Quality surveillance of immediate release aceclofenac tablets (100 mg) available in local market

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Abstract: Aceclofenac is considered to be an effective drug that has been widely prescribed for multi- medical complaints globally. Owing to high demand many generic counterpart of aceclofenac tablets are now available in the commercial market. The aim of the present work is to evaluate and compare the quality attributes of various national/local brands of aceclofenac immediate release tablets (100mg) with the standard multi-national brand available in Pakistan. Physico-chemical evaluation was performed by determining the average tablet weight, thickness, hardness, disintegration time, percent dissolution and assay. Moreover, brands and reference formulation were exposed to multi-point dissolution. The in vitro drug release pattern was examined in various pH environment (1.2, 4.5 and 6.8) using USP dissolution apparatus 2 (paddle) at 50 rpm. The data was then analyzed by model dependent (Zero-order, first-order, Higuchi, Hixson-Crowell, Korsmeyer & Peppas, and Weibull model), pair wise procedure (f_1 & f_2) and one-way ANOVA methods. Results showed that the all aceclofenac brands and the reference tablets followed Weibull kinetics at pH 6.8. f_1 & f_2 were also found to be within the acceptable FDA limits. Furthermore, the values of One-way ANOVA also confirmed the absence of any significant difference among various aceclofenac brands.

Keywords: Aceclofenac, tablets, quality control, NSAID, dissolution studies.

INTRODUCTION

Being a lower middle income country, Pakistan is now facing multiple healthcare issues regarding availability and affordability of drugs (Sumner, 2010). It is estimated that the daily income of the Pakistani population (60.3%) is less than 2$ (Anwar and Sun, 2011). Owing to poor economical status, people are more concerned to the cost of therapy. Currently the objective of pharmaceutical industries is to develop products not only with good quality attributes but cost effective too. The trend of brand marketing has been growing worldwide to provide large access of the medicines. Selection and levels of excipients greatly characterize the in vitro formulation properties as well as in vivo behavior of drugs (Bushra *et al.,* 2008). Brand marketing allows the larger access of medicines to the public with feature restoration of product against the innovator. Such drugs' alternatives are being prepared with the expiration of patents and occupy a valuable place played in healthcare sectors both nationally and internationally (Reddy *et al*., 2014).

FDA and other regulatory bodies recommend the similar physical, chemical and biological characteristics of the generic formulations to the patent product (FDA, 1997a). The assessment of in vitro drug release is considered to be the most sensitive tool to forecast *in vivo* drugs' behavior. Recently the multi-point dissolution with various dissolution media has been utilized for better reflection of drugs' performances especially for the new product development (Shargel *et al.,* 2005; Tsong *et al*., 1997). These in vitro drug release curves are particularly useful to estimate the resemblance of the test/trial formulations to the reference products over specific time course (FDA, 1997a; FDA, 1997b; EMEA, 2000).

Chemically, aceclofenac is a 2-[2-[2-[(2,6-dichlorophenyl)amino]phenyl]acetyl] oxyacetic acid derivative, structurally similar to diclofenac and belongs to non-steroidal anti-inflammatory (NSAIDs) group (Batlle-Gualda *et al.,* 2007). Being a class II candidate it possesses high permeation and poor dissolution leading to variable *in vivo* drug's availability. Currently lipid based carriers have been utilized to improve the drug's solubility and bioavailability as well (Shakeel *et al.,* 2009). It is commonly prescribed for the symptomatic relief of pain and inflammation including osteoarthritis, rheumatoid arthritis and ankylosing spondylitis (Noh *et al.*, 2015; Shakeel, 2007). The potent anti-inflammatory effects are mediated via inhibiting cyclo-oxygenase enzyme (COX-II) and blockage of prostaglandin E2 synthesis (Brogden and Wiseman, 1996). However; prolong administration would causes gastro-intestinal discomforts, bleeding and ulcers (Noh *et al*., 2015; Solanki and Dahima, 2011).

