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Comparative Quantitative Evaluation of Marketed Available Dexibuprofen Product: Assessment of Quality, Effectiveness and Interchangeability

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Abstract: NSAIDs are the most consumable class of drugs used in daily life for a number of ailments like analgesia, anti-inflammatory, antipyretic effect. One of the racemic NSAIDs of the parent drug ibuprofen is Dexibuprofen. As reported in numerous studies, Dexibuprofen is more potent in effect. Dexibuprofen can be interchanged in the clinical practice. This research focuses on the comparative analysis of different commercial brands of Dexibuprofen from different perspectives, including physicochemical properties, pharmacokinetic properties, and pharmacopeial properties. A comparison of Dexibuprofen will provide significant aspects of this product and show its cost effectiveness and interchangeability. Different tests were performed on six marketed common brands of Dexibuprofen. The results were compared and analyzed using different statistical tools and presented in tables are graphs. All the brands followed USP/BP guidelines and their properties lie within acceptable ranges, it has been observed in research through statistical tools that all these six brands in terms of hardness, thickness, weight variation, and dissolution profile (at different pH media) showed significance, which indicates that all the brands have similarities in their properties and significant variations in drug performance of all marketed brands in different pH as dissolution medium at different time intervals. Although in certain points of percentages the results indicate the superiority of brands 01 (DS) in many properties but due to the high price of this brand it might not be preferred in common population, while study concludes that all brands are similar in comparative analysis in different properties and followed by guidelines, they exhibit acceptable properties and are safe to use.

Keywords: Dexibuprofen, non-steroidal anti-inflammatory drugs, marketed brands, comparative analysis.

市售右布洛芬产品的比较定量评价：质量、有效性和互换性评价

摘要: 非甾体抗炎药是日常生活中使用最多的一类药物，可用于镇痛、抗炎、解热等多种疾病。母体药物布洛芬的外消旋非甾体抗炎药之一是右布洛芬。正如许多研究报告的那样，右布洛芬的效果更佳。右布洛芬在临床实践中可以互换使用。本研究重点从不同角度对右布洛芬的不同商业品牌进行比较分析，包括理化特性、药代动力学特性和药典特性。右布洛芬的比较将提供该产品的重要方面，并显示其成本效益和互换性。对六个市售常见品牌的右布洛芬进行了不同的测试。使用不同的统计工具对结果进行了比较和分析，并以图表形式呈现在表格中。所有品牌均遵循美国药典/英国药典指南，其性能均在可接受范围内，通过统计工具研究观察到，这六个品牌在硬度、厚度、重量变化和溶出曲线（在不同 pH 介质）方面均显示显着性，这表明所有品牌在其性质上具有相似性，并且所有上市品牌在不同 pH 作为溶出介质在不同时间间隔的药物性能存在显着差异。尽管在某些百分比点上，结果表明品牌 01(DS)在许多属性中具有优势，但由于该品牌的价格较高，它可能不会受到普通人群的青睐，而研究得出的结论是，所有品牌在比较分析中都相似不同的特性并遵循指南，它们表现出可接受的特性并且可以安全使用。

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关键词: 右布洛芬，非甾体抗炎药，上市品牌，比较分析。

1. Introduction

The multi-task performing drugs used for treating different minor and major ailments to produce different pharmacological actions like analgesic effect, anti-pyretic, anti-thrombotic effect, and anti-inflammatory effects in higher doses are considered in the category of non-steroidal anti-inflammatory drugs (NSAIDs) [1]. The term NSAIDs include steroidal drugs as these drugs also have similar eicosanoid-inhibiting action, leading to the above mention effects they produce.

It is necessary to keep a vigilant monitoring in the formulation of any dosage form and quality control measures during the manufacturing of any dosage form, all the safety and efficacy profile are mandatory to be taken in consideration. With the advancement in the medical field, the increase in medicinal research has also led to the increased generic drug production and its marketing across the globe; extreme rise in generic drugs has completed the selection of suitable equivalent products [2].

Many generic drugs have different brands available in the market, which are pharmaceutical and bioequivalent, proving their therapeutic equivalency. Although it has been observed that selection or preference of a generic drug for a particular ailment differs throughout the globe either considering the views of physicians or patients due to many reasons contributing; like economic value of drug, availability of drug, safety and efficacy profile of drug, quality of the available brand and patient compliance.

Most of the commonly used NSAID is ibuprofen; ibuprofen is available in different forms mostly available as a racemic mixture of both isomers. One of the dextrorotatory active enantiomers of Levibuprofen (NSAID) is Dexibuprofen [3].

