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THE EFFECT OF DIFFERENT EXCIPIENT ON ACECLOFENAC

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Keywords:
Aceclofenac, excipients and different hydrophillcity (starch, betadex, lactose (Hydrophilic) and DCP, MCC)

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ABSTRACT

By using conventional method of preparing solid oral dosage form like tablets, poorly water soluble drugs were formulated by using different excipients. Hence, in present investigation Aceclofenac poorly water soluble drugs, whose absorption is dissolution rate limited, were selected as model. Five excipients having different hydrophillcity, viz. starch, betadex, lactose (Hydrophilic) and DCP, MCC (Hydrophobic), were selected as diluents. The present study was aimed to evaluate the influence of these different excipients (Hydrophilic and Hydrophobic) on the dissolution profiles of selected poorly water soluble drugs. This would help in early stage of formulation development of poorly soluble drugs, to achieve desired dissolution profiles simply by careful selection of different excipients.

INTRODUCTION:

Aceclofenac belongs to a group of medicines called non-steroidal anti-inflammatory drugs (NSAIDs) and it is an inhibitor of prostaglandin synthesis and used in rheumatoid arthritis. The effects of granulation method, moisture content, and excipients on disintegration and dissolution of norfloxacin tablets by Rangaiah et al.[1]

Torrado et al investigated the effect of different excipients on release characteristics of aspirin from compressed pellets prepared with cellulose microcrystalline (Avicel PH-101; MCC), wheat starch, and alpha-D-glucose monohydrate (dextrose monohydrate) in varying proportions.[2]Desai et al studied the dissolution of capsule and tablet formulations containing various drugs, hydrophobic and hydrophilic lubricants, and starch-derived disintegrants.[3]Taneja et al prepared solid dispersions of ketoprofen with polyethylene glycol 6000 and poloxamer 188 and evaluated for *in vitro* characteristics and bioavailability.[4]

MATERIALS AND METHODS-

Multimedia Solubility Study:

Procedure: Solubility of each API in different selected media was determined by dissolving the known quantity of API in cumulative manner with the aid of sonication till the API remains insoluble in the media.

Multimedia solubility study showed the solubility of API in different media. From these studies selection of dissolution media can be done, as it depends on solubility of API in media.The solubility of each API in different selected media was found and described in table no1.

Determination Of λmax

The absorption maxima of each API were determined by running the spectrum of API solution in double beam ultraviolet spectrophotometer. Absorption maxima of each The spectrum of this solution was run in 200-400 nm range in U.V. Spectrophotometer.

Absorption maxima of API have shown in figure, which are obtained from U.V. spectrophotometer. (Fig. no.1)

Linearity and Range

Linearity

The linearity of an analytical procedure is its ability (within a given range) to obtain test results which are directly proportional to the

concentration (amount) of analyte in the sample.

A linear relationship should be evaluated across the range of the analytical procedure. It may be demonstrated directly on the active substance (by dilution of a standard stock solution) and/or on separate weighing of synthetic mixtures of the product components, using the proposed procedure. table no3.

Range

The specified range is normally derived from linearity studies and depends on the intended application of the procedure.

Standard calibration curve of Aceclofenac was prepared in phosphate buffer pH 6.8 media. The equation of line was found to be y= 0.0253x -0.0146 (R^2=0.9996). The equations obtained from these curves were used to calculate cumulative % release of each drug from tablet dosage form in dissolution study..

Preformulation Study

Preformulation studies are the first step in the rational development of dosage form of a drug substance.

Organoleptic Characteristics

The color and odor of the drug were characterized and recorded using descriptive terminology; the result was **Properties:**

Description-Crystalline, Odor- Odorless and Color- White

Microscopic Examination

In this study, pure drug was examined under compound microscope for crystal morphology.

Bulk Density

The bulk density is calculated by following formula:

$$\textbf{Bulk density} = \frac{\textbf{Weight of powder}}{\textbf{Bulk volume}}$$

Tapped Density

The tapped density is calculated by the following formula:

$$\textbf{Tapped density} = \frac{\textbf{Weight of powder}}{\textbf{Tapped volume}}$$

The results are shown for drug and excipients in table no. 4 and 5 respectively.

