

Dexibuprofen: Statistical assessment of drug release kinetics and investigative quality perspective

Anas M Hanif^{1,2}, Ali Akbar Sial¹, Huma Ali^{2**}, Farya Zafar³,
Mirza Tasawar Baig¹, Rabia Bushra⁴, Maqsood Ahmed Khan¹,
Amber Nawab⁵, Omer Mustapha⁴ and Shumaila Shafique⁴

¹Faculty of Pharmacy, Ziauddin University, Karachi, Pakistan

²Institute of Pharmaceutical Sciences, Jinnah Sindh Medical University, Karachi, Pakistan

³Department of Pharmaceutics, Faculty of Pharmacy and Pharmaceutical Sciences, University of Karachi, Karachi, Pakistan

⁴Dow College of Pharmacy, Dow University of Health Sciences, Karachi, Pakistan

⁵Faculty of Pharmacy, Jinnah University for Women, Karachi

Abstract: Healthcare professionals including physicians and pharmacists have been trying since long to come across and work out regarding the issue of generic alternatives, which is highly affected by factors like therapeutic efficacy, cost effectiveness, aesthetic and elegant appearance and implementation of packaging number over the drug product. However, the community pharmacist professionals are also facing difficulty in making decision regarding selection and dispensing the most efficacious brand to the patients. In this regard, the initiation of recent approaches for the development of amenable drug products has led to evolve the concept of generating new avenues for achieving higher patient compliance. Hence, the objective of this study was to evaluate the quality attributes and make comparisons regarding different brands of *Dexibuprofen* available in market of Karachi, Pakistan. The study is based on evaluation of physical chemical parameters of five different brands. Moreover, a comparative dissolution profile of selected brands of *Dexibuprofen* was also performed by applying numerous approaches. DEX-1 was selected as reference while DEX-2-DEX-5 was selected as test brands. Results of all the selected brands met all the compendial requirements. Interpretation of the entire aforementioned test was evaluated using model independent, model- dependent and one – way ANOVA. The work presented in this study has been designed to provide quality standard products easily accessible in Pakistani market.

Keywords: *Dexibuprofen*, Physicochemical, Similarity, Quality, Pakistan, Brands

INTRODUCTION

Drug delivery through oral route is the most challenging, demanding and preferred among all route of administration that has gained considerable significance approximately 50-to 60% owing to its numerous advantages such as ease of administration, reduction in cost, precise dose delivery, enhanced patient compliance and being pain free (Masih *et al.*, 2017). The quality of a pharmaceutical drug product is of paramount importance, depends on the initial development phases, and thus may compromise the overall quality of the formulated finished drug product. Therefore, to evaluate that the drug product includes the desired quality attributes required in any formulation, various quality control parameters are assessed periodically (Jakaria *et al.*, 2016). Several drug products available in the market that do not meet the criteria of acceptance may result in producing serious health issues which includes the minor undesirable affects, resistance, and may sometimes lead to critical conditions and death as well (Sahle *et al.*, 2012). Therefore, it is a matter of great concern to ensure that the drug product must maintain the safety and efficacy

throughout the shelf life period in order to achieve a homogenous effect of desired characteristic or features (Ahmed *et al.*, 2012). A single generic drug product in various strengths and prices is readily available in the market with different brands of renowned pharmaceutical companies. Quality control parameters of each of these brands are taken into consideration in making assessment related to therapeutic outcome and approaches to enhance the patient compliance. In case of over the counter medicines (OTC) the elements of quality added differ from one manufacturing company to another (Qureshi *et al.*, 2016).

Dexibuprofen a derivative of racemic form of ibuprofen chemically known as (2S)-2-[4-(2-methylpropyl) phenyl] propionic acid, is a newly derived non-steroidal anti-inflammatory agent that is known to manage alleviated conditions of pain and inflammation by blocking the synthesis of prostaglandins (Parvin *et al.*, 2014; BNF, 2016). Therapeutically this drug is widely utilized in terms of producing analgesic, anti-inflammatory and antipyretic activity than the conventional NSAIDS recommended by the physicians currently. Moreover, physicians in the treatment of musculoskeletal disorders, arthritis of knee and joint, post-operative pain and dental pain clinically prescribe it. This agent is also indicated in

*Corresponding author: e-mail: humaali80@live.com

reducing fever (Rehnasalim *et al.*, 2013; Drug Bank 2017).