Dexibuprofen is commonly used for multiple NSAID actions and indicated in following pharmacological conditions:

- Sprains
- Arthritis
- Menstrual pain
- Strains
- Dental pain [4]

2. Materials and Methods

The study approaches are to perform comparative analysis on most common marketed brands of Dexibuprofen on different parameter scale to evaluate which available brand is best fit all specification limits.

2.1. Study Design

The study is an in-vitro comparative assessment, to assess different quality control attributes of Dexibuprofen. Tests were performed on three most commonly available marketed brands of 400 mg of film coated tablets of Dexibuprofen. Different tests were performed between these brands to study comparison between them to evaluate physicochemical properties, pharmacokinetic properties, pharmacopeial properties, and pricing [5].

2.2. Sample Collection and Identification

The samples of three different commercially available brands of Dexibuprofen, all three brands were purchased from different pharmacies of Karachi; all three brands were 400 mg film coated tablets. The purchased tablets of Dexibuprofen were than properly labeled with specific codes and all the details present on leaflet of brands were carefully noted, including batch number, manufacturing date, and expiry date. The tablets were then stored according to label instructions before testing begin. The entire tests were thoroughly performed and their results were noted.

2.3. Comparative Analysis of the Selected Commercial Brands of Dexibuprofen

2.3.1. Weight Variation Test

Weight variation was checked on Electronic Balance PA214C between tablets concerning dose and weight which should comply within BP limits. 20 units of each brand were selected at random. From average tablet weight, percent weight variation was calculated. In order to get ahead of weight variation test, each unit should lie in the limits of the percentage divergence permissible by BP/USP. Standard formula was used to determine upper and lower control limits [6]-[7].

2.3.2. Thickness Test

Thickness of each tablet is assessed by determining the level of compaction of 20 units of each brand by using Vernier Caliper. Thickness is an important parameter for consumer's acceptance and to facilitate packaging [8].

2.3.3. Hardness Test

In this test, a sample of 10 tablets from each brand is forced to mechanical stress in order to determine strength of a tablet. A tablet must be rigid enough to stand pressure. Hardness of all the brands was checkered on MH-1 Hardness Tester. The value of each tablet was assessed and mean value was measured and compared with the standard [9].

2.3.4. Friability Test

Ten tablets from each brand of Dexibuprofen were subjected to a uniform tumbling motion in a FB-1004 friabilater for specific time frame, i.e, 25 revolutions per minute for 4minutes that is 100 rpm and the weight loss is measured. This test is performed to check if a tablet can be scraped during shipping and also to observe capping and lamination of tablet. It is determined by calculating % weight loss by the help of initial and final weight [7].

2.3.5. Disintegration Test

This test was performed on 6 tablets from each brand on a disintegration apparatus USP type I DS-0702 which is basket apparatus. Each tablet was placed in a tube of basket rack which was further placed in a 900ml beaker containing 0.1N Hcl medium maintained at 37^{o}C, and disintegration time was recorded [10].

2.3.6. Dissolution Test

The dissolution test was done on tablets from each brand, the dissolution test using multiple point study. Tablet Dissolution Apparatus USP Type II, i.e, paddle apparatus DL-0601 was used for this purpose. In this method, each tablet was placed in a beaker containing 900 ml of dissolution medium; the medium temperature was maintained at 37^{o}C±5^{o}C.The dissolution apparatus was operated at 50 rpm for 90 min. The time selected intervals for this study were 5, 10, 15, 20, 30, 45, 60, and 90 minutes [7], [11].

After a specified time, 5ml volume of a sample was collected, filtered and diluted with dissolution medium making 25ml and analyzed via UV Visible spectrophotometer at 222 nm using respective buffer solution used for dilution. Absorbance of each of the withdrawn sample was noted and the concentration of drug in the samples were calculated as per monograph [11].

2.3.7. Methods of HPLC Analysis, Assay Percentage

- Reagents
  - Methanol
  - Phosphoric acid
- Mobile phase

Table 1 The presentation of preparation of mobile phase for assay percentage analysis

Reagents	Volume
Methanol	750 ml
Water	247 ml
Phosphoric acid	3 ml

Operating conditions

Table 2 The specifications validated for assay percentage analysis of products

Parameters	Specifications
Column	Column (C-18) (5 microns) 0.25 m long and with 4.6nm in diameter
Flow rate	1.0 ml/min
Wavelength	264 nm
Injected volume	20 ul
Temperature	Ambient

2.3.7.1. Standard Procedure

Working standard was weighed equivalent to 100mg of Dexibuprofen, then added in a 200 ml volumetric flask, after it 100 ml diluent was added, the mixture was shaken to dissolve and then was sonicated. The sonicated mixture was further diluted with diluent and then filtered.