Carr's Index [Compressibility Index] and Hausner's Ratio

Carr's index and Hausner's ratio measure the propensity of powder to be compressed and the flowability of powder.

Angle of repose

$$\theta = \tan^{-1} h/r$$

Where, h = height of pile

r = radius of the base of the pile

θ = angle of repose

Loss on drying

LOD of API was tested at 105°C till constant weight achieved by using Halogen Moisture Analyzer.

The results are shown for drug and excipients in table no. 4 and 5 respectively.

Aceclofenac is poor for compression. From all excipients DCP has excellent compressibility, because it has least value among all excipients and which was near to 5%.Whereas aerosil and Mg. stearate had the values more than 40%, therefore they had extremely poor compressibility among all excipients

Formulation Development

***Formulation details*:** For Aceclofenac have summarized in tab. no 6

Procedure:

Weighing & shifting: Aceclofenac.PVP-K 30 (binder) was dissolved properly in the water with constant stirring.Above dry mix was granulated with the granulating (Binder) solution of water by adding drop wise with continuous mixing and it was dried at 45°c - 50°c in tray dryer till LOD obtained 2.0-2.6 % w/w, measured at 105°c for 2 minutes. The blend was sifted through 30# sieve and weighed.

The blend was lubricated with Mg. Stearate.The lubricated blend was compressed on 8-station/12-station compression machine using 8.2 mm round (SC with break line) punches for 178 mg strength.

Evaluation:

Physical characterization

Uniformity of mass, Thickness, Hardness Test, Friability Test, Disintegration time and Wetting time

In-vitro drug release

Dissolution conditions of Aceclofenac tablets:

USP Apparatus **:** Type 2 (Paddle)

Speed **:** 75 rpm

Medium **:** Phosphate buffer 6.8 pH

Volume **:** 900 ml

Time Points **:** 5 min, 10 min, 15 min, 30 min, 45 min, 60min.

Sample preparation:

5ml of solution was taken from each sample and diluted up to mark in 25ml volumetric flask as suitable for absorbance at λmax. Absorbance of the solution was measured at 272 nm. The concentration of Aceclofenac as calculated using slope of calibration curve and cumulative percentage release was calculated.

CONCLUSIONS

Each drug was formulated with each of diluents individually or combinations thereof, by wet granulation method and resulting tablets were evaluated for average weight, thickness, hardness, friability, wetting time, disintegration time and *in vitro* dissolution profiles. *In vitro* dissolution studies were carried out using USP dissolution apparatus II and quantitative analysis of individual drugs in dissolution media were carried out using UV-Visible Double Beam Spectrophotometer at respective absorption maxima of individual drugs.

Rate and extent of dissolution of Aceclofenac varied depending upon the type of excipient used. Initial burst of tablets was observed in batches F 1 and F 2 only. Although betadex and lactose are hydrophilic in nature, could not show release of drug satisfactorily. DCP is hydrophobic in nature, therefore the disintegration time might affect the drug release from tablet and hence the dissolution of Aceclofenac was not satisfactory. As MCC and starch also act as tablet disintegration agent, initial burst was observed. Hence satisfactory dissolution profile of Aceclofenac was found from F2 batch containing starch, as in comparison with dissolution profile of innovator.

Hence it was concluded that without using novel technologies, poorly soluble drugs can be formulated by using hydrophilic excipients, after evaluating selected

excipients. Single excipient can not be better for all poorly water soluble drugs, as compatibility of different excipients may vary from drug to drug. But water soluble excipients are better than water insoluble excipients for formulating the poorly water soluble drugs.

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Tab. no 1: Saturation solubility of API in different selected media.

API	MEDIA				
	N HCL (mg/ml)	Acetate buffer pH 4.5 (mg/ml)	Phosphate buffer pH 6.8 (mg/ml)	Water (mg/ml)	KCL buffer pH 2.0 (mg/ml)
Aceclofenac	0.00018	0.046	1.61	0.38	-

Table no. 2 Absorption maxima of each API

API	Aceclofenac
λmax (in nm)	272

Tab. No 3-Conc. and absorbance of dilutions in linearity study.

