Original Research Article

Comparative Physicochemical Evaluation of Selective Brands of Diclofenac Potassium Tablets Available in Pakistan

ABSTRACT

The purpose of present effort was to conduct physiochemical evaluation of miscellaneous commercially available diclofenac potassium 75mgtablets in the local market of Sindh, Pakistan. Further comparison was made among their different parameters. In study seven brands tagged as RB1 to RB7 were evaluated for diameter, thickness, disintegration time, and assay content and dissolution profile. Obtained results of all brands conformed to the official standard specification for disintegration test, Assay Content. The attained release rate profile during dissolution study revealed that all brands achieved more than 80% in sixty minutes. The spectrophotometric analysis for assay content of all brands was within 90%-110% which in good agreement with specified in the Unites States Pharmacopoeia. In the current study all the assessed products could be regarded as being chemically similar, while no product is found as a false product, these all brands can be used alternatively. The used spectrophotometric evaluation is very simple, reasonable, and easy to adopt for analysis and could be used in routine analysis of diclofenac potassium tablets, particularly in the unavailability of advanced equipment's just like HPLC, LCMS & GC etc. which is not easily available and accusable in many institutions.

***Keywords*:** Diclofenac Potassium, Assay Content, Dissolution Studies, Commercial Brands, Spectrophotometric analysis.

1. INTRODUCTION

The diclofenac active pharmaceutical ingredient is commonly available as potassium and sodium salt for oral tablets while diclofenac diethyl amine used topically. Extensive literature is available on sodium salt [1-3], while a little available for potassium salt [4]. Diclofenac potassium possess outstanding anti-inflammatory, analgesic and antipyretic properties. The dissolution and absorption of diclofenac potassium is faster than sodium salt. As per the biopharmaceutical classification system (BCS) diclofenac potassium falls under the category of class I drug [5]. During the study of dissolution profile of different diclofenac salts Fini et al uses alkaline metals hydroxide or organic aliphatic bases [6]. Now a days, the more emphasis has been giving on dissolution testing by pharmaceutical industry and by regulatory authorities' i.e. FDA, EMA and WHO also [7-8]. The dissolution profile is defined as the amount of drug that released from a dosage unit within specified duration of time. Dissolution release profile is commonly conducted in dissolution apparatus, such as the US Pharmacopeia (USP) I or II dissolution systems [9-10]. Although rapid release solid dosage forms need to test routinely for given parameter such as content uniformity, weight, hardness, friability and disintegration, in-vitro release profile is to be considered as most simulated test with in vivo evaluation [11]. For pharmaceutical solid products, it is believed that absorption of drug from GIT lining is greatly depends upon in-vitro release pattern [12]. Results of in-vitro drug release are considered to be most critical during various drug development stages [13]. The results of in-vitro drug release may helpful in identifying the problems related to the in-vivo studies of a drug product. So, the in-vitro dissolution studies getting significant importance, in order to ensure the in vivo characterization of pharmaceutical products [14]. In vitro release profiles computation has been frequently using during product development process and it is easily adapted for establishing enhanced

pharmaceutical product development process and dissolution specifications. In-vitro release study also proved helpful in predicting the similarity of pharmaceutical products and creating in vitro-in vivo correlations, which have a direct effect on total coast of performance of bioavailability and bioequivalence studies performance [15].

The main aim of the present study is to evaluate the excellence of seven different brands of diclofenac potassium 75 mg tablets (RB1 to RB7), locally available in Pakistan. In present study different quality evaluation tests carried has been carried out i.e., weight variation, diameter, thickness, disintegration, and assay content and dissolution test. The release data profile was analyzing by applying T independent test.

2. MATERIALS AND METHODS

Materials

Diclofenac potassium and Methanol was gifted from Saffron Pharmaceuticals (Pvt.) Ltd. Sodium phosphate dibasic heptahydrate, Sodium phosphate monobasic monohydrate and seven different brands of diclofenac potassium were selected and purchased, which were manufactured in Pakistan. Reference brand was selected and purchased from reputed national pharmaceutical company in Pakistan. While all test brands (RB2 to RB7) were also manufactured locally in Pakistan.