In various Asian inhabitants, pharmaceutical formulations of similar generic may contrast in their quality points of view. Such moieties offer elective decisions in particular social or healthcare setups with differential cost. Selection of such items from physician perspective is generally argued with medication providence gave by the drug maker and generally take similarity details of interest of multisource items. Moreover, pattern of drug release of such formulations likewise is considered essentially vital in deciding the batch consistency of such products. This study was designed to determine the release pattern of various *dexibuprofen* formulations available in Pakistan market. Furthermore, the intention of this study was to assess various quality attributes and similarity potentials of these products. No such data regarding *dexibuprofen* has been reported yet.

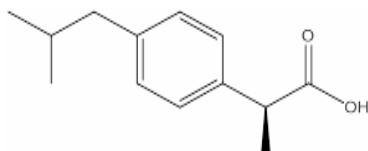


Fig. 1: Structure of *Dexibuprofen*

MATERIALS AND METHODS

Pure *dexibuprofen* was gratefully gifted from Tabros Pharma (Pvt.) Ltd. Pakistan. This study was based on evaluation of five different brands of *dexibuprofen* (200 mg) commercially available in Pakistani market. The test samples were purchased from various pharmacies across the city. In order to maintain the ethical concerns throughout the study the samples were abbreviated as DEX-1, DEX-2, DEX-3, DEX-4, DEX-5. The purpose of coding is to ensure that the identity of the manufacturer was kept blind and confidential. Buffer solutions of pH (6.8 and 7.2) were prepared using potassium dihydrogen orthophosphate (Merck, Germany) and Sodium hydroxide (BioM Laboratories USA).

Quality evaluation tests

Dexibuprofen sample of both tests and reference drug product containing 200 mg were evaluated by various quality control parameters i.e. hardness test (OSK Fujiwara, Ogawa Seiki Co. Ltd., Tokyo, Japan), weight variation test (AUW-220, UNI Blog, Shimadzu, corp.) (B.P, 2013).

However, thickness was measured by Vernier calliper (B.P, 2013) and disintegration time was noted by disintegration test using USP <701> Basket Rack Assembly (Erweka ZT-2 Husenstamm, Germany) (USP, 2013). For Percent recovery (assay) randomly twenty tablets were selected from each brand containing 200 mg were weighed individually, crushed in pestle mortar and

the amount equivalent to average weight of tablet were shaken with methanol and kept in sonicator for 5 minutes. It is then filtered using Whatman Filter Paper No.41. Filtrate is diluted using buffer solution having pH 6.8 to obtain the required concentration 100 µg/mL. Finally, the absorbance was noted at 222 nm using UV- Visible spectrophotometer (UV-1800 Shimadzu Corporation Kyoto, Japan) (Pritesh *et al.*, 2011).

Dissolution profile comparison of dexibuprofen brands

Dissolution profile comparison of both reference (DEX-1) and test (DEX-2 - DEX-5) brands having similar strength i.e. 200mg were conducted using apparatus II (USP) at 50 rpm having capacity of 900mL using dissolution media i.e. phosphate buffer of pH 6.8 and pH 7.2 at 37±0.5°C. The quantity equal to 10mL of sample was drawn and replaced with fresh 10mL of the dissolution medium. Samples were collected at various time intervals i.e. 5, 10, 15, 25, 30, 45 and 60 min. The collected samples were filtered and analysed spectrophotometrically at 222 nm using UV- Visible spectrophotometer (UV-1800 Shimadzu Corporation Kyoto, Japan) (Pritesh *et al.*, 2011).