Aceclofenac is a commonly prescribed drug in different clinical settings of Karachi, Pakistan for various medical conditions. Many brands of aceclofenac tablets (100 mg) are now commercially available in local market. The aim of the present study is to re-evaluate the quality attributes

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of brands prepared by local manufactures and to compare the tablet properties with one the leading multi-national brand of aceclofenac immediate release tablets (100 mg). This study also focuses the estimation of in vitro drug release pattern of aceclofenac tablets in a variety of dissolution media (hydrochloric acid buffer of pH 1.2, phosphate buffer of pH 4.5 and 6.8 using model dependent and independent approaches.

MATERIALS AND METHODS

Chemicals

Aceclofenac ($C_{16}H_{13}C_{l2}NO_4$) pure was kindly provided by Sami Pharmaceutical Ltd, other chemicals including Hydrochloric acid (HCl), sodium hydroxide (NaOH) and potassium dihydrogen phosphate (KH_2PO_4) were of analytical grade (Merck, Damstabt, Germany) and procured from the commercial market.

Procurement of aceclofenac tablets

Six brands of aceclofenac immediate release (IR) tablets 100 mg manufactured by different Pakistani pharmaceuticals were purchased from the local market. These tablets were tagged as B1, B2, B3, B4, and B5, while the multi-national brand was as "S". The date of manufacturing and expiry, batch number, lot number and production license number of all brands were also checked properly.

Evaluation of quality attributes of aceclofenac tablets

All brands were exposed to different physico-chemical testing including measurement of diameter, weight variation, hardness, disintegration, dissolution and content assay.

The diameter of tablets was measured by vernier caliper (Seikobrand, China), weight variation test was performed by assessing the weight of twenty tablets using digital balance (Mettler Toledo B204-S, Switzerland), and the hardness of twenty tablets was evaluated using digital hardness tester (OSK Fujiwara, Tokyo, Japan).

Disintegration test and content assay of tablets

Disintegration time was determined using six rack basket assembly (Erweka ZT-2 Husenstamn, Germany) by taking 900 ml of the distill water as medium.

Assay was performed using by pulverizing 20 units of each brand in mortar and pestle. Aceclofenac powder equivalent to 100 mg was then used to estimate the drug content. The assay was estimated using an isocratic HPLC system (LC-20AT, Shimadzu, Japan) coupled with a UV-visible detector (SPD-20A, Shimadzu, Japan), integrated through CBM-102 Communication Bus Module. Mobile phase was combination of acetonitrile and deionized water (45:55) having a pH of 2.8 adjusted with ortho-phosphoric acid. Sample detection was made at a detecting wave length of 276 nm with a flow rate of 1mL/min (Naz *et al*., 2013).

Dissolution testing

Dissolution test of immediate release aceclofenac was performed using USP 6-station dissolution apparatus II (Paddle method). 900 ml of phosphate buffer (pH 6.8) as dissolution medium was filled in each flask and paddles rotation were set at 50 rpm. Aliquots drawn after specified time intervals were suitably diluted with the same medium and analyzed by UV-spectrophotometer at a wavelength of 273 nm (Shah *et al*., 2008).

Comparison of dissolution profiles of brands

To compare the dissolution profiles of all brands, multi-points dissolution test was carried out at different pH (1.2, 4.5 and 6.8) environment. All buffers were prepared according to the USP monograph guidelines (USP, 2013). Small volumes of samples (5ml) were drawn at time interval of 5, 10, 15, 20, 30, 45 and 60 minutes and were immediately replaced with the fresh medium pre-warmed to 37ºC. All samples were analyzed by spectrophotometer at wavelength of 273nm.

Data analysis of in vitro drug release

The obtained in vitro data was analyzed statistically using ANOVA and other mathematical approaches (model dependent and independent).

ANOVA (Analysis of variation)

SSPS version 17.0 is used to apply one way ANOVA with pos hoc Tuckey testing to compare the difference between the formulations.

Model dependent analysis

These include zero and first order reaction, Hixon-Crowell cube root law, Higuchi, Korsmeyar-Peppas, and Weibul models (Shoaib *et al*., 2010; Costa and Sousa-Lobo, 2001; Higuchi, 1963; Hixson, 1931; Korsmeyer *et al.,* 1983). The in vitro drug release mechanisms were analyzed by software DD-Solver® as "Adds In program" in Microsoft Excel™ 2010 (Microsoft Corporation, USA). The mathematical expression of the applied models is given below in table I; (equation 1-6). Moreover dissolution profiles of aceclofenac brands (B1 to B5) at different pH were also compared with the reference aceclofenac brand (S).