Conc. (in ppm)	Absorbance (in nm)
0	0
5	0.146
10	0.267
15	0.398
20	0.521
25	0.664
30	0.775
35	0.898
40	1.021
45	1.142
50	1.281

Tab. No 4. - Characterization of API

Parameter	API
Loss on Drying (%w/w)	0.16
Bulk Density (gm/ml)	0.58
Tapped Density (gm/ml)	0.83
Compressibility Index (%)	30
Hausner's Ratio	1.43
Angle of repose (θ)	52

Tab. No 5- Characterization of Excipients

Excipient	Parameter			
	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Compressibility Index (%)	Hausner's Ratio
Lactose	0.54	0.80	32.5	1.48
MCC	0.32	0.45	28.88	1.42
Starch	0.46	0.65	29.78	1.42
DCP	0.78	0.82	4.87	1.05
Betadex	0.523	0.754	30.63	1.44
Aerosil	0.03	0.05	40	1.66
PVP-K 30	0.31	0.40	22.5	1.29
Mg. Stearate	0.16	0.28	44.4	1.79

Table No.6 Composition of formulations for Aceclofenac tablets

Category	Ingredients	Batch				
		F1	**F2**	**F3**	**F4**	**F5**
API	Aceclofenac	100 mg	100 mg	100 mg	100 mg	100 mg
Diluents	MCC	30.9 %	-	-	-	-
	Starch	-	30.9 %	-	-	-
	DCP	-	-	30.9 %	-	-
	Betadex	-	-	-	30.9 %	-
	Lactose	-	-	-	-	30.9 %
Binder	PVP-K 30	6.75 %	6.75 %	6.75 %	6.75 %	6.75 %
	Water	q.s.	q.s.	q.s.	q.s.	q.s.
Lubricant	Magnesium Stearate	1.68 %	1.68 %	1.68 %	1.68 %	1.68 %
Disintegrant	Crospovidone	1.12 %	1.12 %	1.12 %	1.12 %	1.12 %
Glidant	Aerosil	3.37 %	3.37 %	3.37 %	3.37 %	3.37 %
-	**Tablet Weight (mg)**	178	178	178	178	178

Tab. No 7- Results of Physical Characterization of Aceclofenac tablets

Parameters	F 1	F 2	F 3	F 4	F 5
Uniformity of mass (mg)	178.8	179.6	181.2	179.4	179.2
Hardness (Kp)	3.2	3.2	6.1	4.3	5.1
Thickness (mm)	3.7	3.7	2.9	4.1	3.6
Friability (% w/w)	0.33	0.22	0.5	0.33	0.56
DT (min)	6	2	15	23	16
Wetting time (sec)	33	52	54	157	39

Tab. No 8- Cumulative % release of Aceclofenac.

Batch	INNOVATOR	F 1	F 2	F 3	F 4	F 5
Time (min)	Cumulative % release					
5	57.1	59.9	60.5	8.9	10.1	16.5
10	89.4	83.5	92.2	20.7	23.2	34.1
15	93.7	90.1	97.3	38.7	37.9	54.6
30	95.5	93.1	98.0	82.3	75.4	93.8
45	95.6	93.3	98.5	94.5	94.7	96.4
60	96.1	94.1	98.7	95.7	94.7	96.6
Similarity Factor (f_2)		70.1	74.5	14.9	14.9	20.3

Fig..1: Spectrum of Aceclofenac in Phosphate buffer pH 6.8.

