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COMPARISON OF DRUG RELEASE PROFILE OF DIFFERENT BRANDS OF DICLOFENAC POTASSIUM

Ghulam Murtaza[1*], Haroon Khan[2], Nisar Ahmad Shahwani[1], Nizam Baloch3,Ghulam Razaque[1],Tahira Bano[1], Noman Ul Haq[1], Ijaz Agha[1], Sohail Riaz[1]

[1]Faculty of Pharmacy, University of Balochistan Quetta, Pakistan

[2]Faculty of Pharmacy, Gomal University,D.I.Khan (KPK) Pakistan

[3]Department of Chemistry,University of Balochistan,Quetta.

Abstract:

Diclofenac Potassium is most commonly used analgesic. To analyze the quality of seven market brands of diclofenac potassium the present study was designed. These seven brands of Diclofenac potassium tablet formulation was manufactured by various pharmaceutical companies. To evaluate their quality these different brands of tablet were checked for varies parameter like disintegration time, weight variation, friability, hardness and dissolution profile by using standard techniques. The results obtained were compared with the standards and all the market brands of diclofenac gave excellent disintegration, hardness, weight variation and friability result. Among all the brands the multinational companies' products showed comparatively better results. The release pattern of diclofenac potassium different brands was within 45 minutes and purity range was 80% to 101%. All the results were within limit and were found satisfactory. Therefore it can be concluded that all the diclofenac potassium different brands that are available in Pakistan fulfill the USP specification for quality control analysis.

Key words: *Quality control, weight variation, Disintegration, Hardness, Release profile.*

Corresponding author:

Ghulam Murtaza,

MPhil Scholar,

Faculty of Pharmacy and health sciences,

University of Balochistan Quetta, Pakistan

(nizam_dua200857@yahoo.com)

QR code

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INTRODUCTION:

Stability study is a very critical factor in the research and development of any drug product. The purpose of the stability testing is to investigate environmental changes i-e Temperature, light, humidity which can effect and may cause changes in factors such as moisture, PH, oxygen, which may influence the quality, safety and efficacy and is liable to change during storage. During well designed stability study the drug Compound should be kept in open atmosphere or in undignified stress conditions such as moisture, PH, oxygen, temperature, humidity and light. Stability study is very helpful for giving the expiry of the drug product, process development and validation, Method development and validation, shelf life of the drug product and susceptible storage conditions, which make it easier for future manufacturing and packing of the drug product in suggested environmental conditions [1].

Diclofenac, a phenyl-acetic acid derivative is a non-steroidal anti-inflammatory drug (NSAID) with analgesic anti-pyretic properties. It is used mainly as the sodium salt for the relief of pain and inflammation in various conditions. NSAIDs mainly inhibit the bio synthesis of prostaglandins. These are released whenever the cells are damaged. They appear in inflammatory exudates[2]. It inhibits cyclooxygenase 1 and 2 activity, hence reducing the production of prostaglandins and thromboxane associated with pain and inflammation. Diclofenac sodium also reduces the arachidonic acid bioavailability and appears to reduce intracellular concentrations of free arachidonate in leukocytes [3]. It has an unpleasant taste and causes gastric irritation [4].

MATERIALS AND METHODS:

Materials

Different chemicals were used in this research work: Sodium Hydroxide (NaOH) (Fluka,Germany),Monobasic Potassium Phosphate (Merk, Germany) and Diclofenac Potassium (gifted by Drug Testing Laboratory, Peshawar, Pakistan).These chemicals were of analytical grade and were used in this research work without any Further processing or purifications. The different brands were purchased from local Pharma markets as given in Table 1.

Instruments/ Equipments

Different instruments used were: UV-Visible spectrophotometer Model No. 1610 Shimadzu, Japan, stability chamber (Model RI-201H. Denmark), Friabilator, and hardness tester (Erweka, Germany).electronic digital balance (Shimadzu, Japan), Pharma Test dissolution apparatus Germany, pH-meter (Denver, USA), disintegration apparatus.