Model independent analysis

f_1(dissimilarity factor) and f_2(similarity factor) are generally used to compare the dissolution profile of two products (test vs. reference). f_1 and f_2 are calculated for all brands of aceclofenac tablets using following mathematical expressions (Moore and Flanner, 1996);

$$f_1 = \left[\frac{\sum_{t=1}^{n}(R_t - T_t)}{\sum_{t=1}^{n} R_t}\right] \times 100$$

and

$$f_2 = 50 \times log\left\{\left[1 + \left(\frac{1}{n}\right)\sum_{t=1}^{n}|R_t - T_t|^2\right]^{-05} \times 100\right\}$$

Where R_t is used for cumulative percentage dissolved at any time of reference product while T_t stands for cumulative percentage dissolved at any time of test formulation. Test formulation is said to be equivalent to standard product if f_1 is up to 15 and f_2 is greater than 50.

RESULT

In the present study, five commonly selling aceclofenac counter parts (B1-B5) manufacture by national pharmaceuticals of Pakistan and a standard multi-national aceclofenac brand (S) were purchased and then exposed to various pharmacopeial and non-pharmacopeial testing. All local brands available in Karachi were found to be almost equivalent to the reference product in terms of physical quality attributes. The diameter and average weight of tablets was found to be in ranged between 8.02 ±0.03 to 9.24 ±0.02mm and 9.24 ± 0.02 to 260.94±1.31 respectively. Tablets were disintegrated in distil water within 15 min. Moreover, the assay of tablets of each brand was also excellent and the summary of the physico-chemical properties of tablets is presented in table 2.

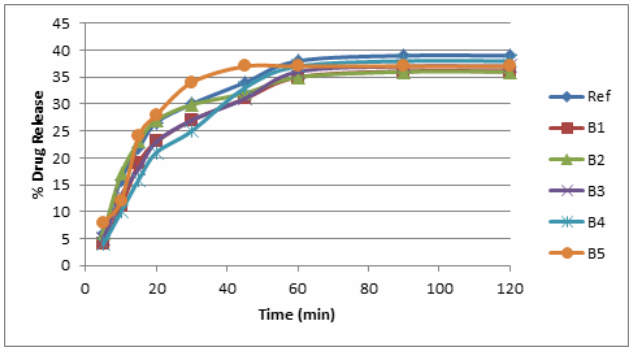

Fig. 1: Release of various aceclofenac brands & Reference at pH 1.2

Multi-point dissolution was also performed to observe the release kinetics of the aceclofenac tablets in different pH environment (pH 1.2, 4.5 & 6.8). The sample collection was continued up to 60 min with the replenishment of the fresh dissolution medium. The drug release at various time intervals was presented in figs. 1-3. The in vitro data was then analyzed by applying various model dependent and independent approaches. f_1 & f_2 were calculated by comparing the drug release of each counterpart against the standard aceclofenac brand. The values of both parameters were found within the official limits at all pH ranges reflecting similarity among brand and other counterparts and the results are given in table 3. The drug release was then studied using various models. The Weibull model showed the higher regression values at all pH while the Korsmeyer Peppas was also valid at lower pH values. The regression values obtained by different drug release models are expressed in table 4.