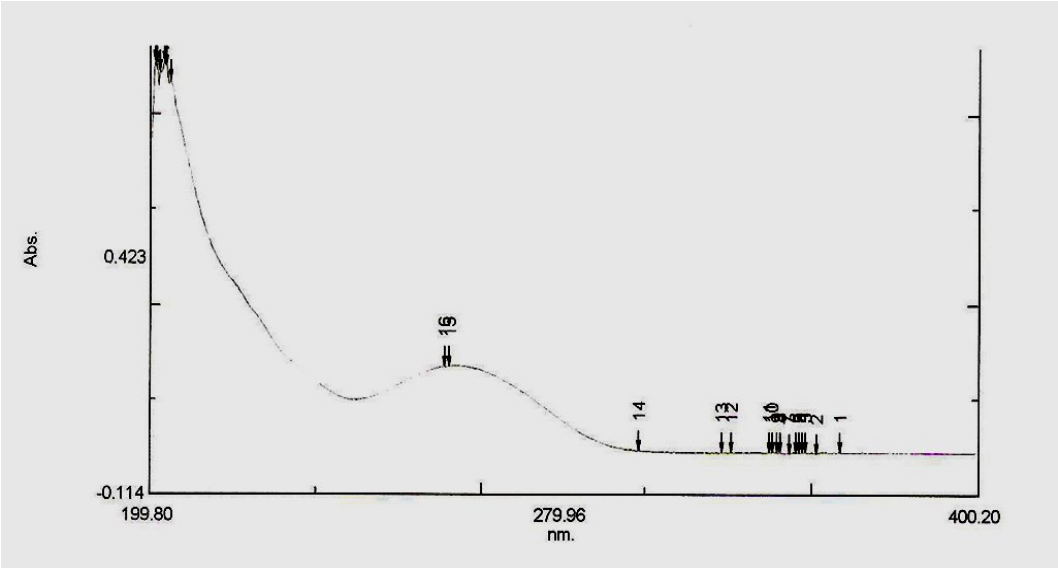
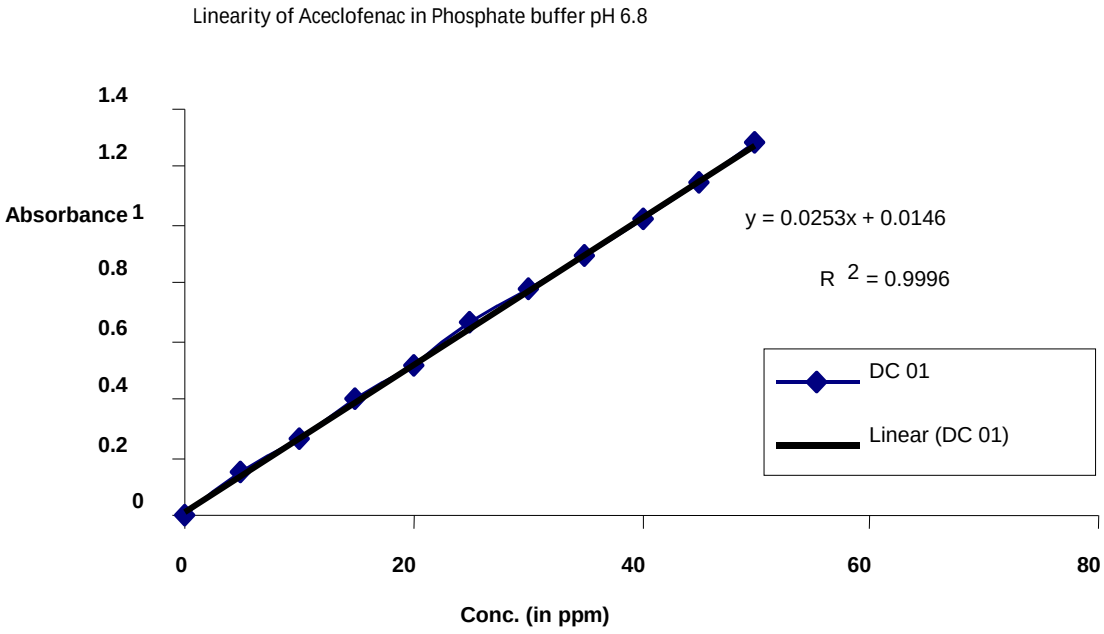