Method

Construction of Diclofenac Potassium Analytical Curve50 ml solution was taken and diluted with phosphate buffer to obtained 1st dilution and this solution was containing 0.2mg of diclofenac potassium. In these way different concentrations dilutions were prepared from the stock solution. From the 1st dilution 50 ml was taken and with buffer it was diluted up to 100ml. The drugs contain in this solution was 0.05mg. 3rd, 4th, 5th dilutions were made in the same way. Each of the respective dilutions containing 0.25mg, 0.0125mg and 0.00625 mg the drug.At fix 276nm of wave length the absorbances of each dilution were determined in triplicate spectrophotometrically.

Table 1: Different market brands of Diclofenac Potassium

S.NO	Brand Names	Pharmaceutical Company
1	**CAFLAM ®**	NOVARTIS PHARMA (PAK) LTDKARACHI
2	**ANTIFLAM®**	WILSHIRE Pharma (PVT) LTD LAHORE
3	**DIC-P®**	SHAHEEN PHARMACEUTICALS SWAT
4	**DICLOKALIUM ®**	ZAFA PHARMACEUTICALCOM (PVT) LTD
5	**DP-MED®**	MEDICRAFT PHARMACEUTICALS (PVT) LTD
6	**GLIZ-K ®**	GlITZ PHARMA (PAK) LTD ISLAMABAD
7	**ARTINIL-K®**	(Global Pharmaceuticals Islamabad Pakistan)

Physical Quality Control Tests

By using Friabilator 20 tablets of each type of market brand of diclofenac potassium friability teat was performed. First of all initial weight of 20 tablets were find out and mark as W1 then in a Friabilator each bran of tablet was place separately. At 100rpm the Friabilator was run for 4minutes. And again the weights of tablet were noted. The limit which is acceptable for friability is < 0.8%[5].

In the hardness tester apparatus diclofenac potassium different brands tablet were subjected. In the hardness tester apparatus 10 diclofenac potassium of each type tablet were used. And for each type of brand of tablet their mean was calculated. 5-10kg/cm2 is the acceptable limit of hardness[5].

With the help of digital electronic balance, each type of tablet weight of diclofenac potassium was determined separately of individual tablets. Each type of brands 0f 20 tablets average weight was determined. The weight variation of tablet in USP acceptable limit is 130.325±75 (USPNF 24, 2000)[6]. Different tablet brands of diclofenac potassium USP method-I was used to determine the disintegration time. From each brand 6 tablets were selected and place one tablet in each of six baskets and rack of disintegration apparatusfor 5 min to dissolve film coating and then using 0.1 N NaOH as disintegration medium was used to carry out the disintegration time test.

In vitro evaluation

By the use of Pharma dissolution test apparatus and accordance with the USP method-1, Dissolution studies were performed. And in the respective basket the tablets were placed and with the Pharma test dissolution apparatus in each six stations the baskets were mechanically brought down. Each of the satiation having phosphate buffer 900ml and (pH 6.8). As a replacement solution the samples were taken each of 5ml and into station phosphate buffer pH 6.8 was added. By passing through a member filter having size of (0.45µ) to filter the samples. The by using spectrophotometer Shamadzu Japan at fix wavelength 276nm analyzed the samples and from the standard curve their percentage release was calculated.

Chemical Assay

In a 100ml of volumetric flask diclofenac potassium 100mg was taken and with the 0.1NHCL the volume was made up to 100ml. After sonication of 20minutes it was then filter. After preparation of the above solution 1ml of solution was taken and with 0.1NHCL it was diluted. Then at fix wavelength 276nm the solution was spectrophotometrically analyzed. The absorbencies of standard solution and sample solution were determined spectrophometrically at fix wavelength 276nm. For this purpose 5 ml of solution was taken from standard and 5 ml was taken from sample.