$100/200*1000 = 500\ mcg/ml$

2.3.7.2. Sample Preparation

100 mg of Dexibuprofen each brand of tablet powder was transferred to 200 ml volumetric flask and 100 ml of diluent was added in it. The mixture was shaken and then was sonicated. The sonicated mixture was then diluted using similar dilution factor as of standard and filtered.

Limits: The acceptable range is 90-110%.

2.3.7.3. Analysis of Standard and Sample Solutions

The standard and sample solutions were separately injected twice in the HPLC column for analysis.

The observed readings were then placed in formula to obtain assay percentage of sample with respect to standard.

2.3.7.4. Formula to Calculate Assay Percentage of the Sample

$$\%age = \frac{\text{Area of sample peak}}{\text{Area of Standard peak}} * 100$$

2.4. Pricing of the Brands

The marketed brands of Dexibuprofen were lastly, compared according to monetary values of brands. For this price of each brand pack of particular brand was noted carefully. These brands were purchased from authentic pharmacies, were then compared in terms of prices [12].

2.5. Data Processing and Analysis

Successively, performing all tests on selected marketed brands of Dexibuprofen, the data of all tests were recorded in individually and separated on different sheets accordingly to brands and tests performed. The recorded data was analyzed by using proper mathematical equations as mentioned on MS. Excel 2016. The in-vitro release analysis was calculated through different models by DD solver.

2.5.1. Model Independent Methods

In Vitro Measurement of Therapeutic Equivalence

The dissolution profile data was further analyzed to measure therapeutic equivalence of marketed brands

comparatively. The equivalence determined by Pair Wise techniques as mathematical approach to calculate the products similarity such as similarity factor (f_2) and difference factor (f_1) [13-14].

i. $f1=\{[\Sigma t=1\ n|Rt-Tt|]/[\Sigma t=1\ n\ Rt]\} \times 100$

ii. $f2=50\times\log\{[1+(1/n)\Sigma\ t=1\ n\ (Rt-Tt)2]-0.5\times100\}$

2.5.2. Model Dependent Methods

For application of Model dependent method DD solver was used, the method applies:

Table 3 Model dependent method applied through DD solver

First Order	Higuchi	Hixson Crowell	Weibull model	
K1(h–1)	KH(h1/2)	KHC(h1/3)	100.[1−e(t−Ti)β/α]	α and β

3. Results and Discussion

Manufacturing of substandard medicine has become very common in developing countries to fulfill needs of patients, when they are unable to spend on expensive medicines. Pakistan is one of developing country where majority of population is unable to afford medicine, where substandard medicine is manufacturing and risking life of consumers. It has been observed that many innovator brands available in market are twice costly comparative to test brands available commercially. Therefore, it is necessary to take certain measures, in regular monitoring of all the pharmaceutical services to ensure minimization of health risks and maximization of safety and efficacy profile of pharmaceutical brands available for commercial use [15].

This study aims to evaluate the quality attributes of commercially available six brands of Dexibuprofen to regulate the inter-changeability of these of these brands according to their pharmaceutical quality profile. The six were subjected to different pharmacopeial tests, pharmacokinetic test, compared in terms of their monetary profile. The innovator brand DS for this study was considered as reference brand for comparison. The selected brands were coded for better identification and all the necessary package information are presented in Table 4.

Table 4 Different brands selected for the study of Dexibuprofen

No.	Brand Name	Code Number	Batch number	Expiry (years)	Pricing
1	Brand 01	DS	005D	2	411
2	Brand 02	DF	8465T	2	377
3	Brand 03	DG	043F56	2	344
4	Brand 04	DO	0456G	2	265
5	Brand 05	DI	678T	2	270
6	Brand 06	DH	023N25	2	330

Table 5 Pharmacopeial evaluation of different brands of Dexibuprofen

Brand Name	Code Number	Weight variation	Thickness	Hardness	Friability	Disintegration time	Assay (%)
Brand 01	DS	781.2 ± 5.98	6.719 ± 0.03	14.87 ± 0.72	0.051	1 min	99.31
Brand 02	DF	971.5 ± 9.82	6.746 ± 0.08	2.83 ± 0.25	0.147	3 mins	94.98
Brand 03	DG	727.9 ± 8.61	6.442 ± 0.06	17.79 ± 0.44	0.136	6 mins	97.42
Brand 04	DO	721.2 ± 2.69	6.672 ± 0.10	16.71 ± 0.12	0.126	2 mins	98.48
Brand 05	DI	775.5 ± 5.45	6.371 ± 0.03	19.56 ± 0.23	0.145	3.5 mins	95.42
Brand 06	DH	764.6 ± 2.34	6.458 ± 0.05	2.09 ± 0.17	0.115	4 mins	96.38

