ISSN : 2320 4850

BI MONTHLY

Asian Journal of Pharmaceutical Research And Development

(An International Peer Reviewed Journal of Pharmaceutical Research and Development)

AJPRD

Volume - 03 Issue - 06 NOV-DEC 2015

website: www.ajprd.com
editor@ajprd.com

Asian Journal of Pharmaceutical Research and Development
(An International Peer-Reviewed Journal of Pharmaceutical Research and Development)
www.ajprd.com
ISSN 2320-4850

Research Article

"DESIGN DEVELOPMENT AND EVALUATION OF WATER DISPERSIBLE TABLET OF ACECLOFENAC USING SYNTHETIC SUPERDISINTIGRANTS"

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Received: June 2015 *Revised and Accepted: September2015*

ABSTRACT

Aceclofenac has been shown to have potent analgesic and anti-inflammatory activities, similar to indomethacin and diclofenac and due to its preferential cox-2 blockade it has better safety than conventional NSAIDs with respect to adverse effects on gastrointestinal and cardiovascular system. Aceclofenac is superior form other NSAIDs as it has selectivity for cox-2, a beneficial cox inhibitor, well tolerated, better GI tolerability and improved cardiovascular safety when compared to other selective cox-2 inhibitors. Aceclofenac has a faster and more potent effect than the other NSAIDs. Aceclofenac has an outstanding anti-inflammatory profile, involving a classical inhibition of prostaglandins E_2, a decrease in the expression of several cytokines including interleukin and tumor necrosis factor. It also inhibits activated oxygen species production and influences cell adhesion. Thus it can be concluded that Aceclofenac may be a better option for the management of pain.

KEYWORDS: *NSAIDs, Adverse effects, Anti-inflammatory, Management of pain.*

INTRODUCTION

Aceclofenac, a non steroidal anti-inflammatory drug (NSAID) has been indicated for various painful indications and proved as effective as other NSAIDs with lower indications of gastro-intestinal adverse effects and thus, resulted in a greater compliance with treatment. Aceclofenac is practically insoluble. For poorly soluble orally administered drugs, the rate of absorption is often controlled by the rate of dissolution. The rate of dissolution can be increased by increasing the surface area of available drug by various methods (micronization, complexation, solid dispersion).

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Many patients express difficulty in swallowing tablets and hard gelatin capsules, resulting in non-compliance and ineffective therapy. Recent advances in novel drug delivery systems (NDDS) aim to formulating a dosage form of drug molecules for convenient administration and to achieve better patient compliance. One such approach leads to development of fast dissolving/disintegrating tablets. Advantages of this drug delivery system include convenience of administration and accurate dosing as compared to liquids, easy portability, ability to provide advantages of liquid medication in the form of solid preparation, ideal for pediatric and geriatric patients and rapid dissolution/absorption of the drug, which may produce rapid onset of action. Some drugs are absorbed from mouth, pharynx and esophagus as the saliva passes down into the stomach and in such cases bioavailability of the drug is increased: pre-

gastric absorption can result in improved bioavailability and as result of reduced dosage, improved clinical performance through a reduction of unwanted effects. [1,]

Advantages of Fast Dissolving Drug Delivery System FDDTs, [2,3,4,5]

- Improved compliance/added convenience
- No chewing needed
- Better taste
- Improved stability
- Suitable for controlled/sustained release actives
- Allows high drug loading.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Adaptable and ameanable to existing processing and packaging machinery
- Cost effective.

LIST OF CHEMICALS USED

Materials	Company Name
Aceclofenac BP	Amoli organics PVT LTD
Microcrystalline cellulose pH 200	Gujarat Microvea, Ahemedabad
Colloidal cilicon dioxide	Cabot India Pvt Ltd
Sodium lauryl sulfate	Signet chemicals
Pharmatose DCL	DMV Netherland
Pearlitol 200 SD	Signet chemicals
Aspartame	Central Pharmacy
Cross carmellose sodium	FMC Biopolymers
Sodium starch glycolate	Signet Chemicals
Cross povidone XL	ISP Technologies
Magnesium Stearate	Komal Pharmaceuticals A'bad
Hydrochloride Acid	Finar reagents Mumbai.