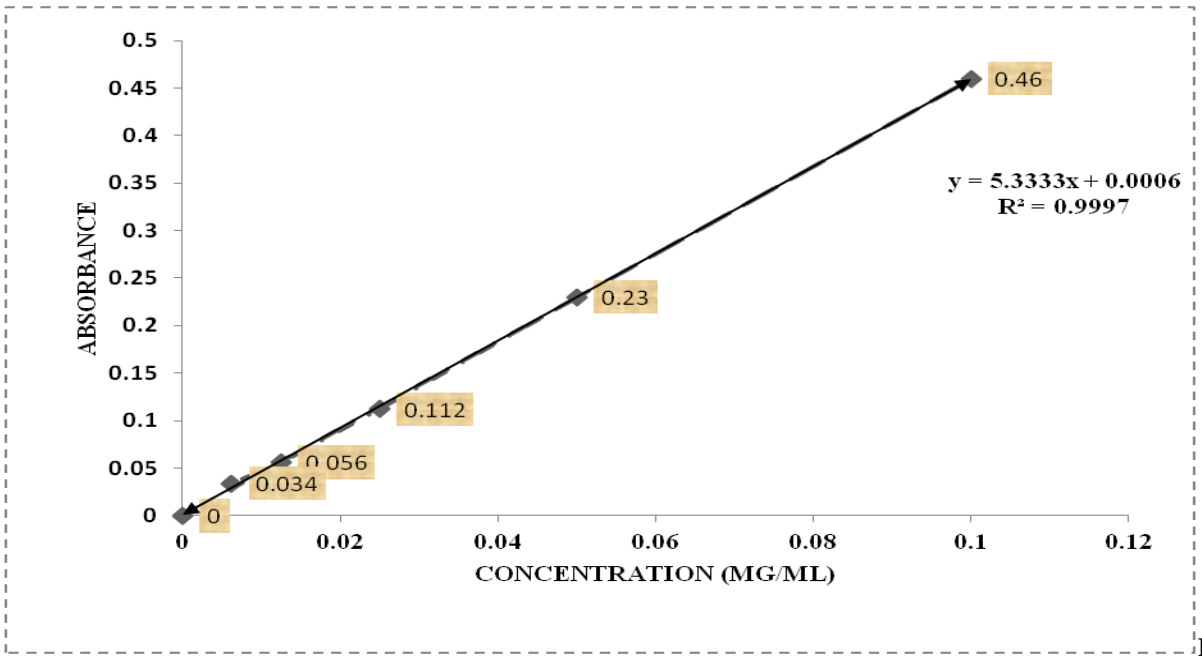
RESULT AND DISCUSSION:

Analytical Curve of Diclofenac Potassium

In the table No.2, the respective absorbencies of different dilutions concentrations are shown. When on Y-axis abdornaces are plotted and on the X-axis concentrations are plotted resulted the formation of straight line showing that a direct proportionality between the two parameters. The coefficient of determination) R^2 value was 0.997 and the equation of regression (y=5.3333+0.00006) result shown in the table No.2 and figure No.1.

Table 2: Different dilutions mean absorbance of respective concentration

S.No	Concentration	Abs-1	Abs-2	Abs-3	Mean Abs
1	0.1	0.48	0.47	0.46	0.47
2	0.05	0.23	0.25	0.24	0.24
3	0.025	0.115	0.113	0.114	0.113
4	0.0125	0.056	0.055	0.057	0.057
5	0.00625	0.037	0.033	0.35	0.035



