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COMPARATIVE STUDY AND IN VITRO EVALUATION OF SUSTAINED RELEASE MARKETED FORMULATION OF ACECLOFENAC SUSTAINED RELEASE TABLETS

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ABSTRACT

Aceclofenac is a newer non-steroidal anti-inflammatory drug (NSAID's) with good analgesic and anti-rheumatic properties. In the present study five brands of marketed SR tablets of Aceclofenac were taken and subjected to evaluate the different parameters as well as to perform the bio-equivalence study of the same tablets. The preformulation studies were carried out first. The drug showed absorption maxima at 275 nm in phosphate buffer pH 7.4. The linearity were observed between 1-10 mcg/nm. The FTIR spectra of Aceclofenac also comply with the standard monographs and principle peaks were shown. After the preformulation studies of the drug, the tablets were evaluated for the uniformity of weight, hardness, friability, drug content and in-vitro release study. All tablets were found within the acceptance criteria as per the official standards. The in-vitro dissolution test was carried out for 12 hours using USP-2 (paddle) dissolution test apparatus at 50 rpm. All tablets have shown the excellent in-vitro release profile. The all marketed tablets released the drug in a sustained pathway. The Af_4 marketed formulation showed the maximum cumulative drug release. On the basis of in-vitro release study, the all marketed formulation of aceclofenac were found to be bio-equivalent.

KEYWORDS: Sustained release tablet, Aceclofenac tablets, NSAIDs.

INTRODUCTION

Sustained release drug therapy

Sustained release dosage forms are designed to release a drug at a predetermined rate by maintaining a constant drug level for a specific period of time with minimum side effects. In recent years, focus on the development of controlled release drug delivery systems has been increased.[1,2] SR of drugs in gastrointestinal tract following oral administration is not affected by the absorption process. SR oral dosage forms have become more important in therapy as a means of reduced dosing frequency, hence potentially improving patient compliance and consequently efficacy.[3] Non-steroidal anti-inflammatory drugs (NSAIDs) are considered to be the first-line drugs in the symptomatic treatment of rheumatoid arthritis, osteoarthritis and spondylitis, Aceclofenac is one of them[4]. Among the various routes of drug delivery oral route is most

widely used route of drug delivery. But conventional dosage form offers few limitations which could be resolved by modifying the existing dosage form[5,6].

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used for their anti-inflammatory, analgesic, and antipyretic effects, which are exerted by cyclooxygenase (COX) inhibition.[7] Aceclofenac is a non-steroidal anti-inflammatory drug (NSAID). Aceclofenac exhibits very slight solubility in water and aqueous fluids. It is freely soluble in acetone.[8] Aceclofenac and 4-hydroxy aceclofenac are the conversion products of aceclofenac and major metabolites in human. However, for rats diclofenac is the major metabolite[9]. At therapeutic doses, these drugs can also have diverse effects on osteoblasts, inhibiting their proliferation and differentiation and modulating their antigenic profile or some of their immune functions, e.g., phagocytic capacity.[10]

MATERIAL AND METHOD

Marketed formulation of aceclofenac

S.No.	Brand Name	Formulation	Manufacturers
1.	Aceclo SR 200 mg	Tablet	Aristo pharmaceutical pvt.ltd.
2.	Aroff SR 200mg	Tablet	Unichem Laboratories ltd.
3.	Aceclowoc SR 200mg	Tablet	Wockhardt ltd.
4.	Topnac SR 200mg	Tablet	Systopic Laboratories pvt. Ltd.
5.	Vriace 200mg	Tablet	Vrinda life

Method

Preformulation Studies

The following preformulation studies of Aceclofenac were carried out.

I. Fourier Transform Infra-red(FTIR) spectroscopy
II. Loss on drying
III. Melting point determination
IV. Partition Coefficient
V. Calibration curve of drug

Fourier transform infrared (FTIR) spectral studies

Infrared spectra of the Aceclofenac were recorded on a FT-IR spectrophotometer (Agilent Technologies, India)Measurements were attempted with the accumulation of 3 scans and a resolution of 4 cm^{-1} over the range of 400 to 4000 cm^{-1}.

The technique is based upon the simple fact that a chemical substance shows marked selective absorption in infrared region. After absorption of IR radiations, the molecules of a substance

vibrate at many rate of vibration, giving rise to closed packed absorption bands which was called an IR absorption spectrum which may extend over a wide wavelength range.