LIST OF INSTRUMENT USED

Equipments	Company Name
UV Spectrophotometer	Systronic 1601 UV/Vis double beam Spectrophotometer (Japan).
Tablet compression machine	Multipunch tablet compression machine, Cadmach Machinery Co. Pvt. Ltd., Ahmedabad, India. Rimek minipress-ii MT.SF
Dissolution test apparatus	Dissolution test apparatus-TDT-06T, Electrolab, Mumbai, India.
Disintigration test apparatus	Electrolab mumbai
pH meter	Lab india Baroda
Balance	Contech mumbai.
Sartorious electronic balance	Model CP- 224 S, Labtronic.
Roche Friabilator	Camp-bell Electronics, Mumbai, India
Hardness Tester	Sbital Scientific Industries Ahemedabad
Stability Chamber	Thermolab Mumbai
Tap density tester (USP)	JEL A'bad

METHODS

PREFORMULATION STUDIES

Organoleptic Properties

The drug (Aceclofenac) powder was examined for its organoleptic properties like colour and odour. The sample of Aceclofenac was identified from its organoleptic properties. This was shown in table 1.

IR Spectroscopy

The spectrum of the Aceclofenac shows the following functional groups at their frequencies. The IR spectrum of pure drug was found to be similar to the standard spectrum of Aceclofenac. The results was shown in figure 1 & 2.

Solubility study

This study includes selection of suitable solvent to dissolve the pure drug as well as excipients used for the design of tablets. The sample was qualitatively tested for its solubility in various solvents. It was determined by taking 1 mg of drug sample in necessary amount of solvent as water,buffer 1.2 pH, buffer 6.8 pH, 0.5%w/v SLS in Water, 1 %w/v SLS in Water, 1.5 %w/v SLS in Water, 1.5% w/v SLS in 0.1 N HCL, 1.5% w/v SLS in Phosphate buffer pH 6.8 etc., in small test tube and well solubilized by shaking, according to IP. This was shown in table 2.

Melting point determination

The melting point of aceclofenac was determined using open capillary method. Aceclofenac was packed into capillary. The capillary filled with drug powder was placed in melting point apparatus and heated it when drug is melt the melting point of drug powder was noted. The average of three values was taken as the melting point of drug. The melting point of aceclofenac was 156-158˚C.

Partition Co-efficient

The results of partition coefficient determination carried out in n-octanol saturated with acidic buffer (pH 1.2) and n-octanol saturated with phosphate buffer (pH 7.4). The Log P values of prodrugs were found to be higher than the parent drug in both pH. The study showed that the major fraction of the prodrugs was partitioned towards the organic phase. High partition coefficient of synthesized prodrug as compared to the parent drug indicates the increase in lipophilicity of the compound. This may lead to the higher absorption of the compound through lipoidal cell membrane. The results of partition coefficient determination were 1.86.

UV Spectroscopy

Determination of λmax

A solution of 10 µg/ml Aceclofenac was prepared in 6.8 pH Phosphate buffer and UV spectrum was taken using Shimadzu UV-1601 UV/Vis double beam spectrophotometer. The UV maxima of Aceclofenac was found to be 274 nm in 6.8 pH Phosphate buffer.[6]

Preparation of standard calibration curve of ACECLOFENAC

Aceclofenac (100 mg) was dissolved in 6.8 pH Phosphate buffer and volume was made up to 100 ml in 100 ml volumetric flask. This solution (1000 mcg/ml) was further diluted with 6.8 pH Phosphate buffer to obtain solution of 100 to 1000 mcg/ml. Absorbance of each solution was measured at 274 nm using Shimadzu UV-1601 UV/Vis double beam spectrophotometer and 6.8 pH Phosphate buffer as reference standard.