Apparatus

Shimadzu digital analytical balance, Mettler Toledo digital top loading balance, Disintegration Apparatus, USP Type II Dissolution Apparatus (China) and UV Spectrophotometer (Schimadzu).

Evaluation

Uniformity of weight

All selected brands were subjected for weight uniformity test, 20 tablets taken from each brand and individually weighed by using a digital analytical balance. The average weight for each brand tablets was determined and their deviation in percentage (%) of the individual tablets from the mean was calculated.

Disintegration Test

Disintegration is first step for tablets consumption in body, bioavailability depends upon dissolution and ultimately dissolution profile is dependent upon disintegration. The disintegration is directly proportional to amount of drug reach at site of action in unchanged form. Tablet disintegration time was observed at 37°C by using disintegration apparatus (Curio), and basket oscillation was adjusted al 28- 32 oscillation per minute. The sample size for each selective brand was n= 06, distilled water was used as disintegration media due to its inertness. The disintegration time end point was taken to be the time no residue and hard mass of any tablet was present on the mesh unless fluffy mass [16].

Assay of diclofenac potassium tablets

Assay analysis is used to quantify the amount of drug in a particular dosage form, this test ensures uniform distribution of API in each dosage form. Uniformity of API is an integral part of evaluations because it imparts profound effect on final therapeutic response of dosage form. Assay of pharmaceutical dosage form can be conducted by following sequence [17].

Standard solution preparation of Diclofenac Potassium drug

An amount of 31.5 mg of Diclofenac Potassium pure standard was taken in volumetric flask (50ml Capacity), dissolve Diclofenac Potassium in it completely and bring the volume to 50ml with further addition of methanol, Now vortex and sonicate the solution, vortex ensure the complete mixing and sonication ensure de-aeration, as presence of air bubble interfere with UV

absorbance. Draw 2ml of prepared solution, transfer it to volumetric flask having 50 ml capacity and bring the final volume to 50ml with methanol, vortexing and sonication was done. Take the absorbance of the solution at 282nm wavelength. Methanol was used as blank.

Sample preparation of diclofenac potassium tablet

The solution was prepared by little modification in previously available method, for preparation of standard solution 20 tablets of Diclofenac Potassium 75mg was taken and ground in motor and pestle. From the crushed tablet powder an equal amount to 31.5 mg of Diclofenac potassium was precisely weighed and transferred to volumetric flask (50ml capacity), The sample was dissolved appropriately and methanol was added to make up the 50 ml volume, vortex and sonicate the mixture if necessary, vortex ensure the complete mixing and sonication ensure de-aeration, as presence of air bubble interfere with UV absorbance. Filter this solution in order to remove any undissolved excipients of tablets or any other impurities. From prepared solution 2ml was transferred to volumetric flask 50ml and methanol was added to bring the final 50 ml, vortexing and sonication was done. . Take the absorbance of the solution at 282nm wavelength. The methanol was used as blank.

Preparation of Diclofenac Potassium standard curve

A 100 mg of Diclofenac Potassium was weighed and transferred to100ml volumetric flask having methanol (60 ml) and mixed to dissolve completely with the help of magnetic stirrer. Then bring the volume of sample up to100 ml with methanol. This dilution has the concentration of diclofenac potassium 1000 µg/ml that is equivalent to 1mg/ml. From this solution 10 ml was taken and diluted up to 100 ml with methanol, this dilution gives the concentration 100µg/ml that is equivalent to 0.1mg/ml. From this solution further make dilutions containing various concentrations. Absorbance was taken at 282nm [18].

