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RESEARCH ARTICLE

COMPARATIVE *IN VITRO* EVALUATION OF ACECLOFENAC AND PARACETAMOL COMBINATION TABLETS MARKETED IN ANDHRA PRADESH

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ABSTRACT

Aceclofenac in combination with Paracetamol is now available in the market and indicated in pain, fever etc. These tablets manufactured and marketed by various multinational and local companies. In this study eight marketed brands of Aceclofenac & Paracetamol combination tablets have been evaluated using physicochemical properties and *in vitro* dissolution test with the object to assess bioequivalence and select a potent generic brand for reducing cost of the treatment. A simple high performance liquid chromatographic (HPLC) method was developed for the simultaneous determination of Aceclofenac & Paracetamol. The retention time of Aceclofenac & Paracetamol were found to be 4 ± 0.2 and 3 ± 0.2. The *in vitro* dissolution studies were performed in USP Dissolution Apparatus II using pH 6.8 phosphate buffer solutions separately for 45 minutes. The amount of Aceclofenac & Paracetamol released at different time intervals were estimated by HPLC method. *In vitro* dissolution of all the brands was satisfactory, the brand Spanac-p® showed higher drug release, respectively 79.32 % of Aceclofenac & 95.04 % Paracetamol within 45 minutes. The f1 and f2 values were in the range of 5 – 13 and 64 – 86 respectively. This suggests that release of Aceclofenac & Paracetamol from all brands were similar with reference. Therefore it is evident that test products were bioequivalent to the reference product and the brand Spanac-p ® could be used as a best generic substitute which reduce the dose and cost of the treatment.

INTRODUCTION

Paracetamol is one of the most popular over the counter drugs. It has analgesic and antipyretic properties with weak anti inflammatory activity and it is used in the symptomatic management of moderate pain and fever. It could also be used in the management of more severe pain like pain in cancer in combination with other drugs (Kalakuntla *et al.*, 2010). Aceclofenac, [(2-{2,6-dichlorophenyl)amino} phenylacetooxy acetic acid] is a non-steroidal anti-inflammatory drug (NSAID) indicated for the symptomatic treatment of pain and inflammation with a reduced side effect profile, especially gastro intestinal events that are frequently experienced with NSAID therapy. At present, beside paracetamol, a new paracetamol / aceclofenac formulation is designed to deliver faster dissolving and more quickly absorbed drug product.

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Paracetamol is often prescribed with aceclofenac for greater patient acceptability, increased potency, multiple activity, fewer side effects and quick relief (Liu *et al.*, 2011). Reducing pharmaceutical care cost with generic drugs while maintaining quality of health care is an important societal goal in developed and developing countries. Health care providers and policy makers also support the practice of prescribing low cost generic products principally for economic reasons. Generic drugs are less expensive than equivalent innovator brands because generic manufacturers do not have to conduct costly clinical trials to test the safety and effectiveness of a generic version of a drug that has been safely and effectively used for several years. It is therefore important that generics substitutes are analyzed for their physicochemical and biopharmaceutical equivalence, strength, quality, purity, and releasing profile of active ingredient in comparison to the innovator drug (S.M. Ashraful Islam *et al.*, 2011). The study was conducted to assess the comparative *in-vitro* quality control parameters through the evaluation of weight variation, hardness, friability, disintegration time and dissolution profile between the

commercially available tablet brands of Aceclofenac & paracetamol combination in Andhrapradesh.

MATERIALS AND METHODS

Aceclofenac & Paracetamol Combination Tablets were purchased from local market at Andhra Pradesh. Aceclofenac and Paracetamol were purchased from Yarrow chem Products, Mumbai. NaOH from S.D. Fine Chem. Ltd, Mumbai, HCl and Potassium Dihydrogen Phosphate were obtained from Qualigens Fine chem, Mumbai and all other ingredients used were of analytical grade.

Experimental method

Eight brands of tablets containing Aceclofenac & Paracetamol as main active ingredients was selected and procured from the local market in Andhra Pradesh. All the brands contained label strength of 100 mg Aceclofenac and 325 mg Paracetamol. The physicochemical equivalence of eight brands of tablets was determined through the evaluation of both official and non-official standards. All tests were performed within product expiration dates. The strength of Aceclofenac and Paracetamol, other details were given in Table 1.

Invitro evaluation of tablets

The physicochemical equivalence of eight brands of tablets were determined through the evaluation of both official and non-official standards according to the USP pharmacopoeia including uniformity of weight, friability, hardness, disintegration, dissolution rate and drug content (Osadebe and Akabogu, 2004).

Visual Inspection: The shape and color of the different brands of tablets were examined visually.

Thickness and Diameter: Three tablets from each brand were used for thickness determination. Thickness & diameter of each tablet was measured in mm using Vernier Calipers (Mitutoyo Dial, Mitutoyo, Japan). The mean and standard deviation values were calculated and reported.

Hardness Test: The crushing strength of the tablets was determined using hardness tester (Lab India). Sample tablets (10) of each brand were taken, a tablet was placed between the spindle of the Lab India hardness tester machine until the tablet breaks and the pressure required to break the tablet was then read off the machine and recorded (Arcot, Chan, *et al.,* 2011).