Figu

Fig 1: Analytical Curve of Diclofenac Potassium

Drug Release Profile

In Pakistan pharmaceutical market present the different brands of diclofenac potassium drug release profile was determined after purchase means at zero time and after six months Exposer to accelerated condition of stability at 40C±2C and 75%±5%.. Diclofenac Potassium distinctive tablet brands discharged the medication 98.3, 99, 98, 99%, 98.1, 98.66 and 98.89 in day and age of a hour, when concentrated subsequent to taking from market as given in figure no. 2 and 3. The brands discharged the medication 97.9, 98.87, 96.2, 97.9, 97.52, 98.1 and 96% in a hour following 3 months presentation to quickened dependability condition as given in figure no. 4 and 5. Following 6 months presentation to quickened strength condition, the diverse brands discharged the medication 97.3, 95.6, 97.1, 92.4, 94.9, 94.77 and 92.98% in a hour as appeared in figure no. 6 and 7. The outcomes gone in worthy cutoff points given in authority detail USP-NF-24 (USP-NF-24, 2000).

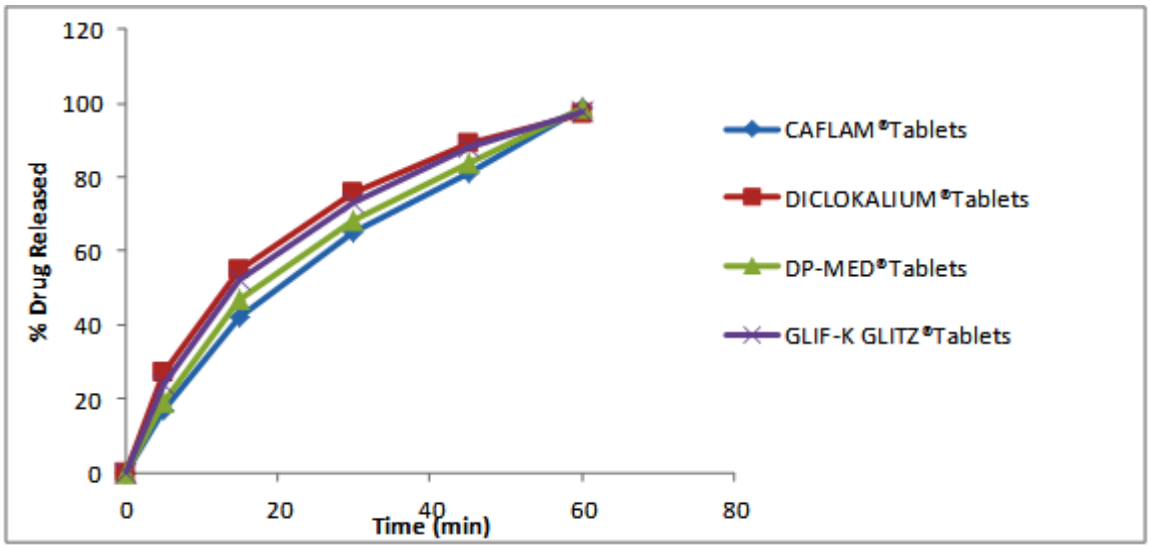


Fig 2:At Zero Time,Diclofenac Potassium Market Brands (Caflam®, Diclokalium®, DP-Med® and Glif-K® tablets) Drug Release Pattern