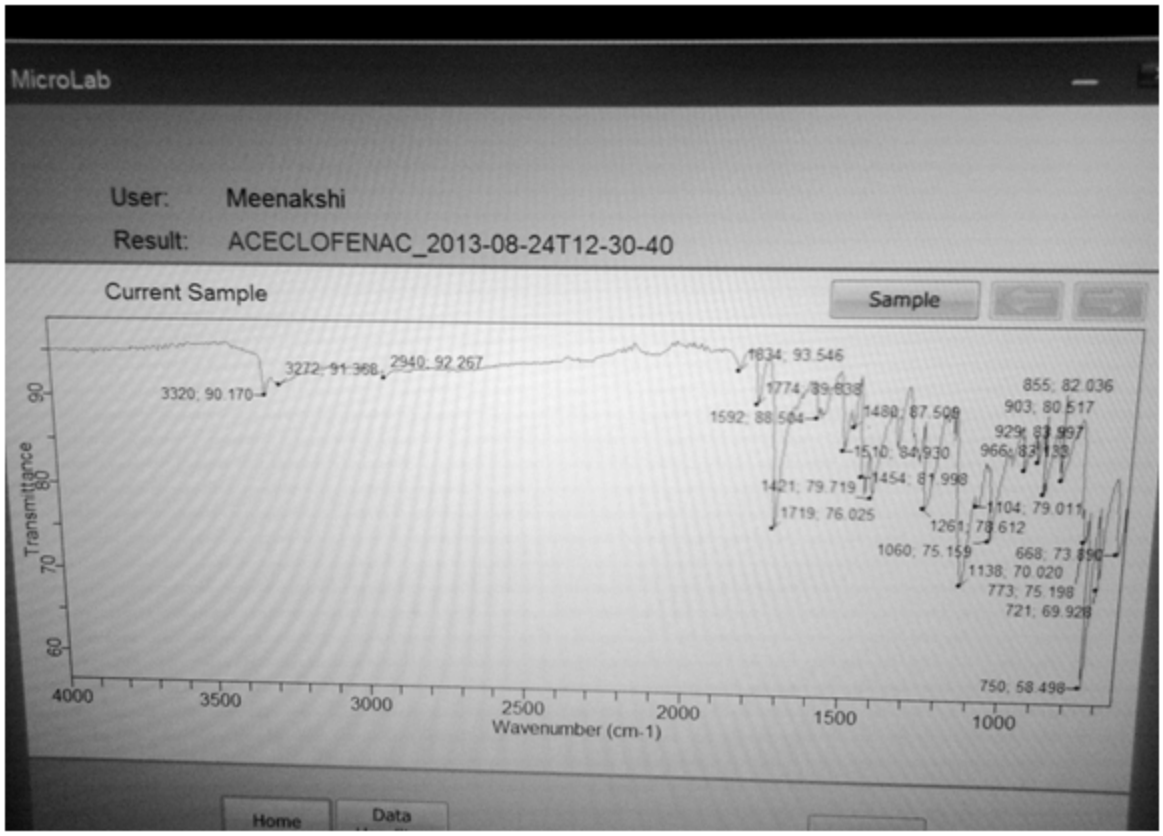

Fig. 1. FTIR spectra of Aceclofenac

Functional group	Range (cm-1)	Drug sample (cm-1)	Reference
C-H	3200-2500	2940	I.P. monographs
C=C	1600-1400	1592	I.P. monographs
N-H	3700-3000	3320	I.P. monographs
C-Cl	800-600	773	I.P. monographs
C-N	1600-1400	1480	I.P. monographs
C=O	1700-1600	1719	I.P. monographs

Table 1.IR peak range of Aceclofenac

Loss on drying

The Test is designed to measure the amount of water and volatile matters in a sample when the sample is dried under specified conditions.1.0 g of drug was weighed accurately. It was placed in

a tray dryer (Oven) at 105°c for 4 hrs. After 4 hrs. The drug was reweighed. The LOD of drug was fond to be 0.012 %.

Melting point determination

Melting point of the aceclofenac was determined by using digital melting point apparatus. (MEPA, Lab India apparatus).

The melting point was found to be 148.7.

Partition Coefficient

The partition coefficient of Aceclofenac was determined by using n-octanol and water (both are immiscible solvents).100 mg of drug was weighed and transferred to a volumetric flask containing 20 ml n-octanol and 20 ml water. The flask was then closed with the stopper and shaken on the magnetic stirrer. After 24 hrs. Both phases were separated by the separating funnel. Then both samples were taken and absorbance was determined by the UV at 275 nm. The partition coefficient was found to be 1.84.the amount of drug was found more in octanol than water. So we can say the drug is lipophilic.

Method for the Estimation of Aceclofenac

A spectrophotometric method based on the measurement of absorbance at 275nm in phosphate buffer of pH 7.4was used in this study for the estimation aceclofenac.

Preparation of calibration curve for aceclofenac

50 mg of aceclofenac was transferred to a 50 ml volumetric flask.then make up the volume with the phosphate buffer (pH 7.4).mixed well and then 10 ml of this solution was further diluted with the same buffer to make the volume upto 100 ml.After that different dilution were prepared (as 1,2,3,4,5,6,7,8,9,10 µg/ml) and examined by using U.V. spectrophotometer(Carywin UV,Agilent Technologies).the ƛ max was first determined and then absorbence of different dilution was determined at 275 nm.