Approaches used for dissolution profile comparison of dexibuprofen

Model-Independent and Dependent Methods

Drug release profile involving the use of similarity and differential factors and different kinetic models such as First Order, Weibull model, Crowell cube root law Hixson – and Higuchi model (Maroof *et al.*, 2016) were used to establish the *in-vitro* release profile of selected brands using software DD-Solver® as “Adds in program” in Microsoft Excel™ 2010 (Microsoft Corporation, USA).

Data analysis procedure

ANOVA test with Tukey’s post hoc test and Dennett’s test were utilized to determine the release pattern of both test and the reference brand. All the statistical analysis was carried out by SPSS 20.0 (SPSS Inc) (Yuksel *et al.*, 2000).

RESULTS

Five selected brands of *dexibuprofen* tablet available in strength of 200 mg potency were procured from local pharmacy. Various pharmacopeia and non- pharmacopeia parameters of quality were performed and evaluated such as variation in weight, thickness, hardness, assay analysis, disintegration time and percent drug release. The data obtained through quality evaluation was analysed by model independent, model dependent (table 2 -5) and ANOVA methods. The result of all five selected different brands was obtained and found to be within the allowed limits. The Mean weights of test samples were calculated, DEX-2; 0.391±1.02 mg, DEX-3; 0.481±1.09mg, DEX-4; 0.422±1.06 mg; DEX-5; 0.446±1.08 mg and DEX-1; 0.62±1.09mg (Reference Brand) (table1). The mean thickness of test samples were measured using Vernier

Table 1: Assessment of Physico-chemical Parameters of *Dexibuprofen* Tablets 200mg (DEX-1-DEX-5)

Brands (200mg)	Thickness (mm)	Hardness (kg)	Weight (mg)	Disintegration time (sec/min)	Assay (%)
DEX-1	5.41±0.16	7.35 ±1.02	0.62±1.09	5	100.59± 0.42
DEX-2	4.73 ±0.11	3.61±0.08	0.391±1.02	13	98.99±0.97
DEX-3	4.65 ±0.05	3.71±0.08	0.481 1±1.04	10	99.67± 0.43
DEX-4	4.84 ±0.03	4.19±0.05	0.422±1.06	7	99.87 ±1.00
DEX-5	4.52 ±0.09	4.25 ±0.07	0.466±1.08	9	97.16±0.98

Table 2: Model Independent methods of *Dexibuprofen* Tablets (DEX-1 to DEX-5)

Reference & Test Brands	pH 6.8		pH 7.2	
	f_1	f_2	f_1	f_2
DEX-1 and DEX-2	6.80	64.28	4.14	68.47
DEX-1 and DEX-3	14.06	52.69	6.85	59.44
DEX-1 and DEX-4	5.41	62.31	7.98	55.47
DEX-1 and DEX-5	3.82	70.15	4.38	67.76

Table 3: *In vitro* release kinetics of *Dexibuprofen* 200mg Tablets at pH 7.2 and pH 6.8

Formulation	First Order		Higuchi		Hixson-Crowell		Weibull model		
	r^2	$K_1(h^{-1})$	r^2	$K_H(h^{-1/2})$	r^2	$K_{HC}(h^{-1/3})$	r^2	α	β
<i>Dexibuprofen</i> 200 mg Tablets									
pH 7.2									
DEX-1	0.9158	0.089	0.7847	10.446	0.9621	0.013	0.9808	5.271	0.701
DEX-2	0.9844	0.080	0.6906	10.819	0.9632	0.014	0.9946	8.562	0.852
DEX-3	0.9060	0.069	0.7565	10.312	0.9412	0.011	0.9768	6.284	0.696
DEX-4	0.9810	0.066	0.7313	11.041	0.9581	0.013	0.9889	10.336	0.861
DEX-5	0.9642	0.075	0.7969	11.138	0.9825	0.013	0.9852	7.900	0.806
<i>Dexibuprofen</i> 200 mg Tablets									
pH 6.8									
DEX-1	0.9696	0.052	0.8421	11.280	0.9759	0.011	0.9774	12.591	0.858
DEX-2	0.9716	0.044	0.8555	11.151	0.9569	0.010	0.9738	16.361	0.891
DEX-3	0.9952	0.034	0.9649	11.076	0.9940	0.008	0.9951	25.863	0.963
DEX-4	0.9874	0.046	0.8416	11.699	0.9728	0.012	0.9856	23.599	1.027
DEX-5	0.9863	0.056	0.8036	11.393	0.9746	0.012	0.9894	13.348	0.901