Table 1. Composition of Commercial Tablets

Brand Name	Aceclofenac & Paracetamol (mg)	Manufacturer	Batch No.	Mfg – Exp Date
Aceclobak-p (Reference)	100 325	May & Baker pharmaceuticals LTD	SHT6018	2016-2018
Acesun forte	100 325	South Healthcare Pvt LTD	T-160404	2016-2018
Dolosaid	100 325	Univentis Medicare Ltd	AB466017	2016-2019
Arcec-p	100 325	Suraksha pharma PVT.LTD	ADR30816	2016-2019
PGI	100 325	Vanguard Therapeutics Ltd	CPT52	2016-2018
Spanac-p	100 325	Spa health care Pvt. Ltd.	SHR81015	2015-2018
XRIF-P	100 325	Saitech medicare Pvt.Ltd	SGT-1923	2016-2018
Movexxplus	100 325	Cipal LTD	AEP5093	2015-2017

Analytical tests for API

Melting Point Determination: Melting point determination of pure drugs Aceclofenac and Paracetamol was done; as it is a first indication of purity of the sample. The presence of small amount of impurity can be detected by lowering as well as widening in the melting point range.

Identification of Pure Drug: FTIR spectroscopy was used for identification of pure drugs Aceclofenac and Paracetamol.

Determination of Isobestic Point: An accurately weighed 10 mg of Aceclofenac & Paracetamol was transferred in a 100 ml volumetric flask. To the flask pH 6.8 phosphate buffer solution was added in small proportion so as to dissolve Aceclofenac & Paracetamol. The volume was made up to 100 ml with pH 6.8 phosphate buffer solution to get a concentration of 100µg/ml. 20 µg/ml solution of Aceclofenac & Paracetamol was prepared in dilution. The resulting solutions were scanned in UV-Vis spectrophotometer from 400- 200 nm to determine the isobestic point (Imad and Ahmed, 2010).

Friability Test: Twenty tablets of each brand were weighed and subjected to abrasion using a Roche friabilator at 100 revolutions for 4 min. The tablets were dedusted and weighed again then percent of weight loss was recorded. The friability of the tablets were then calculated using the following expression (Arcot, Chan, *et al.,* 2011).

% Friability = [(Initial weight – Final weight)/Initial weight]×100

Weight Uniformity: Total 20 tablets from each brand were weighed individually using a digital analytical balance. The average weight was determined and the percentage (%) deviation of the individual tablets from the mean was determined (Pamula, Surender *et al.,* 2010).

$$\% \text{ Weight variation} = \frac{(\text{Average weight} - \text{Individual Weight})}{\text{Individual Weight}} \times 100$$

Disintegration Test: Tablet disintegration was determined at 37 °C using (Lab India) disintegration apparatus. The

disintegration time of randomly selected six tablets of each brand was determined in distilled water. The disintegration time was taken to be the time no granule of any tablet was left on the mesh (Pamula, Surender *et al.,* 2010).

HPLC method

The content of active ingredient (assay) for each of the six brands was determined by HPLC method, using the Waters HPLC equipment. The HPLC method used was a reverse phase chromatographic technique which was developed and validated by Kar and Choudhury (2009). The pump was set up to deliver a mobile phase which was filtered and degassed automatically by the in-built degasser of the HPLC equipment. After the chromatographic conditions were set, the instrument was stabilized to obtain a steady base line.

Table 2. Chromatographic conditions

Parameters	Conditions
HPLC Instrument	Waters- 515
Column	C – 18 ODS
Mobile Phase	Acetonitrile and Phosphate buffer (pH 6.8)
Ratio	50 : 50
Flow Rate	1 ml / min
Wavelength	280 nm
Injection volume	20 µl
Run time	10 min
Column Temperature	37^{o}C ± 0.5^{o}C

Optimised Chromatographic conditions: Acetonitrile of volume 500 ml and 500 ml phosphate buffer (pH 6.8) were measured with a measuring cylinder into a 1000 ml standard volumetric flask and mixed thoroughly to obtain the specified ratio of 50: 50 of acetonitrile and phosphate buffer (pH 6.8) respectively (Kar and Choudhury, 2009). because it was found that it ideally resolve the peaks with retention time (Rt) ACL and PAC at 3 ± 0.2 and 4 ± 0.2 min respectively and the same is shown in Fig Wavelength was selected by scanning all standard drugs over a wide range of wavelength 200 nm to 400 nm. Both the components show reasonably good response at 280 nm.

Calibration curve: Standard stock solution of Aceclofenac and Paracetamol with concentration of 100 µg/ml was prepared separately in the mobile phase. Appropriate aliquots were pipette out from the standard stock solution in to a series of 10 ml volumetric flasks. The volume was made up to the mark with the mobile phase to get a set of solutions having the concentration range of 5, 10, 15, 20 and 25 µg/ml for Aceclofenac and Paracetamol. Each solution was then filtered using sintered glass filter. The samples were injected into an injector of liquid chromatography and the chromatogram for each injection was then recorded. A calibration curve of peak area against concentration was plotted, and the regression equation and correlation coefficient was determined.

Drug content (assay) estimation: Ten tablets from each brand was finely powdered and powder equivalent to 100 mg Aceclofenac and 325 mg of Paracetamol was accurately weighed and transferred to 100 ml volumetric flasks separately containing 50 ml of mobile phase solution. The flasks were shaken thoroughly to get uniform solution. The powder mixture was dissolved in the mobile phase with the aid of sonication and then made up to the 100 ml mark with the mobile phase. The solution was filtered through whatman filter paper and from the above filtrate, 1 ml was taken in a 10 ml volumetric flask and volume was made up to the mark with mobile phase, the solution was then filtered using sintered glass filter. After setting the chromatographic conditions and stabilizing the instrument, the sample solution was injected at flow rate of 1ml/min and a chromatogram was recorded. The average peak area and calibration curve were then used to calculate the amount of drug present (Kar and Choudhury, 2009).