Fig. 2: absorbance vs. concentration of Aceclofenac



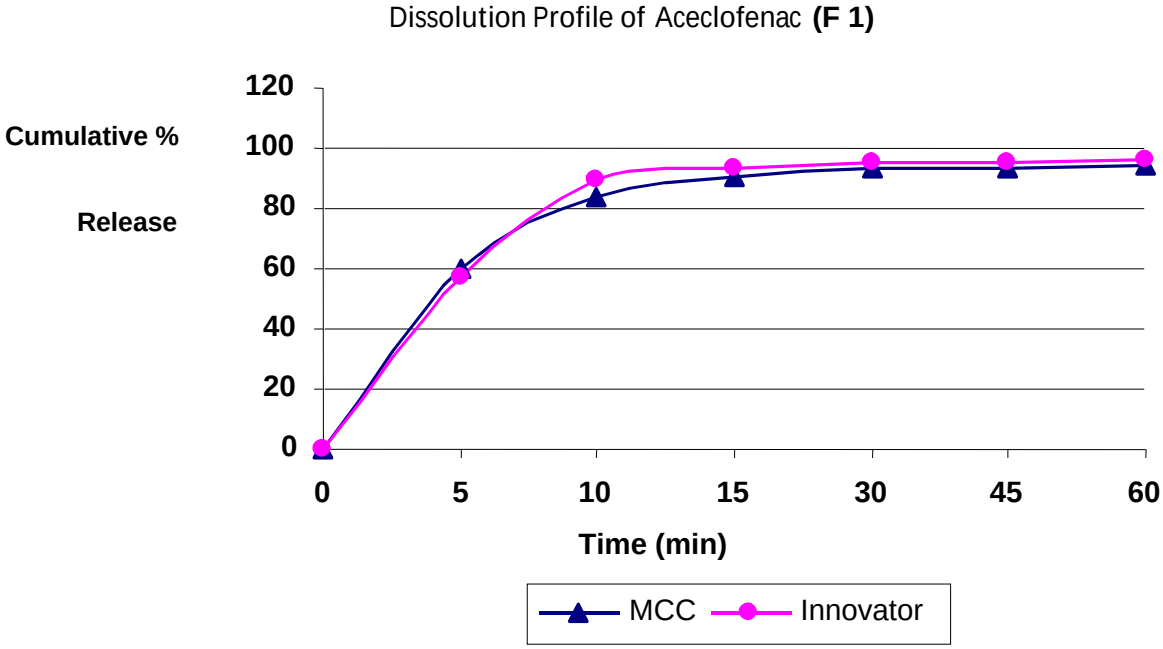


Fig. no 3 Batch F1 with Innovator