Table 5 shows that the brands were prior subjected suitable pharmacopeia in which weight variation, thickness, hardness, friability, disintegration of dosage and assay tests were performed. The evaluated results showed that DS, DF, DG, DO, DI and DH had weights ranging from 721.2 ± 2.69 to 981.2 ± 5.98 mg among three which may due to usage of various excipients in formulation. The Thickness range was found to be 6.371 ± 0.03 to 6.746 ± 0.08 mm in all selected formulations within the pharmacopeial limits while hardness profile ranged from 19.56 ± 0.23 to 2.09 ± 0.17 and friability from 0.051 to 0.147. The disintegration maximum time observed 1-6 minutes. According to USP/BP 2007, all the obtained results of all six brands showed that they are within acceptable limits. The assay was performed according to the guidelines of USP36/NF31, 2013, the evaluated results showed that more than 90% of drug is release is all six tested brands. The similar testing was performed in 2018 and similar test results were obtained [16]. All brands of Dexibuprofen displayed acceptable pharmacopeial range according to USP/BP 2007, as none of the brand did not show any deviation in all pharmacopeial tests category they are considered acceptable for commercial use and will be patient compliant. The obtained results of %Assay showed similarity in the results as adapted Assay technique showed comparable results [16]-[17] all the selected brands of Dexibuprofen showed disintegration in less than 15 min met the criteria [17].

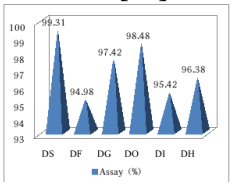

Fig. 1 Assay percent test results by HPLC of marketed brands

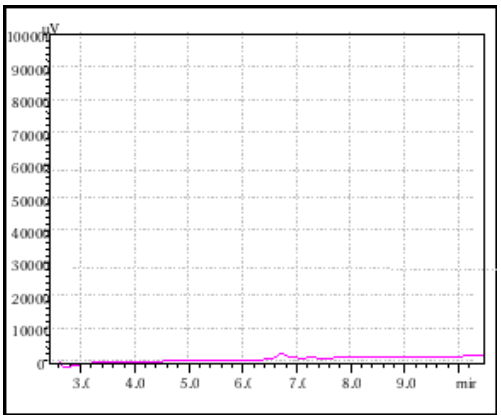

Fig. 2 Peak of blank observed in assay percentage by HPLC brands of Dexibuprofen

Figure 2 shows that no peak has been observed.

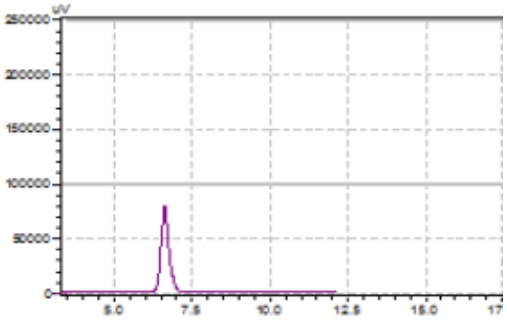

Fig. 3 Peak of pure drug observed in assay percentage by HPLC at 25 ppm

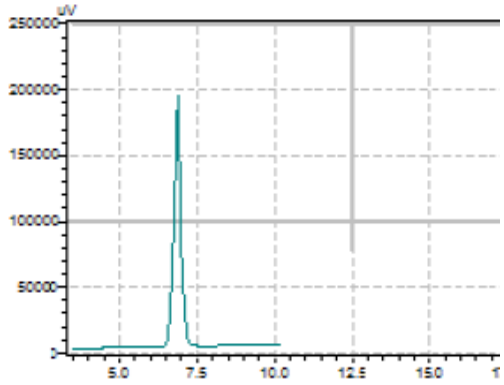

Fig. 4 Peak of pure drug observed in assay percentage by HPLC at 50 ppm

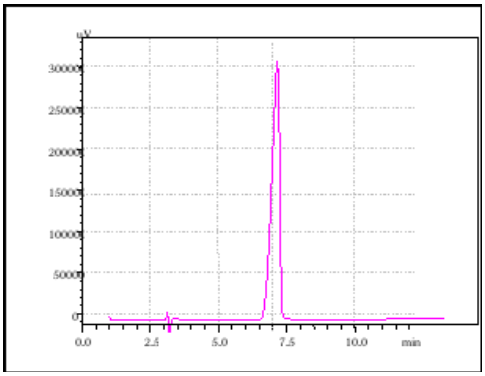

Fig. 5 The peak of pure drug observed in assay percentage by HPLC at 100 ppm

Figures 3 to 5 represent the peaks of pure drug at three different ppm values, 25, 50 and 100pp; it was observed through HPLC analysis that pure drug showed the best peaks at 50 and 100 ppm, which is most suitable observed through different studies [13].