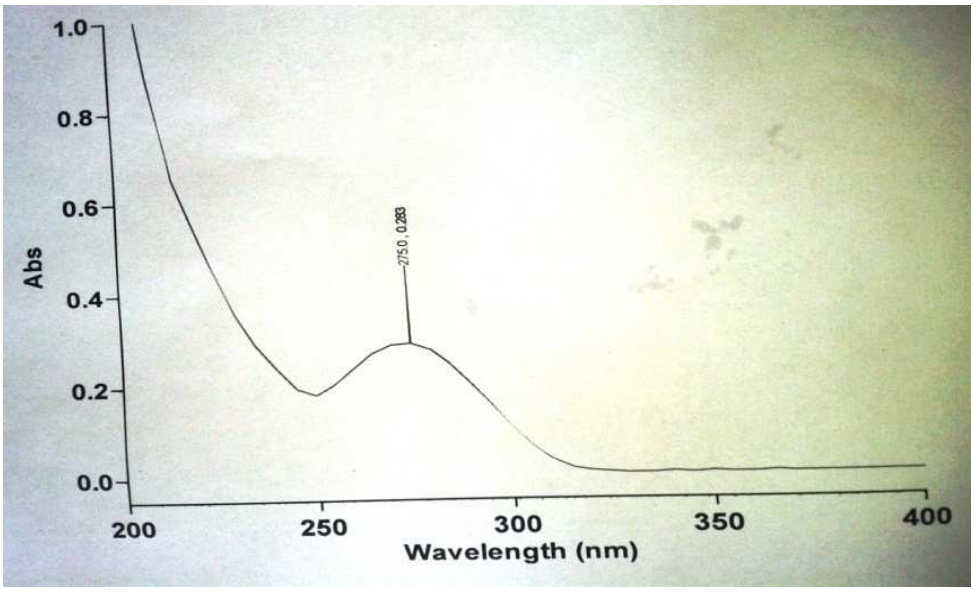

Fig. 2. ƛ Max of the aceclofenac

Conc. (µg/ml)	Absorbance
1	0.0878
2	0.1576
3	0.2208
4	0.2903
5	0.3630
6	0.4238
7	0.4980
8	0.5628
9	0.6340
10	0.7084

Table 2. Calibration curve of aceclofenac

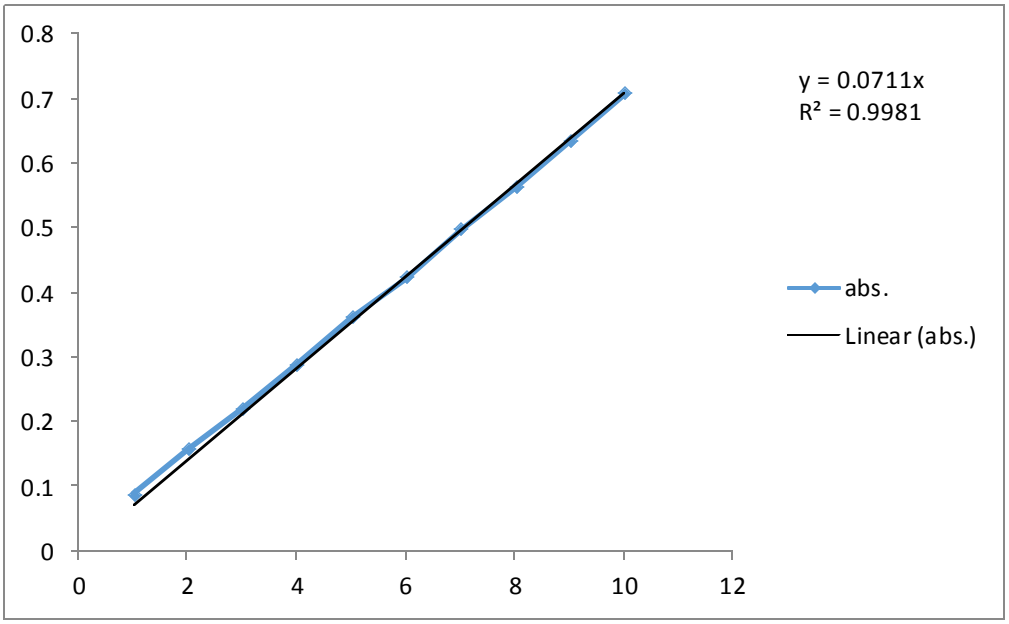

Fig. 3. Calibration curve of aceclofenac.

EVALUATION OF MARKETED FORMULATION

S. No.	Brands name (Aceclofenac)	Marketed formulation code	Strength
1	ACECLO SR	A f_1	200 mg
2	AROFF SR	A f_2	200 mg
3	ACECLOWOC SR	A f_3	200 mg
4	TOPNAC SR	A f_4	200 mg
5	VRIACE SR	A f_5	200 mg

Table 3. Marketed tablets Of Aceclofenac

Evaluation Parameter of Aceclofenac SR tablets

Weight variation

Hardness

Friability

Drug content

In-vitro dissolution study

Weight variation: Twenty tablets were selected at random and average weight was determined. The individual tablets were weighed and compared with average weight. Not more than 2 of the individual weights deviate from the average weight of tablets by more than 5%. As per Indian Pharmacopoeia, 2010.

Average weight of a tablet (mg)	Percentage deviation (%)
80 mg or less	10
>80 mg and < 250 mg	7.5
250 mg or more	5

Table 4. Percentage deviation of doses form

S. No.	Brand's code	Average weight (gm.)	Acceptance Criteria (%)	Observation	Weight variation (%)
1	A f_1	0.341	5	+0.358 , -0.324	+2.63 , -3.22
2	A f_2	0.393	5	+0.413 , -0.373	+1.78 , -3.30
3	A f_3	0.328	5	+0.344 , -0.312	+3.65 , -2.43
4	A f_4	0.412	5	+0.432 , -0.392	+1.94 , -2.90
5	A f_5	0.302	5	+0.317 , -0.287	+2.64 , -3.97

Table 5. Weight variation of Aceclofenac (200mg)

Hardness of Tablet

Tablet hardness was measured by using Pfizer hardness tester. From each marketed formulation six tablets were measured for the hardness and average of six values.