The standard curve was generated for the entire range from 10 to 100 mcg /ml. The results of standard curve preparation are shown in the table 3 and figure 3.

FORMULATION DESIGN

Preparation of Water Dispersible tablets

Different tablets formulations were prepared by direct compression technique. Drug was passed through 60 mesh sieve. All the other ingredients were passed through 40 mesh sieve. Required quantity of drug, and SLS was mixed first than other excipients were mixed thoroughly. Magnesium stearate was finally added as glident and lubricant. The blend was compressed (11/32 diameter, flat punches) using multipunch tablet compression machine (Cadmach, Ahmedabad, India). Each tablet contained 100 mg of Aceclofenac and other pharmaceutical ingredients as listed in table in each section. Data shown in table 5.

EVALUATION STUDIES

EVALUATION OF POWDER BLEND [8, 9, 10, 11, 12]

Angle of repose

The angle of repose of powder blend was determined by the funnel method. The accurately weight powder blend were taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

$$\tan \theta = h/r$$

Where, h and r are the height & radius of the powder cone. The results were shown in the table 4.

Bulk and tapped density

Both loose bulk density (LBD) and tapped bulk density (TBD) was determined. A quantity of 10 gm of powder blend from each formula, previously shaken to break any agglomerates formed, was introduced in to 100 ml measuring cylinder. After that the initial volume was noted and the cylinder was allowed to fall under its own weight on to a hard surface from the height of 2.5 cm at second intervals. Tapping was continued until no further change in volume was noted. LBD and TDB were calculated using the following equations. The results were shown in the table 4.

LBD= Weight of the powder blend/Untapped Volume of the packing

TBD=Weight of the powder blend/Tapped Volume of the packing

Compressibility Index

The Compressibility Index of the powder blend was determined by Carr's compressibility index. It is a simple test to evaluate the LBD and TBD of a powder and the rate at which it packed down. The formula for Carr's Index is as below:

Carr's Index (%)=[(TBD-LBD) x100]/TBD

The results were shown in the table 4.

Drug Content

An accurately weight amount of Aceclofenac powder blend (100 mg) was extracted with 6.8 pH Phosphate buffer and the solution was filter through 0.45µ membrane. The absorbance was measured at 274 nm after suitable dilution using a Shimadzu UV-1601 UV/Vis double beam spectrophotometer. The results were shown in the table 4.

EVALUATION OF TABLETS [13, 14, 15]

Weight variation test

To study weight variation twenty tablets of the formulation were weighed using a Sartorius electronic balance and the test was performed according to the official method.

Drug content

Five tablets were weighed individually, and the drug was extracted in 6.8 pH Phosphate Buffer the drug content was determined as described above.

Hardness

The hardness of ten tablets was determined using the hardness tester and the average values were calculated.

Thicknesses and Diameter

The thickness and Diameter of the tables was determined by using vernier calipers. Five tablets were used, and average values were calculated.

Disintegration time

The disintegration time of the tablet was measured by using USP Disintegration apparatus at 24.5º C

Friability

The friability of tablets was measured by roche friabrator and average values were calculated.

Fineness of dispersion

Place 2 tablet in 100 ml of water and stir until completely dispersed. A smooth dispersion is produced, which passes through a sieve screen with a nominal mesh aperture of 710 µm.

The results were shown in Table 6.

In Vitro dissolution studies [16,17]

The release rate aceclofenac dispersible tablets (n=3) was determined using *The United States Pharmacopoeia* (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of 6.8 pH Phosphate buffer, at 37 ± 0.5°C and 50 rpm.[9] A sample (10 ml) of the solution was withdrawn from the dissolution apparatus minutely for 15 minutes, and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45 µ membrane filter and diluted to a suitable concentration with 6.8 pH Phosphate buffer. Absorbance of these solutions was measured at 274 nm using a Shimadzu UV-1601 UV/Vis double beam spectrophotometer. Cumulative percentage of drug release was calculated using the equation obtained from a standard curve. Results were shown in table 7 & Figure 4.

