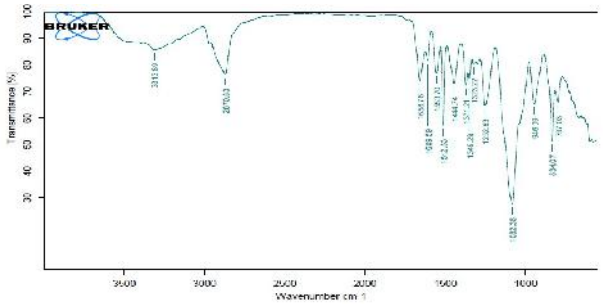

Fig 8: FTIR spectra of aceclofenac + polaxomer

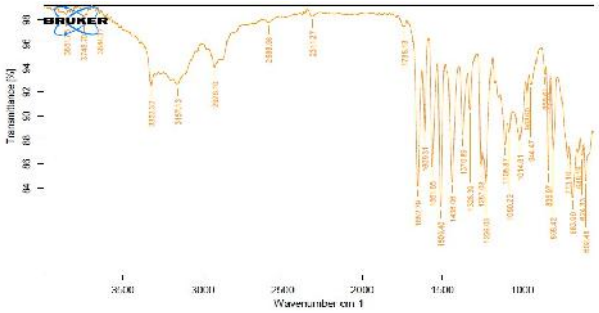

Fig 9: FTIR spectra of aceclofenac + HPMC E5

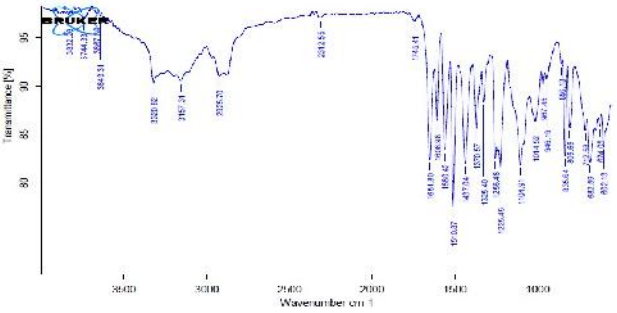

Fig 10: FTIR spectra of aceclofenac + HPMC E15

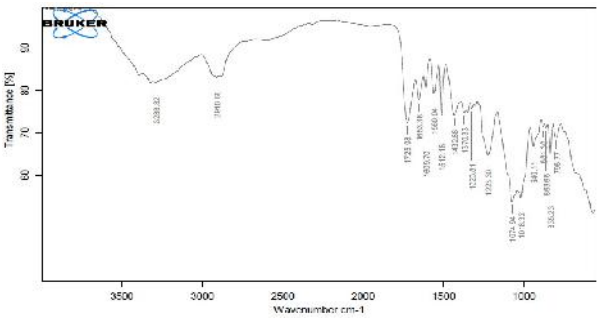

Fig 11: FTIR graph of mixture

Table 3: Assay of physical mixtures of aceclofenac

S.No.	Formulation	%Assay
1	A	100
2	B	99.7
3	C	98.9
4	D	102
5	E	98.6

Table 4: Comparative Dissolution profile of aceclofenac formulations

S.No	Time (min)	% Drug Dissolved					SD
		A	B	C	D	E	
1	0	0	0	0	0	0	0
2	5	55.24	78.47	77.13	63.54	68.988	0.05
3	10	68.26	82.46	80.66	79.04	78.194	0.03
4	15	76.23	86.22	84.14	88.13	84.144	0.03
5	20	78.98	89.59	86.84	93.8	89.308	0.03
6	30	84.82	91.83	89.76	99.3	94.921	0.01
7	45	90.15	95.2	94.3	102.33	97.56	0.01
8	60	96.1	99.3	97.39	106.99	100.366	0.02

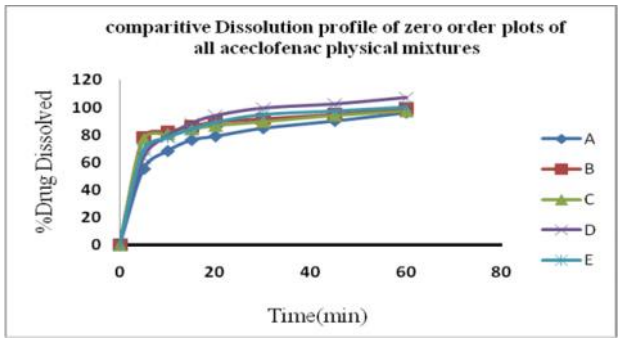

Fig 12: comparative dissolution profile of zero order plots of all aceclofenac physical mixtures