S. No	Marketed formulation code	Hardness (kg)
1	Af_1	10.2
2	Af_2	9.0
3	Af_3	5.5
4	Af_4	10.8
5	Af_5	5.4

Table 6. Hardness of aceclofenac tablets

Friability of Uncoated tablets

The friability of tablets was determined using Veego friability Apparatus. Ten Tablets were weighed accurately and transferred in friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up 100 revolutions. Than tablets were weighted again. The friability was calculated as the percentage weight loss.

% Friability = (W1 – W2) x 100/W1

Where

W1 = Initial weight of the 10 tablets.

W2 = Final weight of the 10 tablets after testing

% friability of the tablets less than 1% are acceptable

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S. No.	Marketed formulation code	Before friability weight	After friability weight	% friability
1	Af_1	3.40 gm.	3.40 gm.	0 %
2	Af_2	3.36 gm.	3.36 gm.	0 %
3	Af_3	3.26 gm.	3.26 gm.	0 %
4	Af_4	4.13 gm.	4.12gm	0.2%
5	Af_5	3.01gm	3.01gm	0 %

Table 7. Friability of aceclofenac tablets

Estimation of drug content

20 tablets were weighed accurately and powdered. The powder was equivalent to 100mg of aceclofenac was transferred to 100mL volumetric flask and made the volume to mark with phosphate buffer pH 7.4.Then filtered through Whatman filter paper No. 41.5 mL of the filtrate was transferred into a 50 mL. Volumetric flask and made the volume up to the mark with buffer solution. Aliquots of the sample were removed and diluted to 10 mL. With buffer solution. The absorbance was determined at 275 nm against the buffer solution as blank. The different marketed formulations of different manufacturers were used for study.

S. No.	Aceclofenac Brand's code	Drug content (%)
1.	Af_1	97.60
2.	Af_2	98.27
3.	Af_3	98.48
4.	Af_4	97.64
5.	Af_5	98.75

Table 8. Drug content of Aceclofenac

Determination of in-vitro dissolution

The dissolution study of different brand tablets was carried out using USP type 2 Dissolution apparatus (paddle type).The test was carried out for 12 hours. For the first two hours the .1 N Hcl (pH. 1.2) was used as the dissolution medium and for 3 to 12 hrs. 7.4 pH phosphate buffer used as dissolution medium. The bath temperature of the dissolution apparatus (DS 8000, Lab India) was maintained 37±.5 .The complete test was done at the 50 rpm. The time interval was taken as 0, 1,2,3,4,5,6,7,8,12 hrs. And the 5 ml sample was taken after each time interval respectively. Each sample was filtered (through Whatman filter paper 41) and diluted 10 times with dissolution media and the absorbance was checked out using UV spectrophotometer (Cary 60, Agilent technology) at 275 nm.

Time (hrs.)	Abs.	Conc. (mcg/ml)	Amt. in 5ml (mg)	Amt. in 900ml(mg)	C.R. (mg)	%CR
0	0	0	0	0	0	0
1	0.0234	3.295775	0.016479	2.966197	2.966197	1.483099
2	0.026	3.661972	0.01831	3.295775	3.312254	1.656127
3	0.173	24.3662	0.121831	21.92958	21.94789	10.97394
4	0.2842	40.02817	0.200141	36.02535	36.14718	18.07359
5	0.3987	56.15493	0.280775	50.53944	50.73958	25.36979
6	0.482	67.88732	0.339437	61.09859	61.37937	30.68968
7	0.6208	87.43662	0.437183	78.69296	79.03239	39.5162
8	0.7387	104.0423	0.520211	93.63803	94.07521	47.03761
12	0.9458	133.2113	0.666056	119.8901	120.4104	60.20518

Table 9. In-vitro release study of Aceclo SR (Af_1):