Dissolution studies

Dissolution studies are important parts in developing a pharmaceutical dosage form. Extent of dissolution directly relevant to therapeutic activity of pharmaceutical drug, as absorption of drug from GIT to systemic circulation depend upon amount of drug dissolved in body fluid. In present project seven formulation were subjected the dissolution studies, dissolution studies were performed using USP40, Apparatus 2 commonly termed paddle over disc apparatus. Rotation speed of paddles were adjusted at50±1 rpm. Phosphate buffer having pH: 6.8, was used as dissolution medium, diclofenac potassium is also soluble completely in water but when water is using as dissolution media fluctuation in pH can accrue, which can alter the dissolution profile at any step. The temperature of dissolution medium was adjusted about to internal body temperature i-e. 37±0.5 °C. The acceptance criterion for diclofenac potassium was not less than 80% in 60min.Total volume for dissolution media was 900ml in each basket. During dissolution studies of all brands, 5ml sample solution were withdrawn at multiple time intervals of 10, 15, 20, 30, 45 and 60min. All collected samples were filtered through filter paper. Make a suitable dilution of each sample and analyze the released amount of drug during specified period of time, in dissolution media. Quantification of released drug conducted by taking absorption at UV-VIS Spectrophotometer. The same dissolution medium was used in preparation of standard solution having same concentration [19].

3. RESULTS AND DISCUSSION

In physicochemical evaluation, test for uniformity of weight is conducted to confirm the presence of uniform amount of API in each tablet. The test was conducted for all seven brands RB1 to RB7. Result of evaluations depicted in Table 1, revealed that the consistency of weight of all the brands was in the specific limits provided by the official reference books for uniformity of

weight, as any brands was not differed and falls under ±5% from the mean value as shown in (Table 1) [20]. Time taken by a tablet to break into their respective granules and broken granules must pass through mesh is called disintegration time, the test is important as it imparts great effect on drug dissolution profile. All studied formulation subject to conduct the test for disintegration. The results obtained from disintegration studies showed that time obtained for RB1-RB3 (film coated) brands was less than six minutes while the disintegration time obtained for RB4-RB7 (Sugar coated) brands was less than eighteen minutes and complies with official specification for film and sugar-coated tablets. It is found that results of dissolution rate profile indicated that all of the brands i.e. RB1 to RB7 attained more than 75%. The dissolution result of brand RB1(99.16%) at 60 minutes found to be highest among all brands. The brand RB6 showed the minimum result (90.08%) (Table 2) [21].

In order to ensure the uniformity of drug distribution in each brand the assay has been conducted, obtained results showed that the spectrophotometric analysis of Diclofenac Potassium tablet for brand RB1 was 99.95% while the lowest assay content among the selected brands was 97.42% for brand RB7. The use of spectrophotometric analysis to all seven brands revealed that their assay values are within the range as specified in the official books i.e. USP (90–110%w/v).

Statistical Analysis

Test "t" with 95% confidence level for 10 degree of freedom was $t_{0.025\ (10)} = 2.228$. There is no profound difference in release profile of reference product and brands RB1, RB2, RB3, RB4, RB5, RB6 and RB7

Table 1. Physicochemical parameters of seven different brands

Brands	Manufacturer	Average weight of	Thickness (mm)±SD	Diameter (mm)	Disintegration Time (Min.)	Assay (%)

		Tablet (mg) ±SD		±SD		
RB1	Hilton Pharma	403±4.10	4.50±.010	9.75±0.10	04	99.95
RB2	Pliva Pharma	215±4.69	3.40±0.12	8.10±0.13	06	98.99
RB3	Biorex Pharma	180±4.08	3.35±0.15	8.00±0.12	05	97.50
RB4	Tabros Pharma	289±5.66	5.05±0.18	7.55±0.10	15	99.30
RB5	Batala Pharma	222±3.56	4.05±0.11	8.20±0.11	18	98.78
RB6	QueperPvt, ltd.	260±5.27	4.65±0.13	8.35±0.13	17	99.11
RB7	Jawa Pharma	210±3.80	3.50±0.14	8.00±0.10	16	97.42