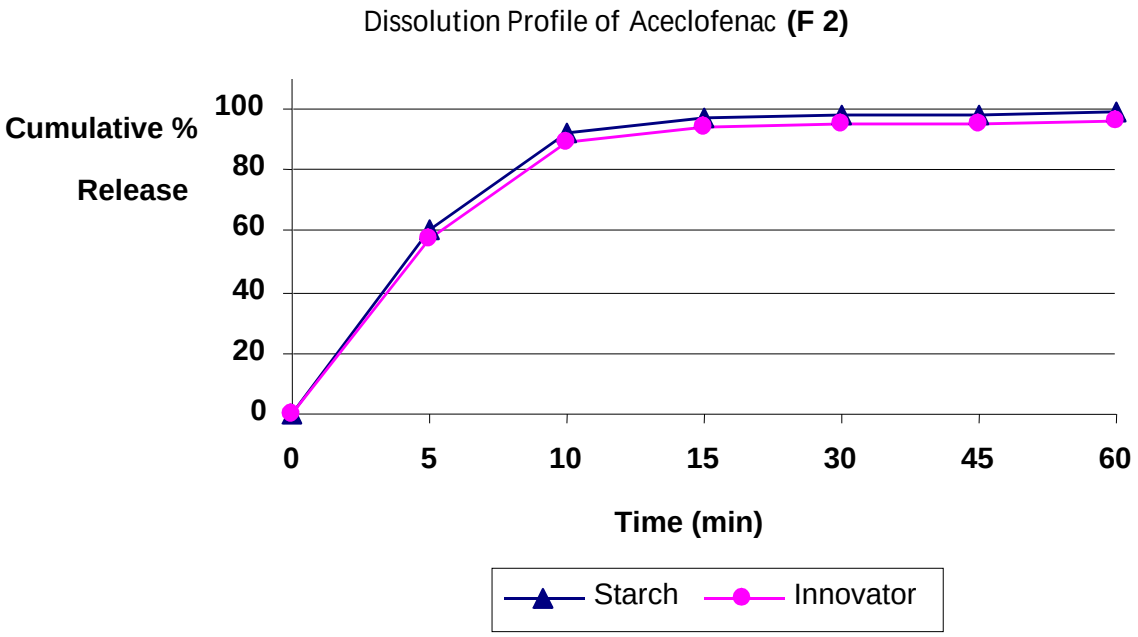


Fig. 4 Batch F2 with Innovator

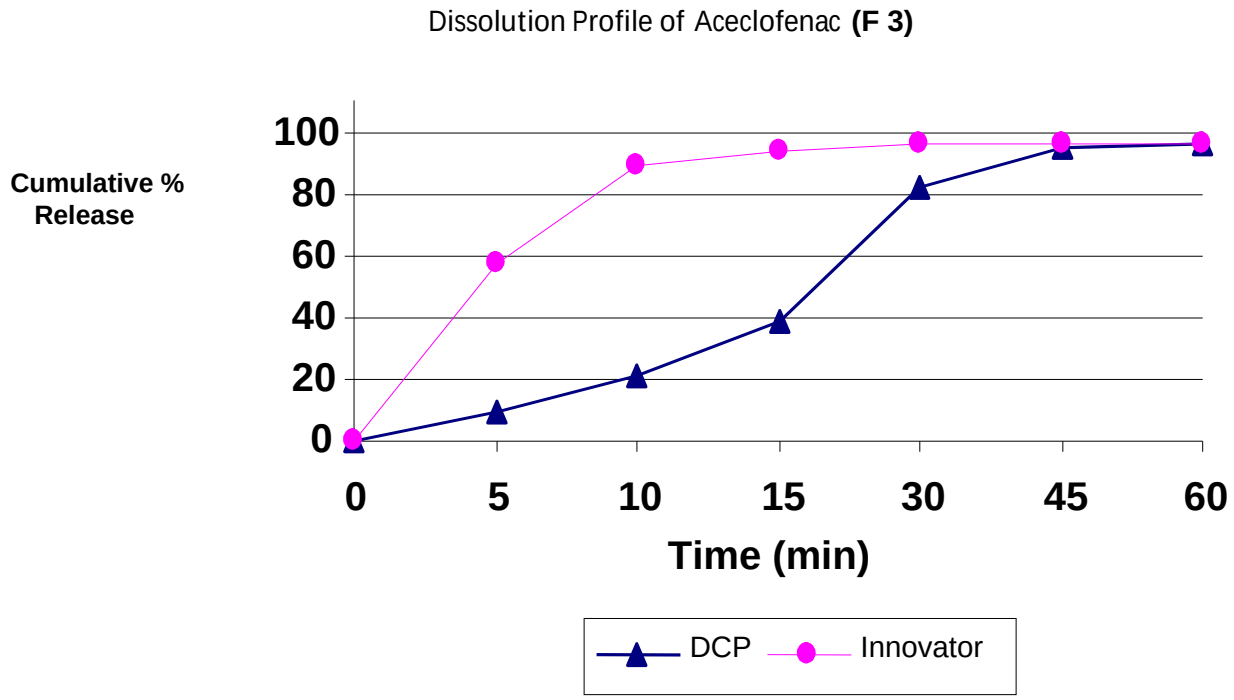


Fig. no. 5: Batch F3 with Innovator