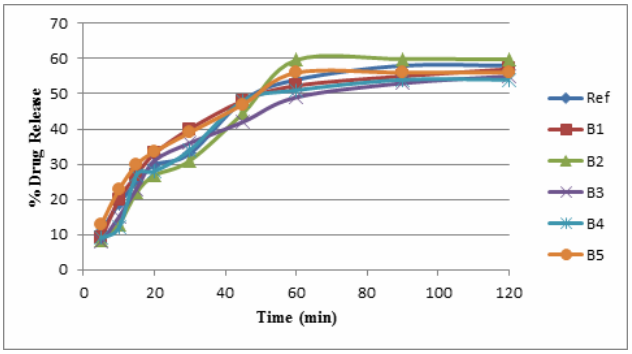

Fig. 2: Release of various aceclofenac brands & Reference at pH 4.5

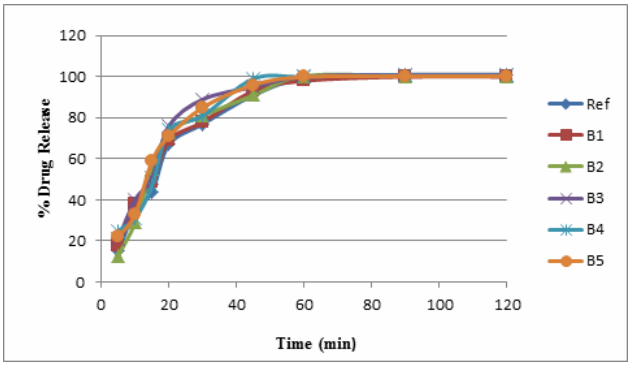

Fig. 3: Release of various aceclofenac brands & Reference at pH 6.8

Lastly the quality attributes of brands and the reference products were also compared using statistically using ANOVA approach. The results of ANOVA also confirmed the Similarity among these aceclofenac brands and the results are presented in table 5.

DISCUSSION

An analysis was conducted by generic pharmaceutical association in United State (US), showing 22% saving in one year and collectively about 10% cost reduction in last ten years. The utilization of brands has been growing and the trend of brand prescription is being increasing globally. It was estimated in 2011 that about 80% of the prescriptions written in US were retailed with brands other than patent (Shargel and Kanfer, 2014). Analgesics are one of the most selling categories of the drug, available with or without prescription. Aceclofenac is a relatively new and effective NSAID used in a variety of painful conditions and other medical problems. Owing to the popularity and excessive utilization of the compound, many brands are now available in pharmacy retail stores of Pakistan. These brands are manufacturing by local and multi-national pharmaceuticals as well. No matter whatever the technique, formulation, equipment, and facility is used to make products, they must be equivalent physically (tablet quality and characterization) and therapeutically (pharmaceutical drug response).

Table 1: Mathematical Approaches for Model Dependent Analysis

S. No.	Mathematical Model	Equation
1	Zero-Order Kinetics	$Q_t = K_0\, t$
2	First-Order Kinetics	$\mathbf{Log\ Q = LogQ_0 - \frac{kt}{2.303}}$
3	Hixon-Crowell cube root law	$\mathbf{Q_0^{1/3} - Q_t^{1/3} = K_{HC} \times t}$
4	Higuchi Model	$\mathbf{Q = kt^{\frac{1}{2}}}$
5	Korsmeyar-Peppas Model	$\frac{M_t}{M_\infty} = Kt^n$
6	Weibull Model	$\mathbf{m = 1 - exp\left[-\frac{(t-Ti)^\beta}{\alpha}\right]}$

Table 2: Physico-chemical analysis of aceclofenac IR brands

Code	Diameter (mm) Mean± S.D	Weight (mg) Mean± S.D	Hardness (kg) Mean± S.D	Disintegration Time (min)	Assay (%)
S	8.23 ± 0.01	219.35 ± 0.57	8.27 ± 0.18	09.50	100.93 ± 0.32
B1	8.20 ± 0.02	238.83 ± 0.93	7.87 ± 0.11	08.50	98.7 ± 0.26
B2	9.24 ± 0.02	260.94 ± 1.31	8.55 ± 0.31	14.50	99.23 ± 0.25
B3	8.26 ± 0.02	211.31 ± 0.83	7.66 ± 0.13	07.50	98.1 ± 0.36
B4	8.02 ± 0.03	191.52 ± 0.96	6.71 ± 0.23	13.50	100.50 ± 0.29
B5	8.14 ± 0.05	205.01 ± 1.21	7.21 ± 0.36	15.00	98.98 ± 0.96

Table 3: Model independent approaches on dissolution profile of aceclofenac tablets at pH 1.2, 4.5 and 6.8