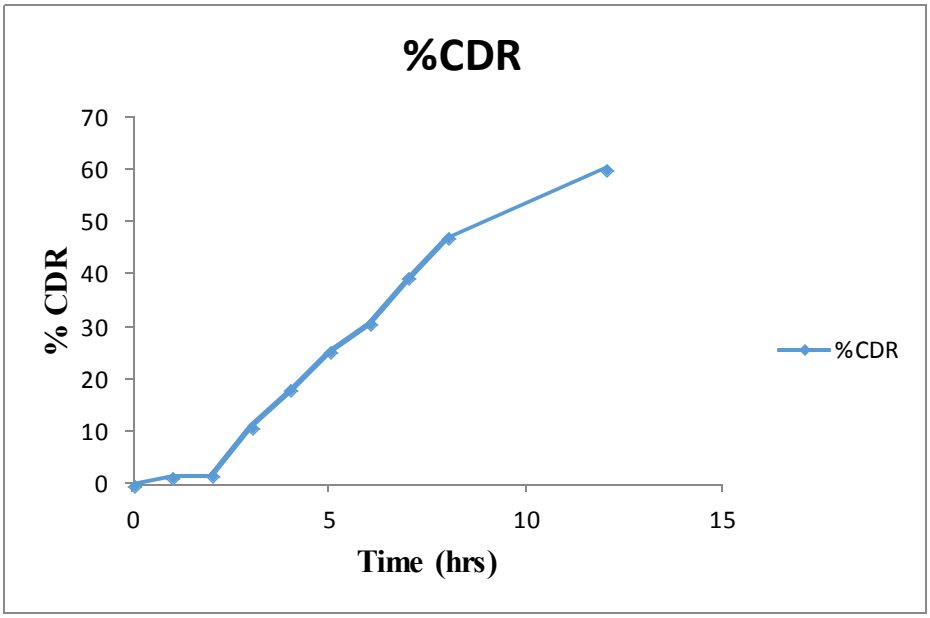

Fig. 4. Dissolution profile of Af_1

Time (hrs.)	Abs.	conc. (mcg/ml)	Amt. in 5ml (mg)	Amt. in 900ml (mg)	CR (mg)	% CR
0	0	0	0	0	0	0
1	0.0234	3.295775	0.016479	2.966197	2.966197	1.483099
2	0.0598	8.422535	0.042113	7.580282	7.596761	3.79838
3	0.1138	16.02817	0.080141	14.42535	14.46746	7.233732
4	0.2368	33.35211	0.166761	30.0169	30.09704	15.04852
5	0.3678	51.80282	0.259014	46.62254	46.7893	23.39465
6	0.4932	69.46479	0.347324	62.51831	62.77732	31.38866
7	0.5185	73.02817	0.365141	65.72535	66.07268	33.03634
8	0.6798	95.74648	0.478732	86.17183	86.53697	43.26849
12	0.9438	132.9296	0.664648	119.6366	120.1154	60.05768

Table 10. In-vitro release study of Aroff SR (Af_2)

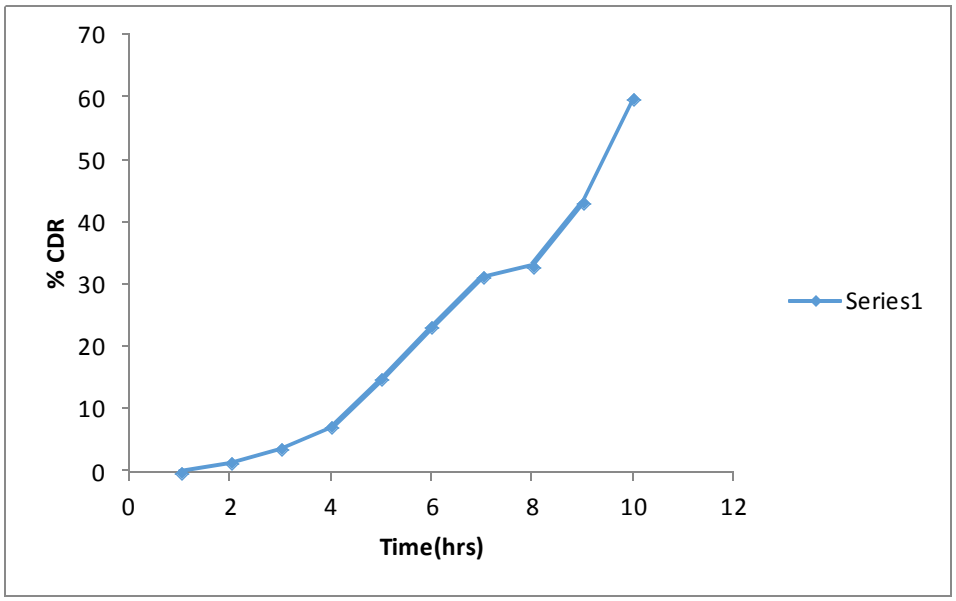

Fig. 5. Dissolution profile of Af_2

Time (hrs.)	Abs.	Conc. (mcg/ml)	Amt. in 5ml (mg)	Amt .in 900ml (ml)	CR (mg)	%CR
0	0	0	0	0	0	0
1	0.0293	4.126761	0.020634	3.714085	3.714085	1.857043
2	0.0373	5.253521	0.026268	4.728169	4.748803	2.374401
3	0.1554	21.88732	0.109437	19.69859	19.72486	9.86243
4	0.2608	36.73239	0.183662	33.05915	33.16859	16.5843
5	0.3568	50.25352	0.251268	45.22817	45.41183	22.70592
6	0.472	66.47887	0.332394	59.83099	60.08225	30.04113
7	0.5839	82.23944	0.411197	74.01549	74.34789	37.17394
8	0.7132	100.4507	0.502254	90.40563	90.81683	45.40842
12	0.9742	137.2113	0.686056	123.4901	123.9924	61.9962

Table 11. In-vitro release study of Aceclowoc SR (Af_3)