RESULT AND DISCUSION

Water dispersible tablets of Aceclofenac were formulated and evaluated.The following results was found of Water dispersible tablets of Aceclofenac.

Table: 1 API Characterization

TEST	RESULT
Colour	White
Odour	Complies
Form	Crystalline powder

Table: 2 Solubility study of aceclofenac

Solution	Solubility(mg/ml)
D.W	Slight soluble
N HCL	Insoluble
Phosphate buffer pH 6.8	Very soluble
Phosphate buffer pH 7.4	Soluble
0.5%w/v SLS in Water	Sparingly Soluble
1 %w/v SLS in Water	Sparingly Soluble
1.5 %w/v SLS in Water	Sparingly Soluble
1.5% w/v SLS in 0.1 N HCL	Sparingly Soluble
1.5% w/v SLS in Phosphate buffer pH 6.8	Very soluble

Table: 3 Standard calibration curve of ACECLOFENAC in 6.8 pH Phosphate buffer

Sr. No.	Concentration (µg/ml)	Absorbance			Average Absorbance
		1	2	3	
1	0	0	0	0	0
2	5	0.177	0.176	0.176	0.176±0.010
3	10	0.287	0.288	0.287	0.287±0.014
4	15	0.397	0.397	0.396	0.397±0.016
5	20	0.529	0.531	0.531	0.531±0.019
6	25	0.636	0.637	0.637	0.637±0.023

Correlation Co-efficient : 0.9939 Absorbance= 0.0249x + 0.0266

Table 4 Micromeritic properties of powder blend of Batch-A

Powder blend	Angle of Repose (^{0})	Loose Bulk Density (g/ml)	Tapped Bulk Density (g/ml)	Hausner 's Ratio	Compressibiliy Index (%)	Drug Content (%)
A	38.24±0.28	0.36±0.03	0.56±0.08	1.55	23.52±0.30	99.92±0.0

Table 5 Formulation of Dispersible Tablet of Batch-A

Composition	Aceclofenac Dispersible Tablet 100 mg (Batch-A)	(Batch-A)
Drug	Aceclofenac	100 mg
Diluent/filler	MCC pH102	77 mg
Superdisintigrant	Cross carmellose sodium	4 mg
Glident	Colliodal silicon Dioxide	7 mg
Sweetener	Aspartame	10 mg
Lubricant	Mg-Stearate	2 mg
Total	Total wt.	200 mg

Table 6 Evaluation parameter of tablets

Batch	Weight variation test (%)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Diameter (mm)	D.T (sec)	Drug content (%)
A	200±3	2.69±0.03	3-5	0.76%	8.79±0.02	27	100