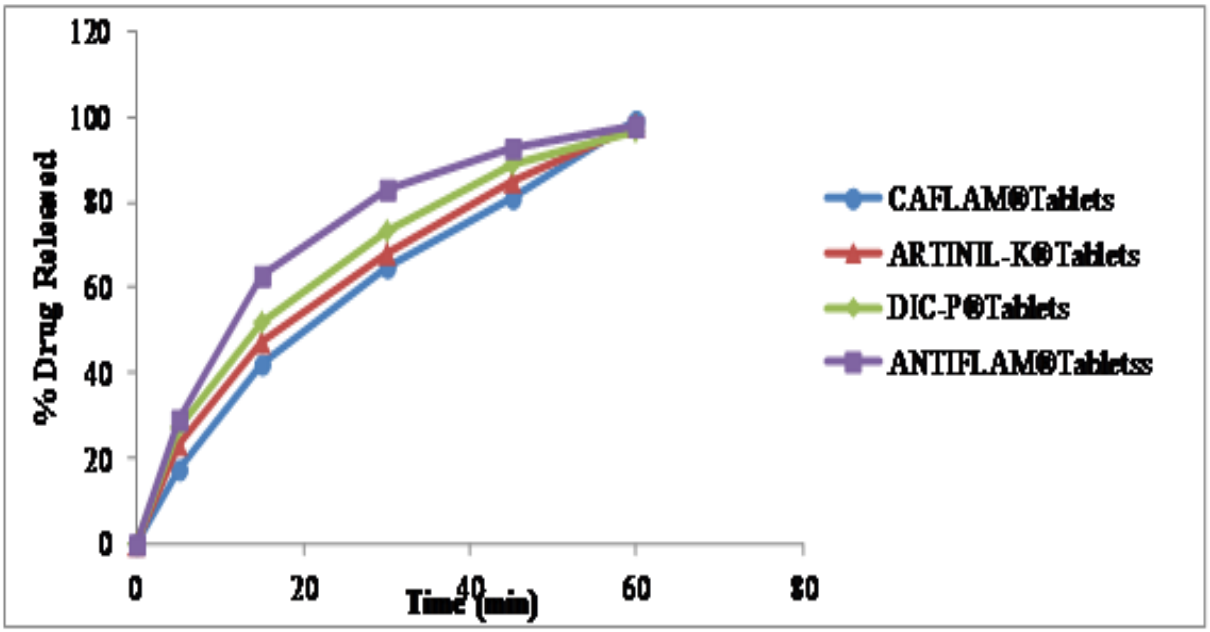


Fig 3: At Zero Time, Diclofenac Potassium Market Brands (Caflam®, Artinil-K®, Dic-P® and Antiflam® tablets) Drug Release Pattern