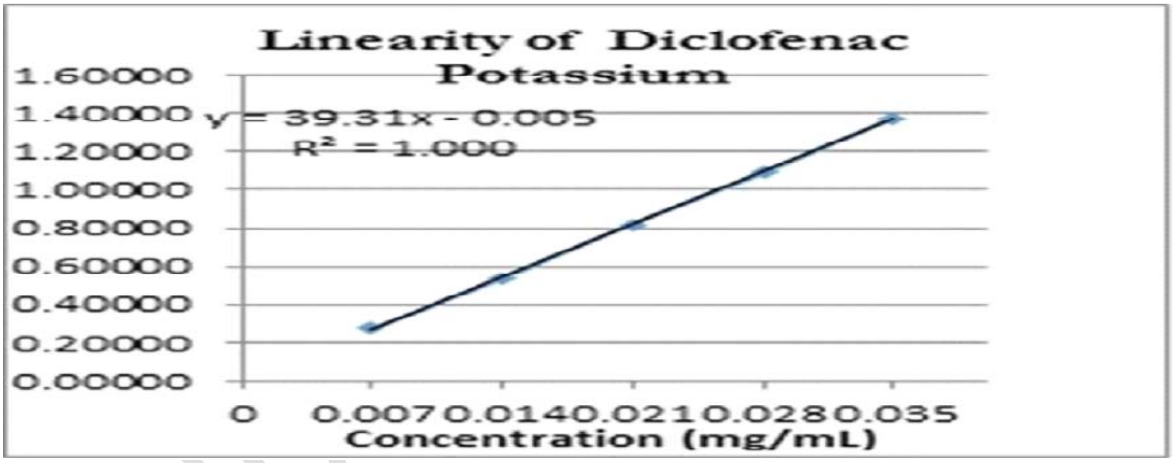

Figure 1. Standard curve of Diclofenac Potassium

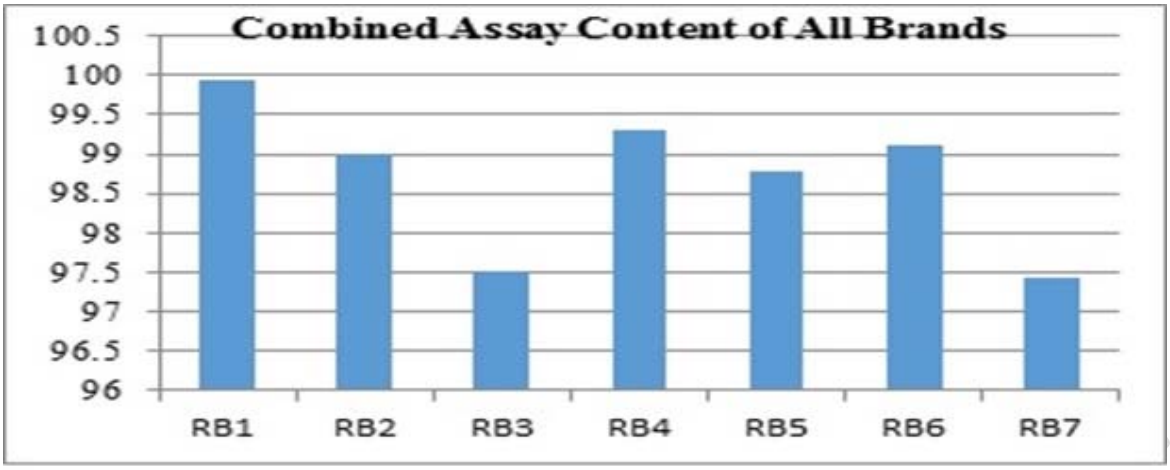

Figure 2. Assay content of All Brands

Table 2. Dissolution data of seven brands of diclofenac potassium 75mg tablets

Brand	Dissolution (%)					
	10min	**15min**	**20min**	**30min**	**45min**	**60min**
RB1	50.13	60.21	72.53	80.53	93.57	99.16
RB2	48.20	59.35	78.40	89.40	90.31	94.64
RB3	55.72	66.69	75.80	86.80	88.62	94.03
RB4	30.16	40.18	61.13	70.13	75.16	91.31
RB5	27.08	38.02	49.66	58.66	76.63	93.75
RB6	28.76	37.59	48.71	57.71	84.59	90.08
RB7	28.60	39.15	40.23	59.23	82.27	91.11

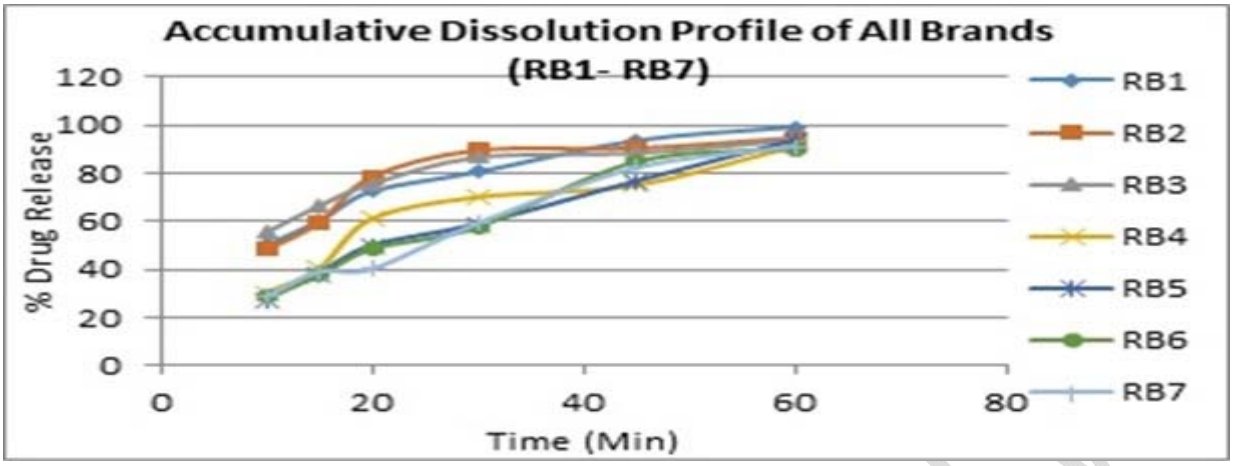

Figure 3. Accumulative Dissolution Profile of All brands (RB1-RB7)

Table 3. Mean difference between reference and test batch

Brand	M	SD	CV	tex	Mean Difference	Standard Error
RB0	75	0	0	0	0	0
RB1	76.02	18.95	24.95	0.514	3.98	7.73
RB2	76.72	18.89	24.62	0.426	3.28	7.71
RB3	77.95	14.67	18.82	0.343	2.05	5.98
RB4	61.35	22.74	37.06	2.09	18.65	9.28
RB5	57.3	24.68	43.07	2.25	22.70	10.07
RB6	57.90	24.87	42.95	2.176	22.09	10.15
RB7	56.76	25.35	44.66	2.24	23.24	10.34

In present study physicochemical parameters of different commercial brands of diclofenac potassium 75mg tablets were evaluated. Tablets of all brands were purchased locally from different drug stores in Nawabshah, Sindh province of Pakistan. Obtained formulations were evaluated by using tests in order to define their quality in respect of Physical and chemical

parameters. All used products were in their shelf life during evaluation. In present project quality of tablets has been determined by conducting quantitative with qualitative means of evaluation. The qualitative evaluation includes organoleptic evaluations of tablets i.e. appearance, color and shape, this observation conducted optically. The quantitative evaluations are uniformity of weight, diameter, thickness and chemical content determination, further in-vitro evaluation of solid dosage forms are disintegration and dissolution tests. The uniformity of weight of all brands was in range of official specification and none of the brands deviated by from official limit, results are shown in Table I. The results of weight variation study revealed that all tables with in each brand comply with prescribed official limits.