Dissolution Test: The dissolution test was undertaken using tablet dissolution apparatus - 2 (Labindia, Mumbai) and 6 tablets of each brand. The medium phosphate buffer pH 6.8 was maintained at 37 ± 0.5°C. In all the experiments, 5 ml of dissolution sample was withdrawn at 0, 10, 20, 30 and 45 min and replaced with equal volume to maintain sink condition. Samples were filtered and assayed by HPLC method. The concentration of each sample was determined from a calibration curve obtained from pure drugs (Kar and Choudhury, 2009). Dissolution was carried out at following conditions:

$$\% \text{ Release of drug} = \frac{AT}{AS} \times \frac{\text{Sd. Dilution}}{\text{Test. Dilution}} \times \frac{900}{1} \times 1 \times 100$$

***In vitro* bioequivalence assessment**

The *in vitro* dissolution used to predict the *in vivo* bioequivalence. Therefore, *in vitro* tests can used to determine bioequivalence of products. The dissolution profile comparison is more precise than others to characterize the drug product. A simple model independent approach uses a difference factor (f1) and a similarity factor (f2) to compare dissolution profiles. The difference factor (f1) calculates the percent (%) difference between the two curves at each point and is a measurement to the relative error between the two curves:

$$f1 = \{[\Sigma n=1\ n \mid Rt - Tt \mid]/ [\Sigma t=1\ n\ Rt\ ]\} * 100$$

Where *n* is the number of time points, Rt is the dissolution value of the reference batch at time t, and Tt is the dissolution value of the test batch at time t.

The similarity factor (f2) is the logarithmic reciprocal square root transformation of the sum of squared error and is a measurement of the similarity in the percent (%) dissolution between the two curves.

$$f2 = 50 \bullet \log \{[1+ (1/n) \Sigma t=1n (Rt - Tt)2]-0.5 \bullet 100\}$$

For the curves to be considered similar, f1 values should be close to 0, and f2 values should be close to 100. Generally, f1 values up to (0-15) and f2 values greater than 50 (50-100) ensures sameness or equivalence of the two curves and thus, of the performance of the test and reference products (Moore and Flanner, 1996).

RESULTS AND DISCUSSION

Analytical tests for API

Melting Point Determination: After performing capillary method melting point of Aceclofenac and Paracetamol found

in range of 152 – 154°C and 167-170°C. The small widening in the melting point range indicates presence of impurity in the API.

Identification of Pure Drug: FT-IR spectroscopy was used to determine the functional group present in the pure drug sample. The spectrum of Aceclofenac are shown characteristic bands at 1769.53 cm-1 (C-O stretching), 1505.48 cm-1(skeleton vibration of aromatic C-C stretching for NH) 1341.80 cm-1 (O-H in plane bending), 1279.65 cm-1 (CN aromatic amine), 962.89 cm-1 (O-H out plane bending) and 779.93 cm-1 (out plane bending for N-H). The presence of above peaks confirms structure of pure drug Aceclofenac and the spectrum is as follows:

The FTIR spectrum of the pure drug Paracetamol displayed characteristic peaks at 3782.69, 3651.24, 3139.60, 1650.86 and 966.62 cm^{-1} due to stretching vibration bands of C – OH stretching, N-H bending, C=O stretching, C=C stretching and C - H stretching respectively. The presence of above peaks confirms structure of pure drug Paracetamol.

Inference: The spectra of drug and tablet formulations were showed a broad peak at the same place of the peak observed at the spectrum of pure drug has been observed, which indicated that the tablet contain pure drugs.

Determination of Isobestic Point: The Acclofenac and Paracetamol in pH 6.8 phosphate buffer solution were scanned