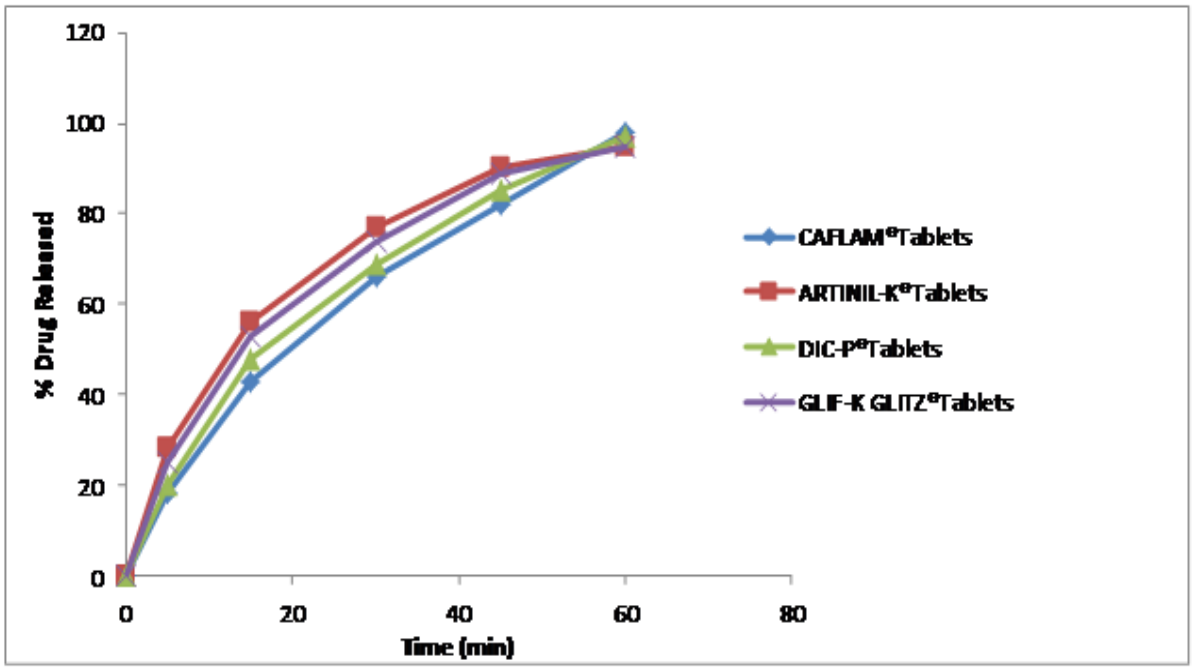


Fig 4: After 3 month Exposer to accelerated stability condition of Diclofenac potassium Tablets brands (Caflam®, Artinil®, Dic-P® and Glif-KGlitz® tablets) Drug release pattern

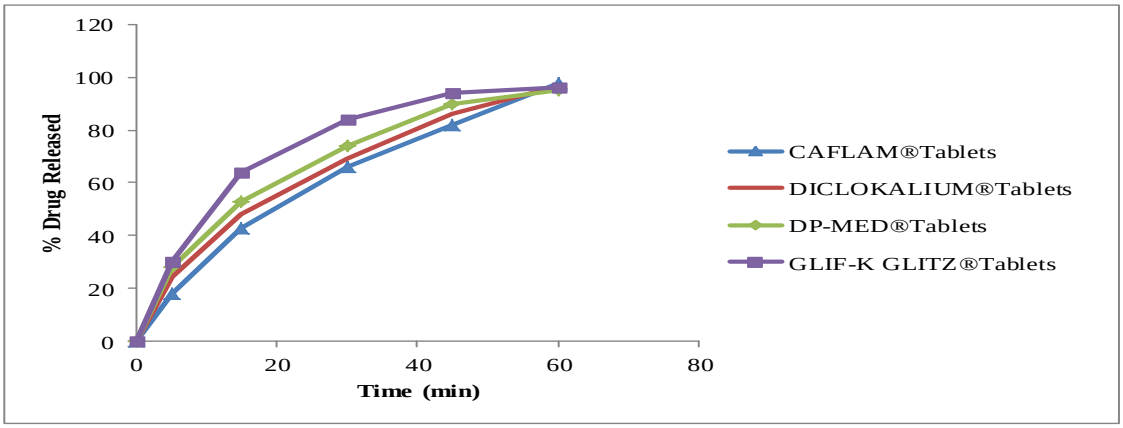


Fig 5: After 3 month Exposer to accelerated stability condition of Diclofenac potassium Tablets brands (Caflam®, Diclokalium®, DP-Med® and Glif-KGlitz® tablets) Drug release pattern