calliper as, DEX-2; 4.73±0.11 mm, DEX-3; 4.65±0.05 mm, DEX-4; 4.84±0.03; DEX-5; 4.52 ±0.09 mm. DEX-1; 5.41±0.16 mm, (Reference Brand) (table1). In this study DEX-1(Reference Brand) hardness was found to be 7.35 ±1.02kg, DEX-2 3.61±0.08kg, DEX-3 3.71±0.08kg, DEX-4 4.19±0.05 and DEX-5 at mean value of 4.25 ±0.07 (table1). Consequently, the release pattern of *dexibuprofen* from reference and test samples was evaluated. DEX-1 was selected as reference product on the basis of excellent physico-chemical features. DEX-2 showed the maximum % drug release of (101.9%) at pH 7.2, DEX-5 (96.9%) at pH 6.8. Furthermore, the study encompasses the comparison of DEX-1(Reference brand) with the test brands purchased from local market (DEX-2-DEX-5) by applying factor of similarity (f_2) and factor of dissimilarity (f_1). Values of f_2 at phosphate buffer pH 6.8 and pH 7.2 found to be in the range of (62 to 70) and (55 to 68) respectively (table 2). Similarly, values of f_1 at phosphate buffer 6.8 and 7.2 were found to be in the range of (6 to 15) and (4 to 7) (table 2). Results of f_2 and f_1 values were observed satisfactory for all the tests products.

Data representing the release profile of the tests samples was further explained in terms of numerous kinetic models as presented in tables (3&4). In this study all formulations followed Weibull kinetics with highest best fitted values followed by Hixson- Crowell model. For First-order kinetic model r^2 values at phosphate buffer of pH7.2 and pH 6.8 were found to be in the range of (0.9060-0.9844) and (0.9696- 0.9952) respectively (table 3). Two models namely Hixon Crowell cube root law and Weibull kinetics were most commonly utilized by formulation scientists and regarded as the efficient simulation models to predict *in-vitro* release pattern. In this study r^2 values for Hixon Crowell kinetic model using, phosphate buffer pH7.2 and pH 6.8, were found to be (0.9412-0.9825) (0.9728- 0.9940). Selection of model terms is detailed in table 3. Statistical assessment using one-way ANOVA (Post Hoc Tukey test) was carried out for both the test and the reference product as presented in table 5. The results revealed that no significant variation between tests and reference brands exists.

Table 4: Model selection criteria for kinetics drug release of *Dexibuprofen*

Models	Parameters	DEX-1	DEX-2	DEX-3	DEX-4	DEX-5
First order	SS	226.1545	53.5575	277.1786	74.0444	126.5926
	MSE	32.3078	7.6511	39.5969	10.5778	18.0847
	AIC	45.3697	33.8460	46.9973	36.4373	40.7278
	MSC	2.2246	3.9115	2.1146	3.7124	3.0790
Higuchi	SS	495.6611	911.3604	615.4407	896.8792	615.2557
	MSE	82.6102	151.8934	102.5735	149.4799	102.5426
	AIC	53.6471	58.5195	55.3787	58.3914	55.3763
	MSC	1.1899	0.8274	1.0669	0.9682	1.2480
Hixson-Crowell	SS	87.2473	108.2989	148.7385	139.9955	52.9397
	MSE	14.5412	18.0498	24.7898	23.3326	8.8233
	AIC	39.7500	41.4792	44.0175	43.5329	35.7532
	MSC	2.9271	2.9574	2.4871	2.82551	3.7009
Weibull	SS	44.1270	15.9829	58.6545	36.8791	44.8363
	MSE	7.3545	2.6638	9.7757	6.1465	7.4727
	AIC	34.2966	26.1722	36.5733	32.8612	34.4241
	MSC	3.6087	4.8708	3.4176	4.1595	3.8670