Table 5: Comparative Dissolution profile of aceclofenac formulations

S.No	Time (min)	Log(% Drug undissolved)					SD
		A	B	C	D	E	
1	0	2	2	2	2	2	0
2	5	1.65	1.33	1.36	1.56	1.45	0.03
3	10	1.50	1.24	1.29	1.32	1.339	0.03
4	15	1.38	1.14	1.20	1.07	1.200	0.03
5	20	1.32	1.02	1.12	0.79	1.029	0.03
6	30	1.18	0.91	1.01	-0.15	0.706	0.01
7	45	0.99	0.68	0.76	-	0.387	0.01
8	60	0.59	-0.15	0.42	-	-	0.02

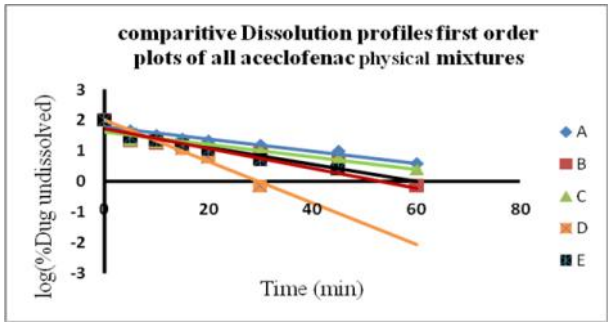

Fig 13: comparative dissolution profile of first order plots of all aceclofenac physical mixtures

Table 6: Evaluation of fast dissolving aceclofenac films

S.No	Formulation code	Thickness (mm)	Folding endurance	Surface pH	Drug content uniformity (%)	Disintegration time (seconds)
1	F_1	0.35 ±0.02	21.3 ±1.70	5.42	98.4 ±0.34	44.7 ±1.25
2	F_2	0.43 ±0.03	20.7 ±0.47	5.47	98.3 ±1.27	65 ±2.16
3	F_3	0.57 ±0.02	14.7 ±0.47	5.49	100.3 ±0.61	80.3 ±1.70
4	F_4	0.35 ±0.02	12.3 ±1.25	5.65	99.3 ±0.46	55.3 ±1.25
5	F_5	0.47 ±0.02	8.7 ±0.94	5.67	99 ±1.52	72.7 ±0.47
6	F_6	0.60 ±0.01	10 ±0.82	5.60	99.3 ±3.48	95.7 ±0.47

Table 7: Comparative Dissolution profile of aceclofenac fast dissolving films formulations

S.No.	Time (min)	% Drug dissolved						SD
		F_1	F_2	F_3	F_4	F_5	F_6	
1	0	0	0	0	0	0	0	0
2	0.5	19.815	30.761	32.782	19.759	26.663	20.882	5.792
3	1	24.867	39.013	43.335	23.408	33.455	24.979	8.394
4	2	31.603	49.061	56.919	30.537	40.248	32.782	10.774
5	3	36.767	67.135	71.626	38.9	46.478	40.36	15.262
6	4	41.988	85.659	81.225	44.121	51.474	45.636	19.739
7	5	47.152	102.612	91.722	52.26	66.406	51.25	23.342
8	10	85.884	116.252	105.082	99.973	99.524	75.106	14.519
9	15	99.131	122.539	122.539	121.753	115.298	89.308	14.201

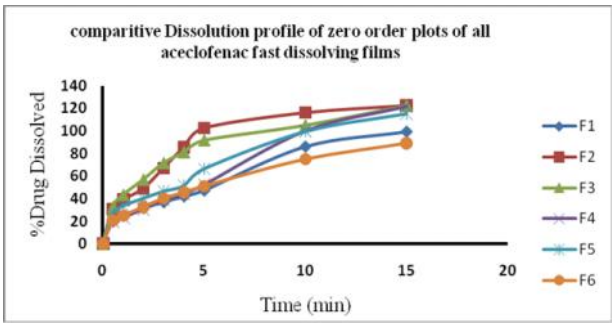

Fig 14: comparative dissolution profile of zero order plots of all aceclofenac fast dissolving films