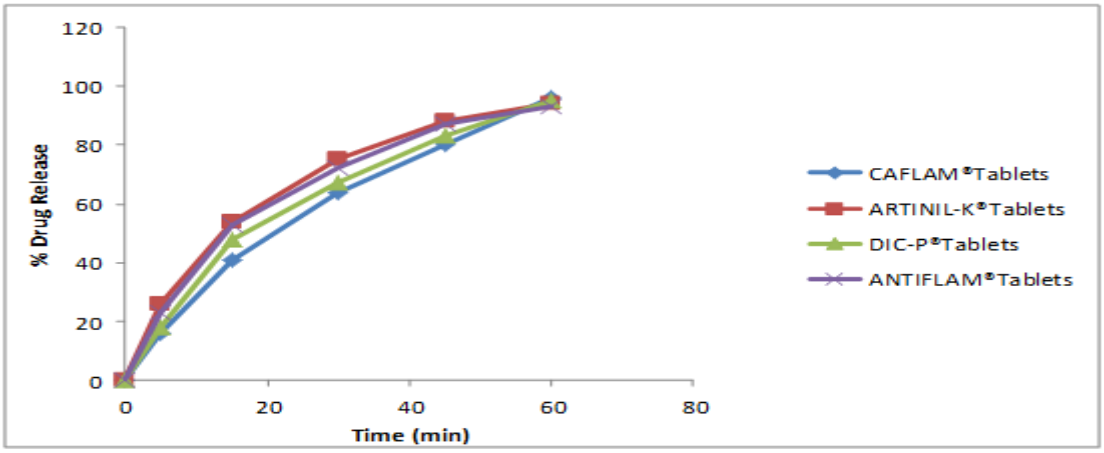


Fig 6: After 6 month Exposer to accelerated stability condition of Diclofenac potassium Tablets brands (Caflam®, Artinil®, Dic-P® and Glif-KGlitz® tablets) Drug release pattern

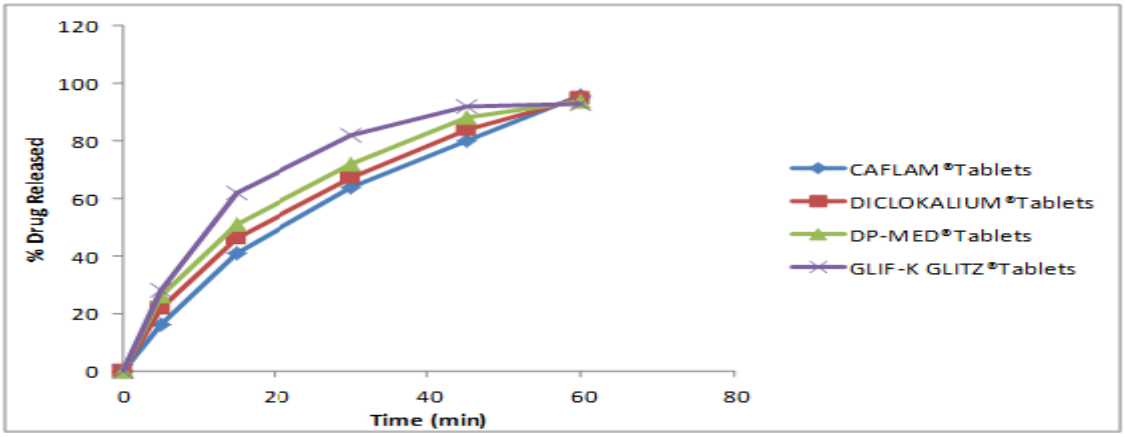


Fig 7: After 6 month Exposer to accelerated stability condition of Diclofenac potassium Tablets brands (Caflam®, Diclokalium®, DP-Med® and Glif-KGlitz® tablets) Drug release pattern

Before And After Exposer To Accelerated Stability The Percentage Purify.

Before exposure to accelerated condition the percentage purity of Diclofenac Potassium different market brands was limit from 99-101. After expose the brands to three month period to accelerated stability conditions, percentage purity was slightly decrease and it limit was found from 97.98-99.97. The percentage purity after expose to 6 month accelerated conditions were found ranged from 97-97.95 and there was found a slight decrease but their result was within the official monograph for percentage purity given in the USPNF-24 (USPNF-24, 2000) that the limit of percentage purity of diclofenac potassium range from 98-101%. The results are given in table No.3-5.

Table 3: Before Exposure to Accelerated Stability Condition Different Brands of Diclofenac Potassium Percentage Purity

S. No	Brand names	Before expose to accelerated stability condition the percentage purity
1	CAFLAM® Tablets	101
2	ARTINIL-K® Tablets	98.55
3	GLIF-K GLITZ® Tablets	97.73
4	DIC-P® Tablets	100.04
5	DICLOKALIUM® Tablets	98.44
6	DP-MED® Tablets	99.1
7	ANTIFLAM® Tablets	100

Table 4: after three month Exposure to Accelerated Stability Condition Different Brands of Diclofenac Potassium Percentage Purity