Table 5: Statistical evaluation of release profiles of *Dexibuprofen* 200mg Tablets

ANOVA						
Factors and medium of dissolution		Sum of Squares	df	Mean Square	F	Sig.
pH 7.2	Between Groups	16337.265	7	2333.895	202.071	0.000
	Within Groups	369.596	32	11.550		
	Total	16706.861	39			
pH 6.8	Between Groups	24110.397	7	3444.342	110.301	0.000
	Within Groups	999.255	32	31.227		
	Total	25109.652	39			
Formulations	Between Groups	0.000	7	0.000	0.000	1.000
	Within Groups	80.000	32	2.500		
	Total	80.000	39			

DISCUSSION

The study has been aimed to assess the quality evaluation parameters among different *dexibuprofen* tablets brands supplied by both local and multinational pharmaceutical companies of Pakistani market. All the selected brands reflected results within the allowed limits and hence assures all aspects of quality standards maintained during manufacturing. It is stated that variation in weight of tablets within same lot reflects non-homogenous distribution of excipients, incorrect ratio of excipients added and in fact the potency of the drug. In the present study conducted the results of all the test samples indicated the satisfactory results of weight variation (table 1). As none of the selected brand showed deviation of more than 5% from their means. A deviation above such pharmacopoeia limits indicates rejection and therefore leads too poor patient compliance (B.P, 2013). Since, weight variation test is not enough compendial parameter to ensure uniformity therefore; assay analysis was performed to check the actual labelled amount stated. The assay values of all the tablets were found to be within limits of (95-105%) (table 1). Bushra *et al.*, in the year

2014 evaluated several physical and chemical parameters of *Aceclofenac* tablets 100 mg. Arshad *et al.* assessed the quality attributes of various marketed brands of *Gatifloxacin* 200 mg tablets available commercially in Pakistani market (Arshad *et al.*, 2011). In our study, the selected tests samples met the official limit of hardness and thickness i.e., not more than $\pm 5\%$ range (table 1).

Disintegration time of all the five brands of *dexibuprofen* was noted to be (less than 15 min) and met the BP specifications) (table 1). Drug release assessment through *in-vitro* testing is considered as highly acceptable tool and depicts *in-vivo* drug product behaviour of pharmaceutical formulation. Thus, applying *in vitro* measures to determine testing of high quality standard of generic drug product available in drug stores serves as a valuable surrogate tool to further investigate the bioequivalence studies. Also biowaiver studies are also carried out using it which tends to decrease problems faced concerning regulatory issues of pharmaceutical industry. In the present study, the release of *dexibuprofen* from all tests samples was immediate release; and hence all the tests (DEX- 2 to DEX- 5) and reference (DEX- 1) met the

compendial requirement of drug release at pH 7.2 and 6.8 respectively (table 2).

The *in-vitro* dissolution release profile of a drug helps to establish a correlation and various modifications in different formulated products. However, it depicts the *in vitro* release profile more clearly than single time point drug release (Zafar *et al.*, 2015). Different formulation scientists reported the release kinetic pattern of sample and reference drug products by applying different mathematical approaches of drug model (Ali *et al.*, 2016). Since the *in-vivo* studies require more time, expensive and shows several ethical concerns. Thus, the two models namely model independent, model dependent methods were utilized, and statistical assessment using ANOVA was carried out to compare the release pattern and therapeutic equivalence perspective (table 3-5).