Table 6: Comparative Dissolution profile of aceclofenac fast dissolving films formulations

S.No.	Time (min)	Log(% Drug undissolved)						SD
		F_1	F_2	F_3	F_4	F_5	F_6	
1	0	2	2	2	2	2	2	0
2	0.5	1.94	1.84	1.82	1.9	1.86	1.89	0.03
3	1	1.87	1.78	1.75	1.88	1.82	1.87	0.05
4	2	1.83	1.7	1.63	1.84	1.77	1.82	0.08

5	3	1.8	1.51	1.45	1.78	1.72	1.77	0.15
6	4	1.76	1.15	1.27	1.74	1.68	1.72	0.27
7	5	1.72	-	0.91	1.67	1.52	1.68	0.33
8	10	1.15	-	-	1.56	0.32	1.39	-
9	15	0.06	-	-	-	-	1.02	-

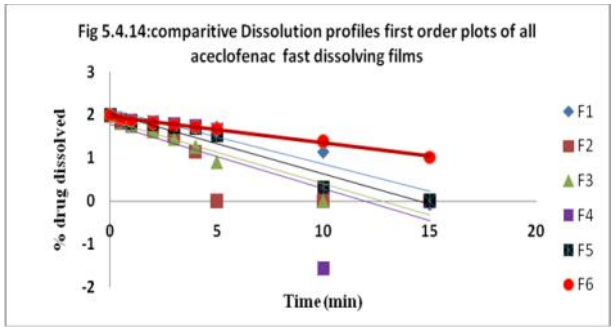

Fig 15: comparative dissolution profile of first order plots of all aceclofenac fast dissolving films.

4. CONCLUSION

Physical mixtures of Aceclofenac were prepared using β-Cyclodextrin, Sucrose, Poloxamer was found to perform better than the pure drug with respect to the dissolution. Formulation with sucrose has shown maximum drug release and apart to mask the taste than the marketed tablet. The physical mixture of aceclofenac prepared with sucrose formulated in to film using HPMC E5 & 15. HPMC E5 of 400mg has shown the greatest dissolution for aceclofenac. However the ANOVA proved that there is no significant difference indicating that both are of similar bioavailability. However *in-vivo* studies are needed to prove that.