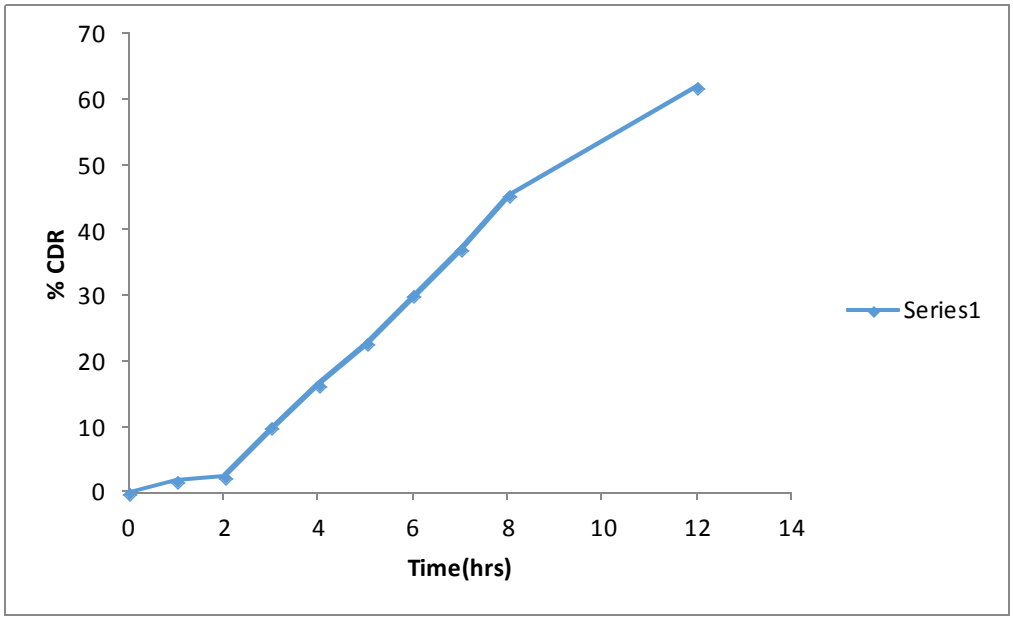

Fig. 6. Dissolution profile of Af_3

Time (hrs.)	Abs.	Conc. (mcg/ml)	Amt. in 5ml (mg)	Amt. in 900ml (mg)	CR (mg)	% CR
0	0	0	0	0	0	0
1	0.0198	2.788732	0.013944	2.509859	2.509859	1.25493
2	0.0276	3.887324	0.019437	3.498592	3.512535	1.756268
3	0.1178	16.59155	0.082958	14.93239	14.95183	7.475915
4	0.2496	35.15493	0.175775	31.63944	31.72239	15.8612
5	0.3378	47.57746	0.237887	42.81972	42.99549	21.49775
6	0.4877	68.69014	0.343451	61.82113	62.05901	31.02951
7	0.6039	85.05634	0.425282	76.5507	76.89415	38.44708
8	0.7124	100.338	0.50169	90.30423	90.72951	45.36475
12	0.9557	134.6056	0.673028	121.1451	121.6468	60.82338

Table 12. In-vitro release study of Topnac SR (Af_4)

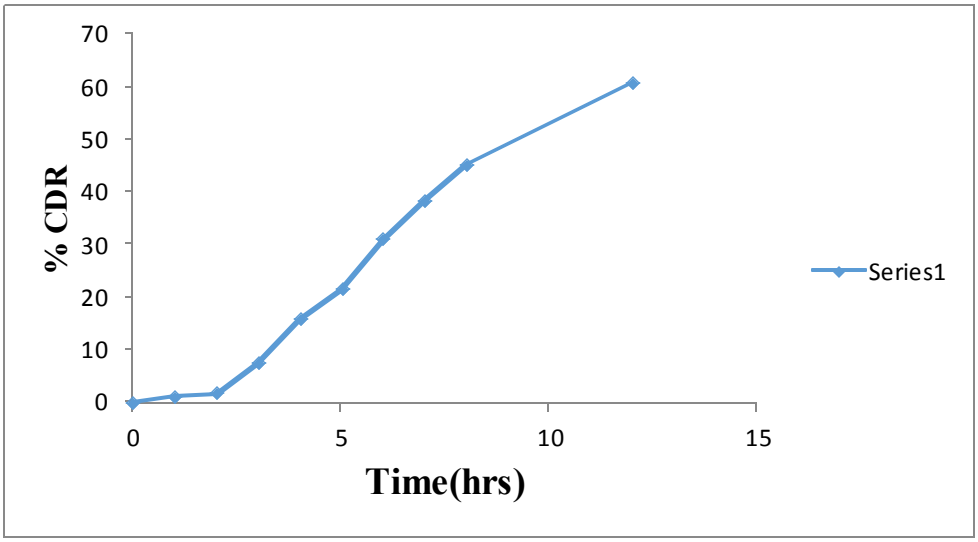

Fig 7. Dissolution profile of Af_4

Time (hrs.)	Abs.	Conc. (mcg/ml)	Amt. in 5ml (mg)	Amt. in 900ml (mg)	C.R. (mg)	% CR
0	0	0	0	0	0	0
1	0.0284	0.4	0.002	0.36	0.36	0.18
2	0.031	0.43662	0.002183	0.392958	0.394958	0.197479
3	0.1285	18.09859	0.090493	16.28873	16.29092	8.145458
4	0.2639	37.16901	0.185845	33.45211	33.54261	16.7713
5	0.3948	55.60563	0.278028	50.04507	50.23092	25.11546
6	0.5263	74.12676	0.370634	66.71408	66.99211	33.49606
7	0.6802	95.80282	0.479014	86.22254	86.59317	43.29658
8	0.7409	104.3521	0.521761	93.9169	94.39592	47.19796
12	0.9285	130.7746	0.653873	117.6972	118.2189	59.10947

Table 13. In-vitro release study of Vriace SR (Af_5)