Code	f_1	f_2	Comments
pH 1.2			
S and B1	11.25	73.59	Similar Profile
S and B2	5.47	83.12	
S and B3	9.35	76.78	
S and B4	11.34	69.97	
S and B5	8.63	77.76	
pH 4.5			
S and B1	6.29	74.93	Similar Profile
S and B2	8.69	71.73	
S and B3	9.56	70.02	
S and B4	7.32	73.00	
S and B5	8.22	72.28	
pH 6.8			
S and B1	2.94	78.83	Similar Profile
S and B2	4.94	65.08	
S and B3	7.07	59.91	
S and B4	5.96	63.31	
S and B5	6.80	58.96	

In the present study, five commonly selling aceclofenac brands manufacture by national pharmaceuticals of Pakistan were purchased and then exposed to various pharmacopeial and non-pharmacopeial testing. The tablet properties are then compared to the reference brand (code S) that is being manufacturing by multi-national pharmaceutical industry. The physico-chemical assessment included the weight variation test, diameter, hardness, disintegration time, percent in vitro drug release and assay. The results of all parameters were found to be within the acceptable limits provided by the official compendia. The hardness of each brand was found to be optimum (6.71 to 8.55kg), the values of average tablet weight were 191.52 to 260.94mg. Least deviations were observed in tablet diameters and the disintegration time was found to be ≤15 minutes for S and B1-B5 aceclofenac tablets. Post market surveillance studies of various pharmaceutical products have been extensively

Table 4: Model Dependent Approaches on dissolution profile of aceclofenac tablets at pH 1.2, 4.5 and 6.8

Batch Code	Zero order		First order		Higuchi		Hixon-Crowell		Weibull Model			Korsmeyer- peppas		
	r^2	$K_o(h^{-1})$	r^2	$K_1(h^{-1})$	r^2	$K_H(h^{-1/2})$	r^2	K_{HC} $(h^{-1/3})$	r^2	α	B	r^2	$K_{kp}(h^{-n})$	n
pH 1.2														
S	0.632	0.238	0.676	0.004	0.759	4.134	0.658	0.001	0.867	13.894	0.435	0.953	12.816	0.251
B1	0.640	0.242	0.692	0.004	0.798	3.972	0.674	0.001	0.862	18.819	0.480	0.933	9.827	0.294
B2	0.541	0.198	0.583	0.003	0.658	3.694	0.568	0.001	0.813	11.840	0.379	0.955	14.602	0.204
B3	0.678	0.246	0.731	0.004	0.827	4.005	0.713	0.001	0.891	18.315	0.479	0.948	9.888	0.296
B4	0.703	0.279	0.764	0.004	0.871	4.221	0.743	0.001	0.936	13.931	0.428	0.925	7.890	0.354
B5	0.462	0.210	0.511	0.003	0.592	3.959	0.494	0.001	0.829	7.140	0.282	0.817	14.031	0.228
pH 4.5														
S	0.792	0.406	0.885	0.008	0.914	6.094	0.856	0.002	0.952	17.627	0.603	0.944	11.136	0.365
B1	0.713	0.357	0.816	0.008	0.860	5.982	0.784	0.002	0.934	13.930	0.546	0.962	14.367	0.304
B2	0.791	0.470	0.875	0.0017	0.916	6.382	0.0865	0.003	0.933	28.434	0.723	0.912	8.322	0.438
B3	0.792	0.406	0.855	0.007	0.909	5.759	0.828	0.002	0.946	18.324	0.588	0.961	11.054	0.361
B4	0.714	0.386	0.811	0.008	0.863	5.870	0.779	0.002	0.959	18.370	0.595	0.904	11.030	0.356
B5	0.720	0.347	0.813	0.007	0.843	5.822	0.783	0.002	0.935	11.349	0.501	0.946	15.788	0.284
pH 6.8														
S	0.634	0.668	0.980	0.047	0.789	11.065	0.975	0.012	0.990	41.897	1.230	0.910	27.625	0.294
B1	0.614	0.625	0.988	0.051	0.757	10.777	0.971	0.011	0.993	31.245	1.159	0.913	30.797	0.268
B2	0.538	0.647	0.957	0.053	0.697	11.243	0.934	0.012	0.982	58.946	1.469	0.867	31.298	0.269
B3	0.540	0.592	0.972	0.059	0.674	10.768	0.932	0.012	0.987	39.501	1.300	0.869	35.351	0.242
B4	0.569	0.623	0.957	0.053	0.710	10.897	0.942	0.012	0.968	44.875	1.285	0.828	30.167	0.278
B5	0.539	0.597	0.973	0.057	0.678	10.797	0.939	0.012	0.989	40.794	1.300	0.851	34.017	0.251