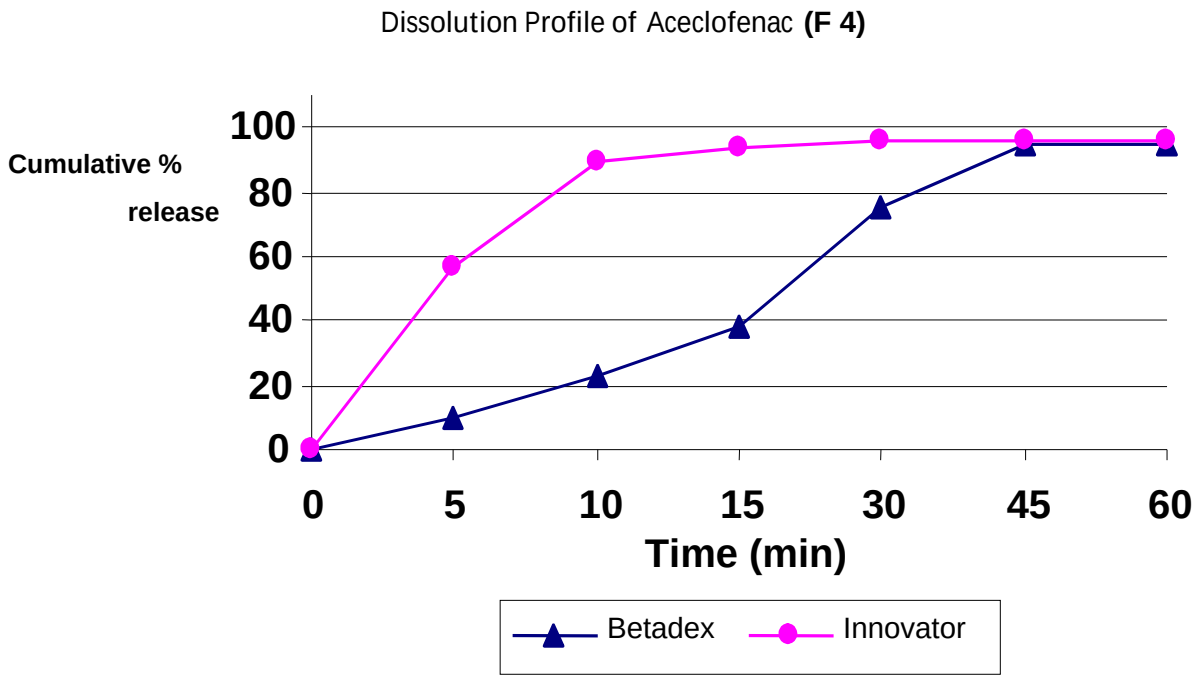


Fig. no. 6: Batch F4 with Innovator

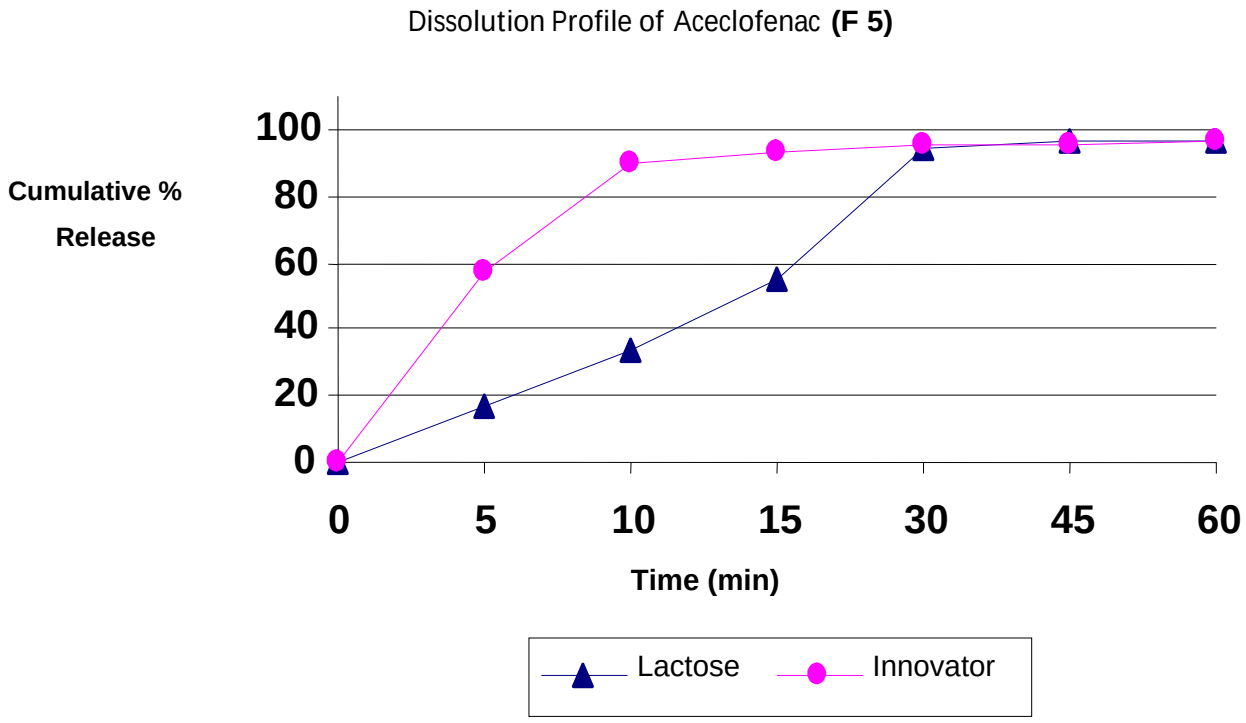


Fig. no. 7: Batch F5 with Innovator