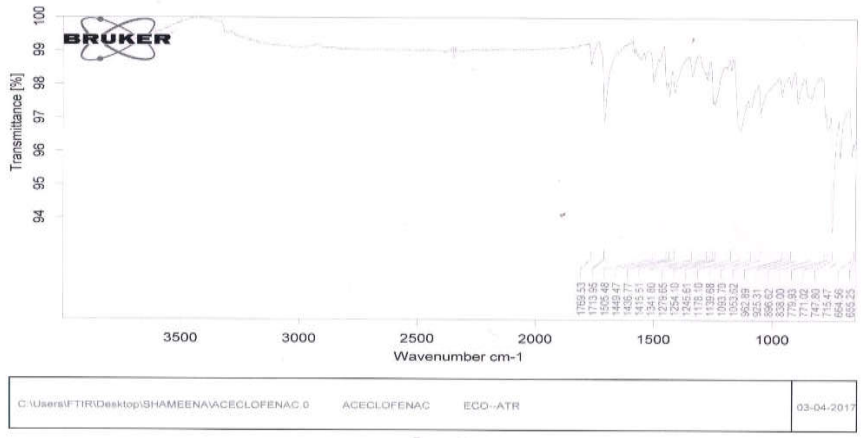

Fig. 1. IR Spectra of Aceclofenac

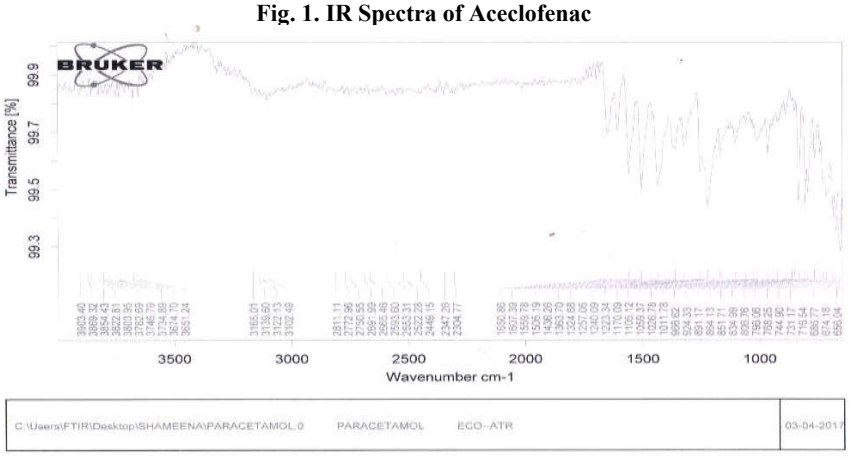

Fig. 2. IR Spectra of Paracetamol

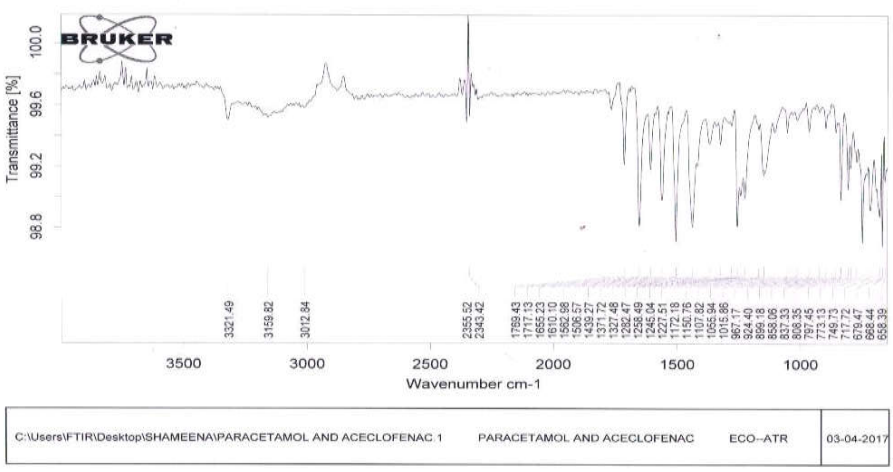

Fig. 3. IR Spectra of Aceclofenac and Paracetamol mixture

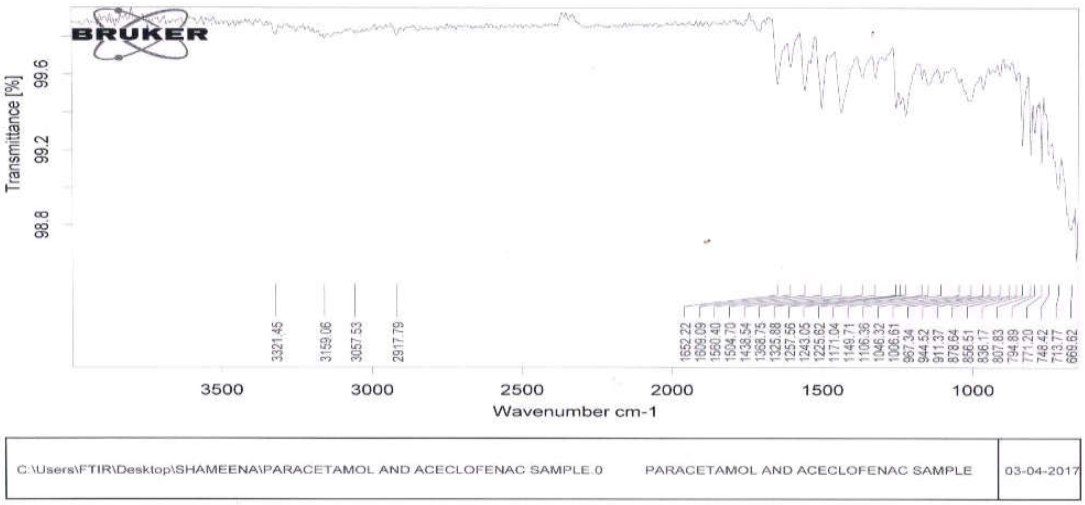

Fig. 4. IR Spectra of Aceclofenac and Paracetamol Combination Tablet

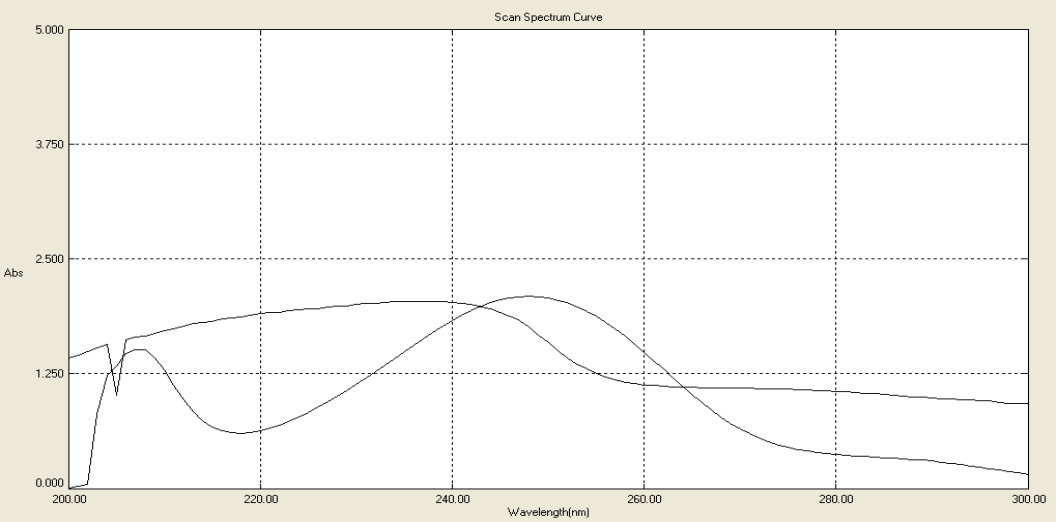

Fig. 5. Isobestic point of Aceclofenac & Paracetamol

in UV - Vis spectrophotometer from 400 – 200 nm to determine the isobestic point. The isobestic point was found to be 280 nm, so the calibration curve of Acclofenac and Paracetamol was developed at this wavelength.

Invitro evaluation of tablets

Visual Inspection: Eight brands of marketed tablets were visually inspected for colour and shape, the qualities was summarized in (Table 3) All the tablet brands have shown orange colour, capsule shape with biconvex surfaces; whereas the PGI ® and Dolasaid-P ® tablets have shown pink and white color, capsule shape with biconvex surfaces.

Table 3. Visual Inspection of Eight brands of Tablets

Brand Name	Colour	Shape	Surface Property
Aceclobak-p	Orange Colour	Capsule	Biconvex
Acesun forte	Orange colour	Capsule	Biconvex
Dolosaid-p	White Colour	Capsule	Biconvex
Arcec-p	Orange colour	Capsule	Biconvex
PGI	Pink Colour	Capsule	Biconvex
Spanac-p	Orange colour	Capsule	Biconvex
XRIF-P	Orange colour	Capsule	Biconvex
Movexxplus	Orange colour	Capsule	Biconvex

Thickness & Diameter: Thickness and diameter uniformity of tablets are necessary not only for consumer requirements but also for packaging. ± 5% variation is permissible. The thickness and diameter values of the all branded tablets were within limit.

Table 4. Thickness & Diameter of Eight brands of Tablets

Brand Name	Thickness (mm)	Diameter (mm)
Aceclobak-p	5.44 0.002	7.96 0.006
Acesun forte	5.21 0.001	7.95 0.005
Dolosaid-p	4.89 0.005	6.93 0.002
Arcec-p	4.85 0.006	7.97 0.001
PGI	5.00 0.001	8.24 0.004
Spanac-p	5.20 0.002	7.99 0.002
XRIF-P	4.08 0.003	12.48 0.001
Movexxplus	3.96 0.004	12.40 0.003

Hardness Test: The hardness of the tablets is an essential criterion in the determination of the ability of the tablets to resist chipping, abrasion or breakage under conditions of storage, transportation and handling. Using Labindia hardness tester, the strength of the tablets was tested. All the tablet brands passed this non-official test according to USP specifications (4-6 kg). The hardness of the tablet was found to be 4.25 – 5.98 kg/cm^2. Brand Spanac-p® required the least