Table 5: Results of ANOVA

pH	Sources of Variation	Sum of Squares (SS)	Degree of Freedom (df)	Mean Square	Variance of F	Significance
1.2	Between Groups	114.741	5	25.948	0.174	0.971
	Within Groups	6314.508	48	131.552		
	Total	6429.249	53			
4.5	Between Groups	135.028	5	27.006	0.087	0.994
	Within Groups	14855.344	48	309.486		
	Total	14990.372	53			
6.8	Between Groups	155.095	5	31.019	0.32	0.999
	Within Groups	46269.942	48	963.957		
	Total	46425.037	53			

documented by authors. Zafar *et al*., in 2014 re-evaluated the quality parameters of various diclofenac sodium brands (sustained release) available in pharmacy stores of Pakistan. Test parameters of such diclofenac sodium SR tablets were found within the official limits as provided by USP (Zafar *et al*., 2014). Similarly Afifi and Ahmadeen designed a comparative study among various marketed brands of metformin hydrochloride (500mg) tablets commonly sold in Saudi Arabia. These metformin alternatives were found to be comparable with an innovator both pharmaceutically and chemically (Afifi and Ahmadeen, 2012). Another study reported the brand analysis of anti-hypertensive drug lisinopril tablets in Yemeni market (Othman, 2014).

In vitro drug kinetics

From past few years, extensive emphasize has been given to dissolution testing by regulatory authorities and official compendia. Single point dissolution testing is considered to be a routine quality control assessment but keeping the drug development view point dissolution profile has been focusing now days. Dissolution profile of any API reflects the pattern of drug release with time and is highly useful in product optimization and comparisons, development of in-vivo-in-vitro correlations and bioequivalence of products (Yuksel, 2000).

Aceclofenac tablets were subjected to multi-point dissolution test to assess the drug release pattern. The in vitro behavior of aceclofenac tablets was estimated in different dissolution media by applying model dependent and independent approaches. The drug release pattern of various aceclofenac brands at pH 1.2, 4.5 and 6.8 are graphically presented in figs. 1-3. Regression analysis of various mathematical models as; zero-order, first-order, Higuchi, Korsemeyer-Pappas, Hixson–Crowell and Weibull model was made for understanding of the drug-release kinetics. The numerical expressions of the studied models are given in table 1. f_1 and f_2 were also assessed to find out the closeness of the test formulation(s) against the standard aceclofenac candidate. In vitro data computation was made by software DDSolver an add-in program of Microsoft Excel™ 2007.

Model dependent method

Qualitative and quantitative modification of excipients in any formulation greatly influences the in vitro drug release characteristics. Hence the drug regulatory authorities have given large emphasis on the drug dissolution to assure product excellence (Mitra *et al*., 2015). The results obtained from in vitro drug release were then analyzed by applying various kinetic models. Since the aceclofenac is a class II drug with pKa value of 4.7 (Patel, 2011), showed poor drug release (less than 40%) in hydrochloric acid buffer of pH 1.2 and also inadequate drug release (up to 60%) was seen in phosphate buffer of pH 4.5. However the drug released was drastically enhanced in phosphate buffer of pH 6.8. The rate constants and the corresponding regression values of various models are shown in table 3. Zero order showed least r^2 Korsmeyer-Peppas models was found to be the best fitted model for reference and different aceclofenac brands with r^2>0.90 in various pH environments. For Korsmeyer-Peppas kinetics, the r^2 values of standard and brands at pH 1.2, 4. And 6.8 were ranged of 0.817 to 0.955, 0.904 to 0.962 and 0.828 to 0.913 correspondingly. However; Weibull model showed the highest regression values in phosphate buffer of pH 6.8. The consecutive r^2 values of Weibull model at pH 6.8 for brands (B1-B5) and reference were found to be 0.993, 0.982, 0.987, 0.968, 0.989 and 0.990 respectively. Similar finding of aceclofenac immediate release brands was reported by another study where aceclofenac (IR) tablets showed drug release similar to Weibull model (Soni and Chotai, 2010). Numerous scientists have conferred the worth of dissolution profiles during product development of pharmaceuticals. Furthermore, the multi point dissolution testing is thought to be more useful from comparison view point of marketed and/or test formulations. Ochekpe *et al*., in 2012 investigated the quality attributes of twelve commonly selling brands of sulphadoxine pyrimethamine in local market of Nigeria. The in vitro drug release of these brands was examined under various environmental conditions and the data was then analyzed using valuable model dependent, independent and ANOVA procedures. Authors observed the dissimilar in vitro drug profile among seven brands