S. No	Brands Names	After 3 month expose to accelerated stability condition the percentage purity
1	CAFLAM® Tablets	99.98
2	ARTINIL-K® Tablets	97.99
3	GLIF-K GLITZ® Tablets	99.91
4	DIC-P® Tablets	99.55
5	DICLOKALIUM® Tablets	100
6	DP-MED® Tablets	99.66
7	ANTIFLAM® Tablets	100

Table 5: After 6 month Exposure to Accelerated Stability Condition Different Brands of Diclofenac Potassium Percentage Purity

S. No	Brands Names	After 6 month expose to accelerated stability condition the percentage purity
1	CAFLAM® Tablets	99.79
2	ARTINIL-K® Tablets	97.96
3	GLIF-K GLITZ® Tablets	99.33
4	DIC-P® Tablets	99.65
5	DICLOKALIUM® Tablets	97.88
6	DP-MED® Tablets	99.23
	ANTIFLAM® Tablets	100

Table 6: Test tablets formulation and reference standard dissolution profile comparison

Comparison of standard and reference	f_2 values
CAFLAM® Tablet	80
CAFLAM® Tablet	59
CAFLAM® Tablet	60
CAFLAM® Tablet	71
CAFLAM® Tablet	83
CAFLAM® Tablet	70

Similarity Factor (f2)

For the determination of drug release pattern similarity factor (f2) was applied between the standard reference (Caflam® Tablet) and other tablet brands of Diclofenac Potassium Dissolution taken test formulations and their dissolution profile was compare with dissolution pattern of Caflam tablet. The limit of the similarity factor (f2) is between 50-100 .By applying similarity factor (f2) the value between this 59-83 indicates that the two dissolution profiles between test formulation and standard reference Caflam are similar. The results are showed in the table No.6.

DISCUSSIONS:

In the official specification of both of physical and quality control analysis the result of market brands table of diclofenac potassium results were within the acceptable range which confirms the finding report of other authors (Khan *et al*,.2013)[6]. Percentage purity (chemical assay) and in-vitro drug release were also determined when it was exposing to accelerated conditions i.e. (40C±2C and 75C±5% RH) and it was found that there is no significant effect on the brands chemical stability and t-test indicates that the level of significance was less than 0.05 which shows that the brands taken from market may good quality and the results obtained are same as shown in the standard monograph. Other authors (Muaz *et al.*,2009) [7] also studied ciprofloxacin hydrochloride post market quality analysis and evaluated the physicochemical features for example chemical assay ,friability, disintegration, weight variation, dissolution and hardness. According to authors when dissolution result are not within the specification then there is no need of in vitro study [8].The author found that specifications given in the USP-NF-25 were not fulfilling the required limit. It was found that they were pharmaceutical equivalent and could be used interchangeably [9]. The author studied another six different brands and found that they could not be used interchangeably for innovator product because in the official monograph such as USP and BP specification did not match with the result studied and statistically they were not significant in their physicochemical characteristics [10]. The specification given in USP, according to those specifications the Chiloquin market brands were investigated. And within the specification author found that one brand was not found within the official monograph[11]. Diclofenac potassium market brand in the present study showed stability in their physiochemical characteristics and can be used with caflam Tablet a innovator product interchangeably.

CONCLUSION:

Diclofenac potassium different market brands were purchased from the local market and their physicochemical characteristics were analyzed and then it was subjected to accelerated stability condition (40C±2C and 75±5RH) to study their affect on the chemical assay and dissolution test. After subjected to the accelerated stability condition the selected brands showed good quality when their physicochemical characteristics such as friability, disintegration, weigh variation, percentage purity and drug release profile. For the determination of dissolution profile equivalency similarity factor (f2) was applied and the CALAM Tablets dissolution profile was taken as standard reference and the f2 value showed that the similarity between the dissolution profiles with standard reference CAFLAM tablets dissolution profile.

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