pressure before fracture while brand Arcec-p® required highest pressure.

Table 5. Hardness of Eight brands of Tablets

Brand Name	Hardness (Kg/Cm^2)
Aceclobak-p	5.61 0.02
Acesun forte	4.58 0.13
Dolosaid-p	4.45 0.05
Arcec-p	5.98 0.06
PGI	5.95 0.11
Spanac-p	4.25 0.12
XRIF-P	4.32 0.23
Movexxplus	4.68 0.09

Friability Test: The friability test is mostly important criteria for tablets to examine that the tablets have a good withstand strength for transportation, packaging, shipping and coating. All the tested brands in this study are uncoated tablets. The friability was tested for these tablets for all brands. The friability was less than 1 % for all the brands, which is an indication of good mechanical resistance of the tablet.

Table 6. Friability of Eight brands of Tablets

Brand Name	% Friability
Aceclobak-p	0.31 0.001
Acesun forte	0.22 0.004
Dolosaid-p	0.21 0.003
Arcec-p	0.22 0.001
PGI	0.94 0.007
Spanac-p	0.84 0.005
XRIF-P	0.67 0.003
Movexxplus	0.21 0.002

Weight Uniformity: Tablets were subject to weight variation study for uniformity of weight. All brands showed different mean weight which indicates the use of different excipients in the different brands. The weight of the tablet varied between 600 0.017 to 860 0.043 mg for all the tablet brands. The variation in weight was within the range of ± 5 % complying with pharmacopoeial specification.

Table 7. Weight Uniformity of Eight brands of Tablets

Brand Name	Mean Weight (mg)	% Variation
Aceclobak-p	600 0.017	0.156 0.002
Acesun forte	740 0.042	0.563 0.011
Dolosaid-p	650 0.023	0769 0.003
Arcec-p	860 0.043	1.785 0.012
PGI	660 0.027	0.625 0.004
Spanac-p	660 0.025	3.188 0.015
XRIF-P	710 0.033	0.338 0.003
Movexx-plus	630 0.022	0.677 0.002

Disintegration Test: The observed disintegration times for all the brands investigated was less than the 15 min limit prescribed by the official pharmacopeia. All tablets of the different generic brands passed the disintegration test. The fastest disintegrated tablets were brand of Spanac-P® while the slowest one was brand Aceclobak-P®. The various brands could have employed different disintegrants to improve the penetration of aqueous liquids.