5. REFERENCES

1. John H.Block, John M.Beale. Wilson & Gisvold's textbook of organic medicinal and pharmaceutical chemistry. 11th edition. Published by Lippincott Williams & Wilkins; 731.
2. Kulkarni Parthasarathi Keshavarao et al. Formulation and evaluation of mouth dissolving films of rofecoxib. International research journal in Pharmacy 2011; 2(3): 273-278.
3. Mogal S., Gurjar P. Solid Dispersion Technique for Improving Solubility Of Some Poorly Soluble Drugs. International Journal of Pharmacy and Pharmaceutical Sciences 2012; 3: 5-8.
4. Parul Saini, Anoop Kumar. Fast Disintegrating Oral Films: A Recent Trend of Drug Delivery. International Journal of Drug Development &Research 2012; 4(4): 2088-2093.
5. Indian Pharmacopeia 1996; 2: 554-555.
6. Raymond craowe , Paul J. sheskey. Hand Book of Pharmaceuticals Excipients. 6th edition. Published by the Pharmaceutical Press 2009; 210-214.
7. M.D. Nehal Siddiqui. A Novel Approach in Oral Fast Dissolving drug Delivery System and Their Patents. Advances in Biological Research 2011; 5(6): 291-303.
8. SwapnilL.Patil. Fast Dissolving Oral Films: An Innovative Drug Delivery System. International Journal of Research and Reviews in Pharmacy and Applied science 2012: 2(3): 482-496.
9. Koland, M, Sandeep. Fast Dissolving Sublingual Films of Ondansetron Hydrochloride: Effect of Additives on in vitro Drug Release and Mucosal Permeation. Journal of Young Pharmacists 2010; 2(3); 216-222.
10. D.akiladevi, P.Shanmugapandiyan, D. Jebasingh, sachinandhan basak. Preparation and Evaluation Of Paracetamol By Solid Dispersion Technique. International journal of pharmacy and pharmaceutical sciences 2011; 3(1): 188-191.
11. M Koland, VP Sandeep, NR Charyulu. Fast Dissolving Sublingual Films Of Ondansetron Hydrochloride: Effect Of Additives On In Vitro Drug Release Andmucosal Permeation. Eur J Pharm Biopharm. 2010; 75(1): 45-47.
12. Anupama Singh. Evaluation Of Enhancement Of Solubility Of Paracetamol By Solid DispersionTechnique Using Different Polymers Concentration. International Journal Of Pharmacy And Pharmaceutical Sciences 2011; 4(1): 177-119.
13. D.Akiladevi. Preparation and Evaluation of Paracetamol by Solid Dispersion Technique. http://www.inventi.in/Article/pndds/471/12.aspx. © 16th February.
14. Mogal S. A, Gurjar P. Solid dispersion technique for improving solubility of some poorly soluble drugs. International journal of pharmacy and pharmaceutical sciences 2011; 3(1): 845-847.
15. Phanijithendra Koganti. Formulation Development And In-Vitro Evaluation Of Midazolam: Solid Dispersions Buccal Flash-Disintegrating Films. Panacea Journal of Pharmacy and Pharmaceutical Sciences 2013; 1: 5-10.
16. Dawn A. Adkin, Stanley S. Davis. The Effect of Mannitol on the Oral Bioavailability of Cimetidine. Journal of Pharmaceutical Sciences 1995; 84(12): 1405–1409.
17. Desai D, Zia H, Quadir A. Evaluation of Selected Micronized Poloxamers as Tablet Lubricants. Drug Deliv. 2007; 14(7): 413-26.
18. Fu Y, Yang S, Jeong SH, Kimura S, Park K. Effect of Poloxamers on the Dissolution of Felodipine and Preparation of Controlled Release Matrix Tablets Containing Felodipine. Eur J Pharm Biopharm 2010; 75(1): 1-1.
19. Kaul G, Huang J, Chatlapalli R, Ghosh K, Nagi A. Quality-By-Design Case Study: Investigation of the Role of Poloxamers In Immediate-Release Tablets By Experimental Design And Multivariate Data Analysis. AAPS PharmSciTech. 2011; 12(4): 1064-76.

20. SabahatJabeen, Ayub Ali. Studies on The Effects of Cyclodextrin Polymer As A Tableting Aid On Some Selected Analgesics. Pakistan Journal of Pharmacology 2006; 23(1): 67-71.
21. Katarzyna Centkowska ,Sznitowska. Comparison of Sublingual Tablets With Nitroglycerin Complexed With N-cyclodextrin or Titrated With Crosspovidone N Technological Approach. Department of Pharmaceutical Technology. Medical University of GdaOsk, Poland; 80-416.
22. Venkatramana M. Rao,John L. Haslam. Controlled And Complete Release of A Model Poorly Water-Soluble Drug, Prednisolone, From Hydroxypropyl Methylcellulose Matrix Tablets Using $(Sbe)_{7m}$-B-Cyclodextrin As A Solubilizing Agent. Journal of Pharmaceutical Sciences 2001; 90(7): 807–816.
23. Reginster JY, Franchimont P. Piroxicam-Beta-Cyclodextrin in the Treatment of Acute Pain of Rheumatic Disease. Eur J Rheumatol Inflamm 1993; 12(4):38-46.
24. Hind Al-Zein, Khalil Sakeer, Fars K. Alanazi. Designing An Extended Release Waxy Matrix Tablet Containing Nicardipine–Hydroxy Propyl B Cyclodextrin Complex. Saudi Pharmaceutical Journal 2011; 19(4): 45–253.
25. Md. Sariful Islam Howlader et.al. Enhancing Dissolution Profile of Diazepam Using Hydrophilicpolymers By Solid Dispersion Technique. International Current Pharmaceutical Journal 2012; 1(12): 423-430.
26. Fudamental of Biostatistics By Khan & Khanum. Publishied By Uaask Publitions. Hyderabad: 375.
27. D. Nagendrakumar et al. Formulation and evaluation of fast dissolving oral films of metoprolol sccinate. International Journal of Engineering and Applied Sciences 2015; 6(4): 28-38.

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