Table 7 Effect of polymer concentration on drug dissolution profile

S. NO	Time(min)	%CDR
1	0	0.00
2	2	15.58
3	4	28.15
4	6	41.83
5	8	53.86
6	10	72.88
7	12	79.82
8	15	79.96

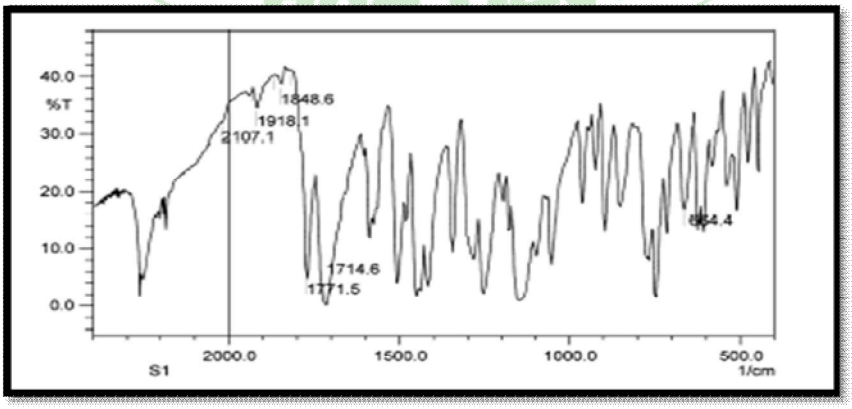

Figure 1 FTIR of Pure drug

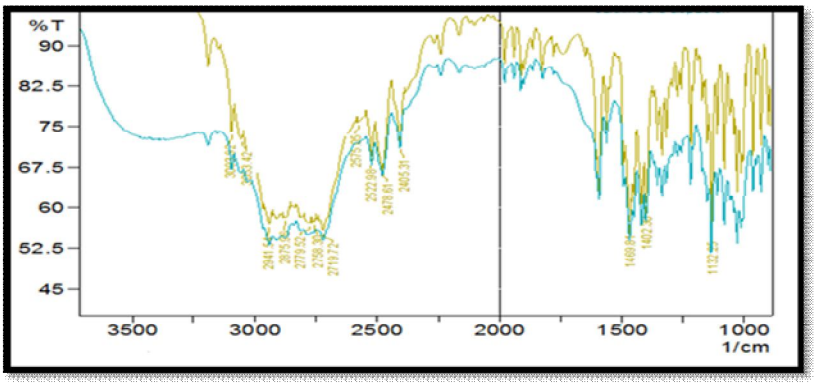

Figure 2 FTIR of drug with excipients

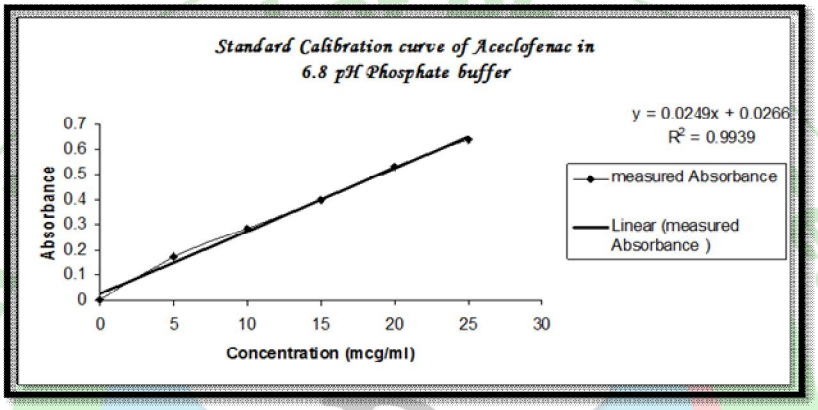

Figure 3 Standard Calibration curve of Aceclofenac In 6.8 pH Phosphate buffer

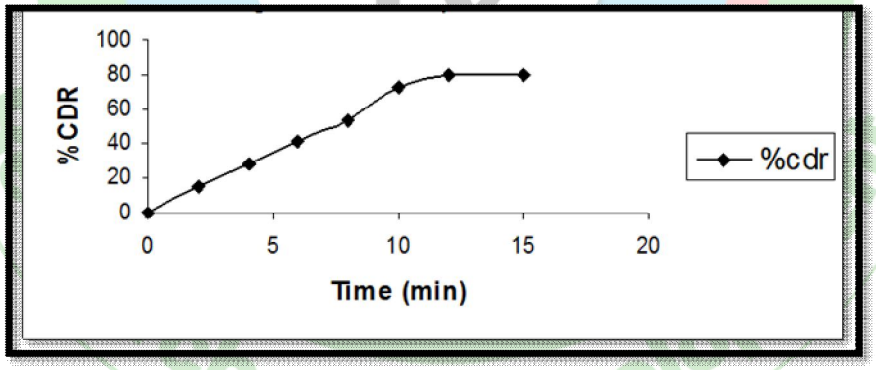

Figure: 4 Dissolution profile of Batch-A

ACKNOWLEDGEMENT

The authors are very thankful to Dr. Mahaveer Prasad Khinchi (pharmaceutics) Principal of Kota college of Pharmacy, Kota, Rajasthan for providing the research facilities. We are also thankful to all staff specially lab staff of Kota college of Pharmacy, Kota, Rajasthan, for providing the regular help and support.

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