HPLC method

Optimised Chromatographic conditions: The chromatographic conditions were optimized to develop assay method for Aceclofenac and Paracetamol in tablet dosage forms. The basic chromatographic conditions were designed to be simple, easy to use and reproduce and were selected after testing the different conditions that affect HPLC analysis, for example column, aqueous and organic components of the mobile phase, proportion of mobile phase components, detection wavelength, diluents and concentration of analyte. Acetonitrile and phosphate buffer (pH 6.8) in 50:50 ratio was injected and observe the chromatogram without tailing and it was found that it ideally resolve the peaks with retention time (Rt) Aceclofenac and Paracetamol at 4 ± 0.2 and 3 ± 0.2 min respectively.

Table 8. Disintegration time of Eight brands of Tablets

Brand Name	Disintegration Time (min)
Aceclobak-p	8.45 0.32
Acesun forte	5.80 0.27
Dolosaid-p	5.28 0.22
Arcec-p	8.07 0.32
PGI	6.46 0.31
Spanac-p	4.58 0.18
XRIF-P	5.06 0.14
Movexx-plus	5.51 0.24

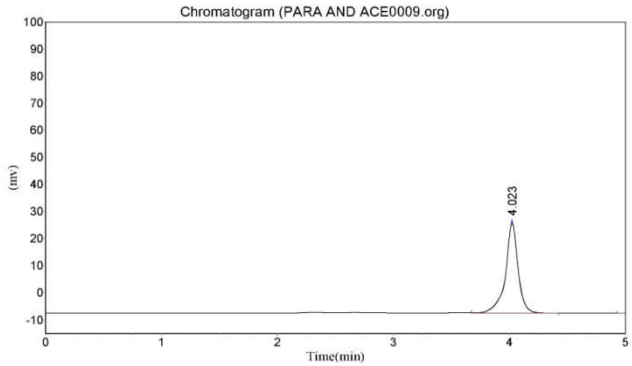

Fig. 6. Retention time of Aceclofenac

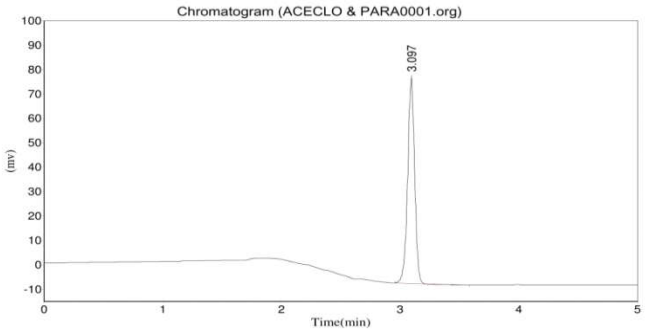

Fig. 7. Retention time of Paracetamol

Calibration of Standard Curve: Linearity of the proposed HPLC method for determination of Aceclofenac and Paracetamol were evaluated by analysing a series of different concentrations of standard drug. In this study five concentrations were chosen ranging between 5-25 µg / ml for both Aceclofenac and Paracetamol. Each concentration was injected three times and obtained information on variation in the peak area response of pure analytes was plotted against corresponding concentrations and result was shown in (Table 9). The linearity of the calibration graphs was validated by the high value of correlation coefficient, slope and the intercept value was shown in Fig.8.

Table 9. Standard Calibration Curve of Aceclofenac and Paracetamol

S.No.	Concentration (µg/ml)	Paracetamol area	Aceclofenac area
1	5	185382	102658
2	10	275491	257841
3	15	398547	445219
4	20	522477	612587
5	25	684544	795554

Table 10. Drug content estimation of Eight brands of tablets

Brand	Aceclofenac		Paracetamol	
	Content (mg)	Area	Content (mg)	Area
Aceclobak-p	98	246632	324	368301
Acesun forte	106	274133	298	268012
Dolosaid-p	102	256889	319	310020
Arcec-p	92	230193	303	305533
PGI	111	279676	342	456830
Spanac-p	103	259730	323	359504
XRIF-P	98	246631	319	310092
Movexx-plus	99	247209	321	336770

Table 11. % Aceclofenac Released from eight brands of Tablets

Time (min)	Average % Aceclofenac Released							
	Aceclobak-p	Acesun forte	Dolosaid	Arcec-p	PGI	Spanac-p	XRIF-P	Movexxplus
10	16.79	16.90	15.46	14.7	17.71	17.4	19.6	18.87
20	28.13	29.28	30.12	30.22	30.9	31.45	32.12	31.83
30	41.69	43.13	45.63	43.96	45.25	48.42	47.76	47.86
45	70.30	70.5	71.03	71.98	72.0	79.32	73.44	74.03

Table 12. % Paracetamol Released from eight brands of Tablets

Time (min)	Average % Paracetamol Released							
	Aceclobak-p	Acesun forte	Dolosaid	Arcec-p	PGI	Spanac-p	XRIF-P	Movexxplus
10	31	33.63	36.70	39.29	36.7	39.29	34.12	31.54
20	40	43.13	46.42	49.0	51.59	53.47	45.73	43.13
30	58.1	60.77	63.35	65.94	68.52	69.08	60.77	61.28
45	76	81.71	84.29	86.88	89.46	95.04	85.19	89.97

Table 13. Area of Aceclofenac Released from eight brands of Tablets

Time (min)	Area of Aceclofenac Released							
	Aceclobak-p	Acesun forte	Dolosaid	Arcec-p	PGI	Spanac-p	XRIF-P	Movexxplus
10	116631	117409	107421	102271	123451	121031	136214	131101
20	195400	203409	209271	209941	215241	218496	223101	221121
30	289607	299607	316948	305400	314213	332451	331758	332491
45	484321	489921	493421	499981	500121	592356	510124	514258