while the remaining five were disqualified owing to failure of the USP dissolution requirement (Soni and Chotai, 2010). Al-Ameri and co-workers evaluated the difference among innovator and generic counter-parts of huge range of drug chemicals using in vitro drug kinetic approach. They found that majority of the generics had dissimilar dissolution (either faster or slower) profile however; the drug releases were found to be within the acceptable pharmacopeial limits (Al Ameri *et al.,* 2012). Moreover; some generic medicines showed incomplete or poor dissolution than the standard products (Ochekpe *et al*., 2012).

In the present study the release profiles of all brands were found to be nearly identical to the reference brand in various discussed above dissolution media.

Model independent method

Model independent analysis using estimation of similarity and dis-similarity approaches has been extensively utilized during product development and SUPAC (Scale-Up & Post Approval Changes) (Tansel and Nursin, 2005; Yuksel *et al*., 2000). In the present study the various national brands of aceclofenac tablets are compared with the multi-national standard product. The values of these fit factors (f_1 and f_2) are mentioned in table 4. The difference factor (f_1) of brands was ranged between 5.47 to 11.34, 6.29 to 9.56, and 2.94 to 7.07 at pH 1.2, 4.5 and 6.8 consecutively exhibiting acceptable difference in marketed products. While the similarity factor (f_2) of brands was ranged between 69.97 to 83.12, 70.02 to 74.93, and 59.91 to 78.83 at pH 1.2, 4.5 and 6.8 respectively. Soni and Chotai explored the brand to brand variation of aceclofenac tablets available in local market of India. The in vitro assessment of these brands was carried out by multi-point dissolution testing and their equivalence was estimated using pair wise procedure. All aceclofenac brands and generic were found to be similar in respect of drug release profiles (Soni and Chotai, 2010). The Hanif *et al*., in 2014 developed nimesulide tablets by direct compression method. The in vitro drug kinetics of these trial formulation batches were then compared against reference product by computing similarity factor (Hanif *et al*., 2014). Lalic *et al*., in 2011 compared the dissolution profiles of lamotrigine oral immediate release tablets available in commercial market using f_1 and f_2 indices. Both indices of lamotrigine tablets were found within the acceptable limits (Lalic *et al*., 2011).

One way- ANOVA method

ANOVA is considered to be one of the sensitive statistical approaches to assess the significant difference among pharmaceutical products (Momin *et al.,* 2015; Fatima *et al*., 2013). The in vitro drug release kinetics of the various brands and the reference formulation was statistically evaluated using one way ANOVA method. Furthermore, Tukey test was also done to assess the difference among brands and standard product. The result of ANOVA is given in table 5. The analysis showed no significant difference among brands and reference drug. The *P* values were found to be 0.971, 0.994, and 0.999 at pH 1.2, 4.5 and 6.8 respectively.

CONCLUSION

The intention of the present study is to assess and compare the quality of various aceclofenac immediate release brands against the reference product. The in vitro drug kinetics showed that all aceclofenac brands followed Weibull drug release model. f_1 and f_2 values were found to be within the acceptable FDA ranges and all brands are so declared to be equivalent to the reference one. Moreover, one way ANOVA was found to be sensitive to evaluate the differences among various products and showed the absence of significant difference among aceclofenac brands.

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