In the current study Higuchi, Hixon-Crowell cube root law, Weibull kinetic model and first order were used to quantify the kinetic model based data. Also, in order to establish a perfect correlation, model independent approaches by means of dissimilarity (f_2) and similarity (f_1) were calculated to compare and contrast among the tests and sample products. Zafar *et al.*, in 2015 compared release kinetic profiles using six commercial brands of Mefenamic acid tablets available in pharmacies using different dissolution media and concluded that all the marketed brands followed weibull kinetic model. Considering DEX-1 to DEX-5 for Weibull kinetic model r^2 values at pH7.2 were found to be (0.9768-0.9946) at phosphate buffer pH 6.8 (0.9738 -0.9894) as shown in table 3. However, applying Higuchi kinetic model r^2 values using phosphate buffer pH7.2 and pH 6.8 were shown as (0.6906-0.7969) and (0.8036-0.9649) (table 3). In the year 2013 Hussain *et al* evaluated *in-vitro* drug release profile in different dissolution media i.e. phosphate buffer pH 4.5, 6.8 and 0.01N HCl and used kinetic approaches of zero order, first order and Hixson Crowell models (Hussain *et al.*, 2013). The drug release profile using similarity and dissimilarity was found to be satisfactory for tests products (DEX-1- DEX-5). Statistical approach using one-way ANOVA with Tukey's post hoc test results showed that the variations were found to be significant at different pH conditions for release patterns of these formulations in this study. However insignificant associations from formulation perspectives were noted (table 5). Numbers of authors have elucidated the degree of difference at various levels of pH and time to demonstrate the formulations efficacy (Zafar *et al.*, 2015; Bushra *et al.*, 2016).

For quantitative assessment of dissolution profile, choice of reasonable model term for suitable fitting of medication release information is the noteworthy concern. They may include coefficient of determination (r^2), the coefficient of adjusted correlation (r^2_{adjusted}), the mean

square error (MSE), sum of squares (SS), weighted sum of squares WSS, Model Selection Criterion (MSC) and the Akaike Information Criterion (AIC) (Naqvi *et al.*, 2018). The customary techniques are the r^2 , MSC and AIC. Best-fitted model may be considered with lesser AIC and higher MSC and r^2_{adjusted} values. table 4 clearly depicted that majority of formulations are following kinetics pattern of Weibull release with acceptable goodness of fit principles followed by Hixon Crowell. Values of MSC were in the range of 3.417-4.870 whereas AIC values were found in order of 26.172-36.573 respectively for Weibull model (DEX-1-DEX-6). In another investigation Naz *et al.*, also applied such model terms for selection of goodness of fit for glimepiride brands (Naz *et al.*, 2014).

CONCLUSION

In this study various physical and chemical parameter were evaluated and also comparison based on *in-vitro* evaluation has been done on different *Dexibuprofen* brands available in the local market. Results were found to be within the acceptable range. Therefore, it could be concluded that the selected brands of *Dexibuprofen* tablet purchased from local market for quality evaluation could be considered as being both chemically and pharmaceutically equivalent drug product. Such studies may result in reducing the burden of patient in terms of providing cost effective treatment option with better patient compliance and therapeutic outcome.

REFERENCES

- Ahmed S, Pal N, Verma G and Singh A (2012). Comparative *in vitro* release study of some commercially available paracetamol tablets. *Der. Chemical Sinica.*, **3**: 1075-1077.
- Ali H, Harris MS, Zafar F, Bushra R, Riffat Y, Shehla S and Zafar MA (2016). Intermediate release formulations of diclofenac potassium tablets for IVIVC. *Pak. J. Pharm. Sci.*, **29**(4): 1287-1298.
- Arshad HM, Harris MS, Ghayas S, Yousuf RI, Hanif M and Khan A (2011). Pharmaceutical Quality Control Studies on *Gatifloxacin* 200 mg Tablets Available in the Pakistani Market. *LAMP*, **30**(10): 1922-1926.
- BNF, British National Formulary; 72nd Edition. 2016. British Medical Association and Royal Pharmaceutical Society of Great Britain, London.
- British Pharmacopoeia (2017). London: Stationary Office London. Appendix XII C pp.V-A382-A386, III-75.
- Bushra R, Harris MS, Ali H, Zafar F, Yousra S and Nousheen A (2016). *In vitro* drug analysis and stability studies of optimized formulations of *Aceclofenac* (100 mg) Tablets. *Lat. Am. Pharm.*, **35**(4): 695-704.
- Drug Bank: *Dexibuprofen* (2017). Drug created on October 21, 2015 09:53 / Updated on August 02, 17:33. <https://www.drugbank.ca/drugs/DB01050>.