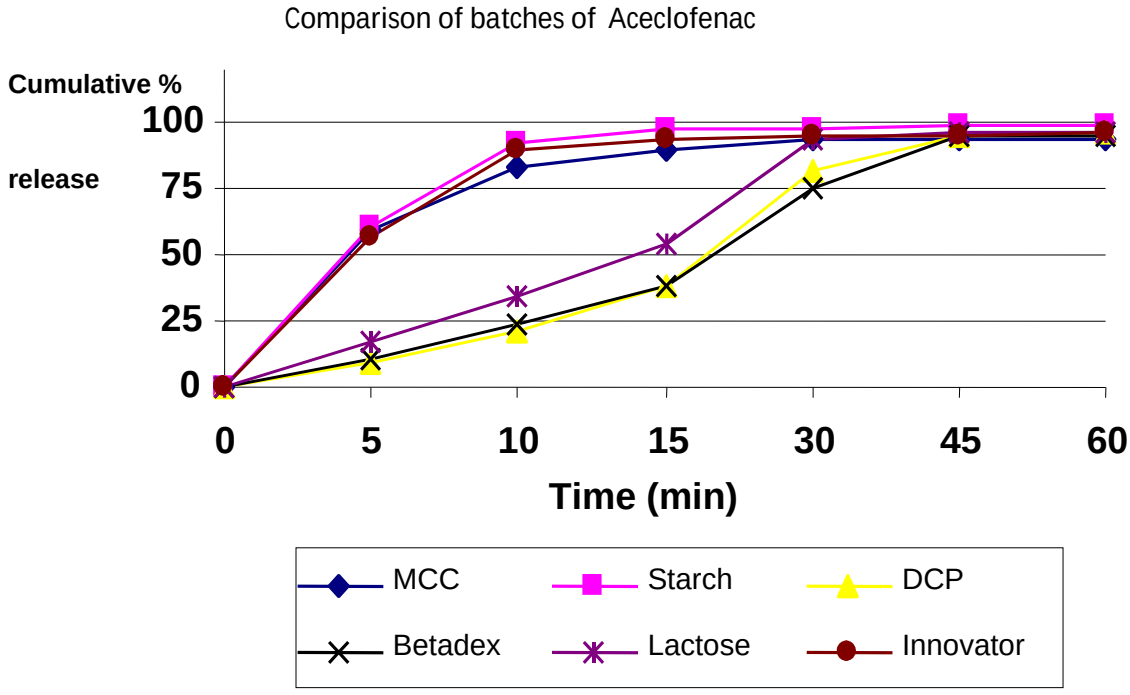


Fig. no 8: Comparison of batches of Aceclofenac with Innovator.

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