In-vitro evaluations are conducted to define the in-vivo performance of brand and to develop in-vivo, in-vitro correlation. Assay content was conducted to ensure the uniform distribution of API in each dosage form. Obtained results showed that the spectrophotometric analysis of diclofenac potassium tablet for brand RB1 was 99.95% while the lowest assay content among the selected brands was 97.42% for brand RB7. The assay content comes in range stated in official book USP (90–110%w/v) (USP, 2017). Results of assay content are computable with study conducted by Huma, Shoaib, Zafar, 2014 [21]. The performed comparative evaluation of diclofenac potassium 75 mg tablets available in market of Pakistan. All selected brands were subjected in-vitro disintegration study, because disintegration time impart significant effect on bioavailability. From finding of this test it can conclude that, all the brands RB1-RB7 qualify the disintegration test and results shown in Table I. The B.P. 2017 specifies 30 minutes for film coated while sixty minutes for sugar coated tablet.

The ability of all brands for disintegration during the time stated limit, this indicates that the drug will show good break down of product in the shape of disintegration in the gastrointestinal tract.

Hence, the tablet may have broken down to facilitate release of active pharmaceutical ingredients into the gastrointestinal fluid, this usually has a direct effect on the dissolution and bioavailability of the drugs. The USP 2017 specifies that not less than 75%w/w labeled content should have dissolved after 60minutes. The obtained outcome during dissolution study of diclofenac potassium tablets elucidate that all of the brands (RB1 to RB7) achieved this specified concentration at 60minutes result of study are number in Table2. Initially release of brands RB4-RB7 was low as compare to brands RB1- RB3 this slow release due to excipients available in sugar coating layer. Sugar coating contain seal coat and talk which is present in major proportion after sugar, hydrophobicity of seal coat and talk provides a shielding effect to dissolution media, which ultimately slow down the release of drug. The result of dissolution study is in good agreement with Petrone, 2014 and Huma et al., 2014 [22] they conduct study on dissolution profiles of diclofenac potassium tablet from Argentinean market.

As obtained result are satisfactory and falls in specified range, so it can predict from in-vitro study brands may exhibit good in vivo bioavailability profile. On bioavailability profile of tablet dosage forms as it can be used to predict the drug release pattern in vivo, the dissolution rate has been described to have a straight effect. Although bioequivalence studies would be required to describe clinical conclusions. One of the other objectives of this study was to provide a simple, less expensive and reliable analytical technique, and to give proof that the locally available brands are of good physical and chemical character. The feasibility of assay method for determination of Diclofenac Potassium tablets was confirmed by applying the method to seven brands of the drug. All of the brands (RB1 to RB7) gave values that ensure to the U.S.P specification of Diclofenac Potassium content. Results of applied t test showed that release profile of all brands not deviate from reference product, because of that all brands are equal in

variance. These release behaviors may be attribute toward the fact that all the pharmaceutical companies working in Pakistan, using same type of excipients and same technique for preparation of tablets.

4. CONCLUSION

This work determined the quality parameters of seven Diclofenac Potassium 75 mg tablets with weight variation, thickness, diameter, disintegration, dissolution and Assay of active pharmaceutical ingredient. During study it was observed that all brands of Diclofenac Potassium satisfied the Pharmacopoeia limits in respect to in vitro dissolution. These in vitro studies can be efficiently used to evaluate quality of commercial tablets. Further bioequivalence and clinical studies need to evaluate completely. Results of present evaluation can conclude that; patients can safely change from one brand to another brand containing diclofenac potassium 75 mg. Pharmacists must be involved to select the proper alternate brand.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

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