- Hussain A, Hanif M, Harris MS, Yousuf RI, Ali T, Muhammad IN, Hussain L, Fayyaz M and Shafi N (2013). Comparative Studies of Ciprofloxacin 250 mg Tablets Available in Pakistani Market. *Lat. Am. J. Pharm.*, **32**(4): 484-89.
- Jakaria M, Mousa AY, Parvez M, Zaman R and Arifujjaman SM (2016). *In vitro* comparative study of different brands of dexamethasone tablet available in Bangladesh. *Int. J. of Pharma. Qual. Assur.*, **7**(2): 24-8.
- Maroof K, Zafar F, Ali H, Naveed S, Shah SN, Khan FA and Siddiqui S (2016). Development and optimization of fast dispersible *Flurbiprofen* 100mg tablets by central composite design. *Lat. Am. J. Pharm.*, **35**: 685-94.
- Masih A, Kumar A, Singh S and Tiwari AJ (2017). Fast Dissolving tablets: A Review. *Int. J. Curr. Pharm. Res.*, **9**: 8-18.
- Naqvi GR, Naqv BS, ShoaibMH, AliH, Zafar F and Parveen S *et al* (2018). Pharmaceutical Surveillance Study of Moxifloxacin Formulations: Therapeutic Perspective in Terms of Quality and Efficacy. *Lat. Am. J. Pharm.*, **37**(6): 1104-14.
- Naz A, Ali H, Zafar F, Shah SN, Shareef H, Shehla S, Zaib UN and Raza GN (2014). Development of spectrophotometric method for dissolution and *in vitro* kinetic study of glimepiride tablets. *Lat. Am. J. Pharm.*, **33**(9): 1418-24.
- Parvin S, Rafshanjani MD, Shuaib A and Abdul KA (2014). Formulation of dexibuprofen solid lipid nano particles and its evaluation by *in vitro* dissolution study. *Inter Res. J. Pharm.*, **5**: 1-5.
- Pritesh GD, Rajan VK, Suprit DS, Shailesh GI, Sandeep CA and Madhuri DG (2011). Development and validation of UV spectrophotometric method for estimation of *dexibuprofen* in bulk and dosage form. *Der Pharma Chemica.*, **3**(4): 361-366
- Qureshi MS, Rukh G, Kirplani PD, Farheen A and Hamid M (2016). A Comparative Study of Quality on Conventional Paracetamol Tablets Available in Pakistan. *Res. in Pharmacy and Health Sci.*, **2**: 205-210.
- Rehnasalim R, Sivakumar K and Sajeeth CH (2013). Biowaiver monographs of *dexibuprofen*. *IJPCBS*. **3**: 424-435.
- Sahle SB, Ayane AT, Wabe NT (2012). Comparative quality evaluation of paracetamol tablet marketed in Somali region of Ethiopia. *Int. J. Pharm. Sci. Res.*, **3**(2): 545-550.
- U.S. Pharmacopoeia-National Formulary* [USP 35 NF 30]. (2012) Volume 1-5. Rockville, Md: *United States Pharmacopeial Convention, Inc.*
- Yuksel N, Kanik AE and Baykara T (2000). Comparison of *in vitro* dissolution profiles by ANOVA-based, model-dependent and-independent methods. *Inter. J. Pharm.*, **209**(12): 57-67.
- Zafar F, Huma A, Shabana NS, Safila N and Shehla S (2015). Quality assessment and dissolution profile comparison studies on 250mg mefenamic acid tablets available in local market of Karachi. *J Chin Pharm Sci.*, **24**(10): 673-677.