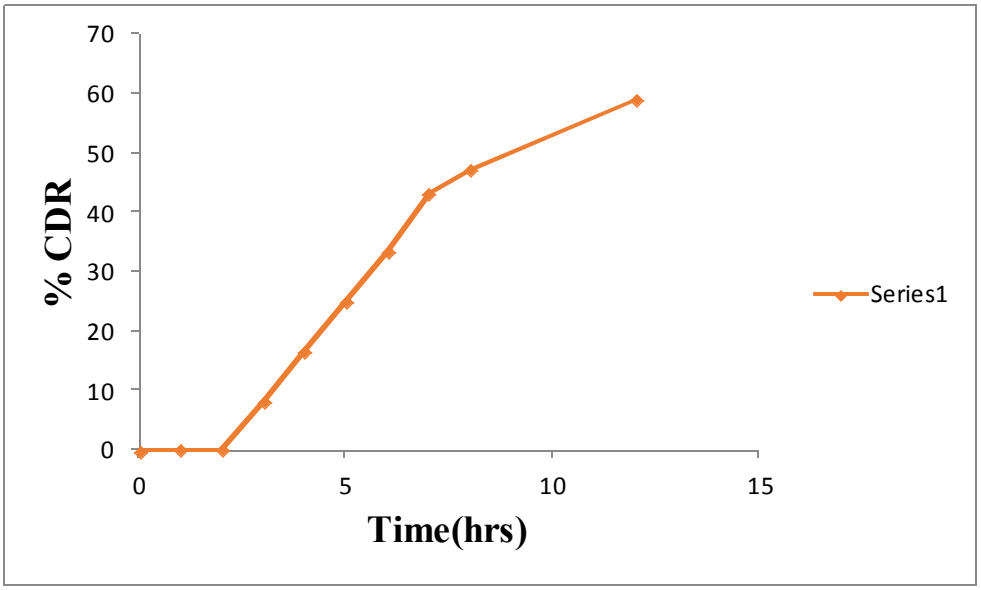

Fig. 8. Dissolution profile of Af_5

RESULT AND DISCUSSION

Preformulation Studies

Aceclofenac		
Property Studies	Results	Inference
Colour	White	crystalline in nature
Analytical Method	UV Visible Spectroscopy λ_{max} 275nm ,slope 0.071	R^2= 0.998
Melting range	148.7° C	Thermostable
Partition Coefficient	1.84	Lipophilic
Loss On Drying	0.012%	Within limit as given in I.P. (0.5%)
IR Spectroscopy	Principal Peaks shown	Complies with monograph

Table 14. Result of preformulation studies of Aceclofenac

Result of Preformulation study are shown in the above table, which are very closely to the actual and standard values of different Preformulation studies of the pure Aceclofenac API. The Preformulation study of any drug is very important tool for the further investigation of the sample. The Preformulation study of aceclofenac API is very useful for the further evaluation parameters of the tablets.

Evaluation studies

S.NO	Brands codes	Weight variation (%)	Hardness (kg/cm^2)	Friability (% loss)	Drug content (%)
1	Af_1	+2.63 , -3.22	10.2	0%	97.60
2	Af_2	+1.78 , -3.30	9.0	0%	98.27
3	Af_3	+3.65 , -2.43	5.5	0%	98.48
4	Af_4	+1.94 , -2.90	10.8	0.2%	97.64
5	Af_5	+2.64 , -3.97	5.4	0%	98.75

Table 15. Evaluation parameter of marketed formulation Results

The all brand's tablets were evaluated for the determination of weight variation, hardness and friability (only for uncoated tablet of brand Af_4) and after evaluation the different parameters was determined successfully and the resulted value of different parameters are shown in above table respectively.

Dissolution of Aceclofenac

The comparative dissolution study of various marketed formulation was carried out. All the marketed formulation showed efficient drug release profile. The release profile of the all brand's tablets are shown in below given table. The release of drug was shown as % cumulative drug release (%CDR) with respect to time interval (hrs.).The resulted graph was shown below to describe the in-vitro drug release of all brand's tablets.

Time (hrs.)	Af_1	Af_2	Af_3	Af_4	Af_5
0	0	0	0	0	0
1	1.483099	1.483099	1.857043	1.25493	0.18
2	1.656127	3.79838	2.374401	1.756268	0.197479
3	10.97394	7.233732	9.86243	7.475915	8.145458
4	18.07359	15.04852	16.5843	15.8612	16.7713
5	25.36979	23.39465	22.70592	21.49775	25.11546
6	30.68968	31.38866	30.04113	31.02951	33.49606
7	39.5162	33.03634	37.17394	38.44708	43.29658
8	47.03761	43.26849	45.40842	45.36475	47.19796
12	60.20518	60.05768	61.9962	60.82338	59.10947