Table 14. Area of Paracetamol Released from eight brands of Tablets

Time (min)	Area of Paracetamol Released							
	Aceclobak-p	Acesun forte	Dolosaid	Arcec-p	PGI	Spanac-p	XRIF-P	Movexxplus
10	120181	130261	142061	152061	142061	152061	132061	122061
20	156948	166948	179648	189648	199648	206948	176984	166944
30	225189	235189	245189	255189	265189	267367	235189	237186
45	296216	316216	326216	336216	346216	386216	329681	348189

Table 15. *Invitro* bioeqivalence assessments using f1 &f2

Brand Name	Aceclofenac		Paracetamol	
	f1 value	f2 value	f1 value	f2 value
Aceclobak-p (Reference)	0	100	0	100
Acesun forte	5	86	9	79
Dolosaid-p	8	80	10	68
Arcec-p	10	79	11	72
PGI	9	81	13	71
Spanac-p	11	72	12	69
XRIF-P	12	69	13	64
Movexx-plus	11	76	12	67

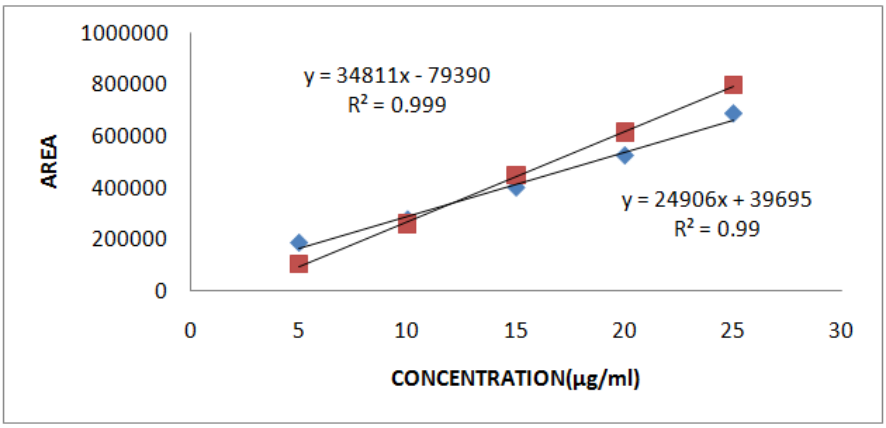

Fig. 8. The Standard Calibration Curve of Aceclofenac & Paracetamol

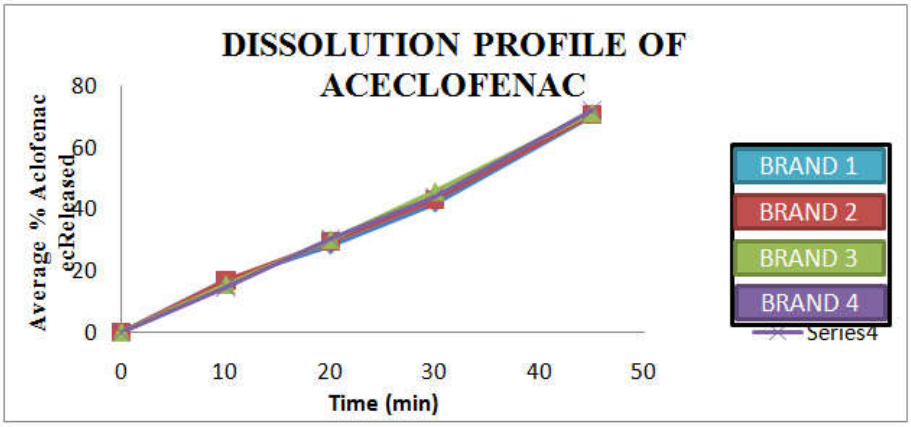

Fig. 9. Comparative Dissolution profile of Aceclofenac Brand 1 – 4

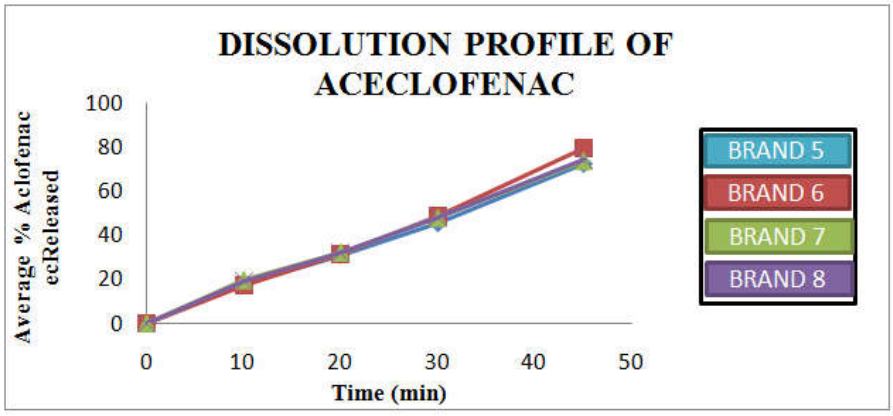

Fig. 10. Comparative Dissolution profile of Aceclofenac Brand 5 – 8

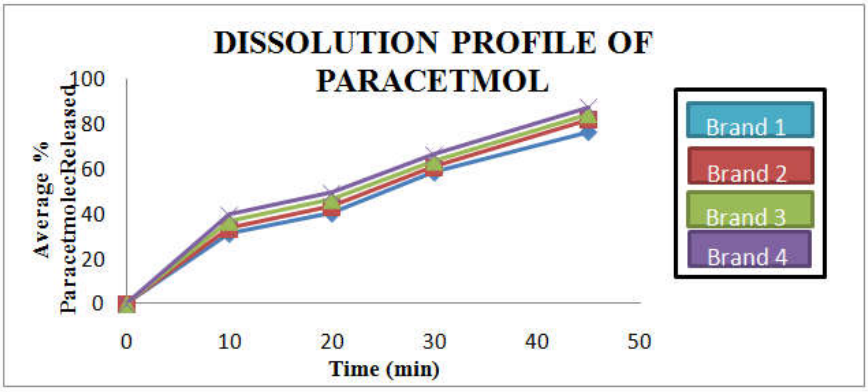

Fig. 11. Comparative Dissolution profile of Paracetamol Brand 1 - 4

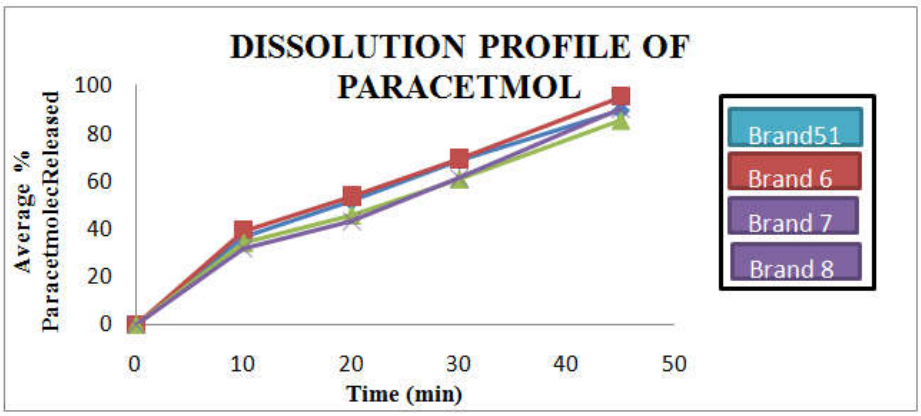

Fig. 12. Comparative Dissolution profile of Paracetamol Brand 5 - 8

Drug content estimation: The drug content of all the brands of tablets was carried out by high performance liquid chromatography. The potency of tablets is expressed in terms of label strength of the product. According to the standards of the British pharmacopoeia, upon assay of a product between 95% and 105% of the label claim should contain the active ingredient. Considering the results obtained from HPLC analysis (Table 10). All the brands with the exception of PGI®, Acesun forte® and Arcec-P® had values which fell within the monograph specifications. The brands PGI® and Acesun forte® had percentage content of active ingredient above the upper limit of 105%. The brands Arcec-P® had percentage content of active ingredient below the lower limit of 95%. Brands PGI®, Acesun forte® and Arcec-P® could be said to be substandard. The deviation from the stated percentage content in these brands could be attributed to factors involved in the formulation process. Some of the possible factors include inaccuracy in weighing the active ingredient, lack of effective mixing during the granulation and incorporation of excess amount of the active ingredient during the formulation.

Dissolution Test: In the present investigation, the release of Aceclofenac & Paracetamol from all tablet brands was immediate release and the percent of drug released at 45mins was more than 70% as shown in Figure 9 to 12. The results obtained from this study revealed that all the brands passed the USP general specifications standard for conventional tablets. The cumulative percentage release in pH 6.8 phosphate buffer solution for all the brands was recorded and the reference Aceclobak-p® showed 70.30 % of Aceclofenac & 76.0 % Paracetamol in alkali fluid for 45 minutes, while the brand Spanac-p® showed higher drug release, respectively 79.32 % of Aceclofenac & 95.04 % Paracetamol within 45 minutes. Hence the brand Spanac-p® considered as better generic brand than others. The higher drug release from these brands was possible may be due to presence of higher concentration of the disintegrant. The cumulative amounts of drug released from all brands are shown in Table 11 & 12.

***In vitro* bioequivalence assessment**

FDA set public standards of f1 & f2 factors to indicate dissimilarity and similarity between brand and generic product. The factor f1 is proportional to the average difference between two profiles, where as factor f2 inversely proportional to the average similarity between two profiles. The percentage dissolution values of all tablet brands used to calculate the f1 and f2 factors.

Assessment Aceclofenac: The higher the f2 values, the more similar the dissolution profiles, so the values cited in (Table 15) shows that Acesun forte® is the most similar local product to the reference product Aceclobak-p®. The similarity factor f2 was 86 and difference factor f1was only 5.

Assessment Paracetamol: Acesun forte® is the most similar local product to the refernce product Aceclobak-p®. The similarity factor f2 was 79 and difference factor.

Conclusion

HPLC method was used for the simultaneous estimation of Aceclofenac and Paracetamol and all the brands had values within the specification range for assay in the British Pharmacopoeia (2013). All the brands of combination tablets sampled complied with the official specifications for identification, uniformity of weight, hardness, thickness, friability, disintegration test and met the pharmacopoeia criterion for dissolution rate test for conventional immediate release tablets. Brand Spanac-p® had the highest dissolution efficiency, while brand Aceclobak-p® had the lowest dissolution efficiency. So Spanac-p® could be used as a best generic substitute which reduces the dose and cost of the treatment. From f1 and f2 analysis, the dissolution profiles of all brands of tablets were similar to that of the reference brand. Therefore it is evident that test products were bioequivalent to the reference product.

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