Table 16. Percentage drugs release profile studies of all brands

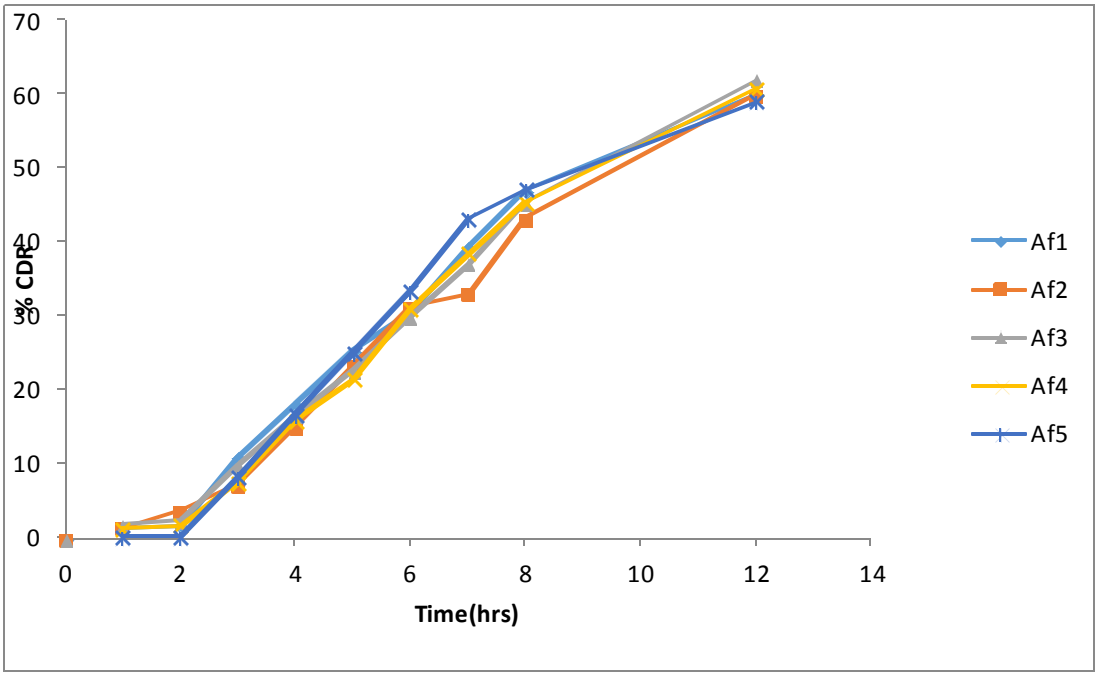

Fig.9. In-vitro release profile of all marketed formulations.

The in –vitro drug release kinetics of the all marketed tablets was shown in the above figure.All marketed tablets release the drug in a sustained manner.The % cumulative drug release were found as 60.20 , 60.05 ,61.99 ,60.82 and 59.10 for the Af_1 ,Af_2 ,Af_3 ,Af_4 and Af_5 respectively.The maximum drug release was found for Af_3 marketed formulation.

CONCLUSION

In the present study we evaluated five marketed SR tablets of aceclofenac. The purpose of this study was to determine different evaluation parameters as well as the drug release kinetics of the SR tablets. This type of study is also sometimes referred as bio-equivalence study. After performing this study we conclude that all brand tablets are of good quality. The tablets were evaluated for different parameters and all of them are under the standard acceptance criteria or limit for the different parameters. after performing different evaluation parameters we conclude that all tablets are under the acceptable limit for weight variation test, no friability was found except Af_4 brand tablets, hardness was also determined successfully and all brand's tablets shown efficient drug release as well as in a sustained release manner. The maximum drug release was shown by the Af_3 brand and minimum was shown by the Af_5 brand. Thus we can say that all the tablets are effective for the use as well as to release the drug in a sustained manner. Or in other words on the basis of drug release profile, we can say that all the tablets are bio-equivalent.

REFERENCES

1. Soni T, et al. MAY 2008, Development of Discriminating Method for Dissolution of Aceclofenac Marketed Formulations**, *Dissolution** Technologies* |, 31-35.
2. Kumar K.P.S.et al. 2010, Innovations in Sustained Release Drug Delivery System and Its Market Opportunities, *Journal of Chemical and Pharmaceutical Research,* 2010, 2(1): 349-360.
3. Chakraborty Santanu et al. 2012 Preparation and preclinical evaluation of aceclofenac loaded pectinate mucoadhesive microspheres", *Drugs and Therapy Studies*; volume 2, 36-42.
4. Tripathi.K.D, Essentials of medical pharmacology, 6th Edition, 2009, J.P. Publication 184-195.
5. Chien YW. Oral drug delivery systems innovel drug delivery pharmaceutical technology. Marcel Dekker Inc. New York.1992; 139-52.
6. Qiu Y, Zhang G. Research and development aspects of oral controlled release dosage forms. Handbook of pharmaceutical controlled release technology. 1st Indian Ed. Replika press. New York. 2005; 465-503.
7. Axelsson, H., Lonnroth,€ C., Andersson, M., Lundholm, K., 2010. Mechanisms behind COX-1 and COX-2 inhibition of tumor growth in vivo. Int. J. Oncol. 37, 1143e1152.
8. Indian Pharmacopoeia. Vol. II. Delhi: Published by the Controller of Publication; 2007:681.
9. Sanchez, C., Mateus, M.M., Defresne, M.P., Crielaard, J.M., Reginster, J.Y., Henrotin, Y.E., 2002. Metabolism of human articular chondrocytes cultured in alginate beads. Longterm effects of interleukin 1beta and nonsteroidal anti-inflammatory drugs. J. Rheumatol. 29, 772–782.
10. De Luna-Bertos, E., Ramos-Torrecillas, J., García-Martínez, O., Díaz-Rodríguez, L., Ruiz, C., 2012. Effect of aspirin on cell growth of human MG-63 osteosarcoma line. Sci. World J. 2012 (2012), 1e6. http://dx.doi.org/10.1100/2012/834246.