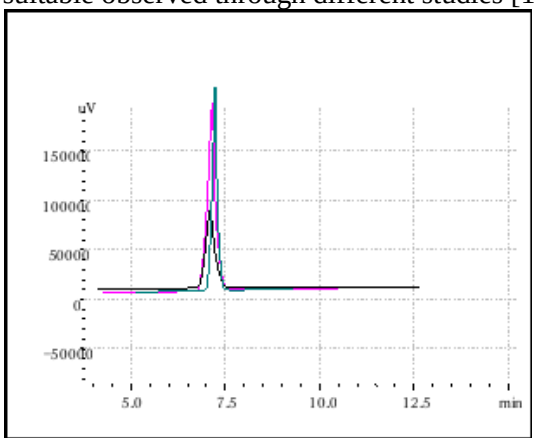

Fig. 6 Overlaid peaks of pure drug observed by HPLC in assay percentage at 25, 50 and 100 ppm

In Figure 6, the overlay of the peak at 25, 50 and 100 ppm of pure drug also gives an insight of the picture of the most suitable ppm values for Dexibuprofen, the overlaid graph helped in selection of a suitable ppm for marketed brands of Dexibuprofen [18].

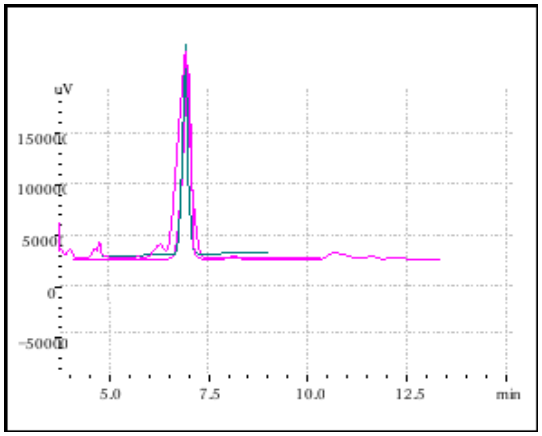

Fig. 7 Overlaid peaks of marketed brands observed by HPLC in assay percentage at 100 ppm

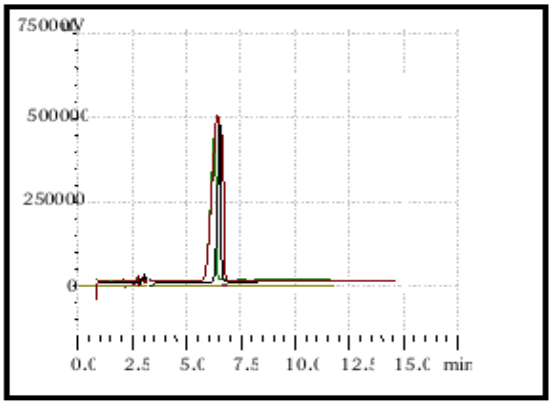

Fig. 8 Overlaid peaks of marketed brands observed by HPLC in assay percentage at 50 ppm

Figures 7 and 8 represent the peak overlay of six marketed brands of Dexibuprofen at 100 ppm and 50 ppm, respectively. It was observed in both graphical representations that all six brands showed similar peak behavior and stability at both ppm. When comparing the graphs of both ppm, at 100 ppm more sharp and stable peaks were observed, of all six brands, which indicated that 100 pm is more suitable range for Dexibuprofen [18].

3.1. Dissolution Test

In-vitro availability of commercial brands of Dexibuprofen 400 mg tablets was studied in different dissolution media, including buffer at pH 1.2, buffer at pH 4.5, phosphate buffer at pH 6.8, and phosphate buffer at pH 7.2. As Dexibuprofen belongs to class BCS-II, which shows limited solubility in water medium, we have analyzed dissolution of marketed brand tablets using buffer of different pH [19]. Dissolution apparatus of Galvano scientific paddle GDT – 6L Pakistan was applied in this analysis, in 900 ml dissolution media separately, previously maintained at particular temperature, i.e, 37°C for 90 minutes, 10 ml of the solution were withdrawn after completing specified time set in the multipoint dissolution test. The volume of dissolution medium was kept constant by adding an equivalent amount of the dissolution media. The absorbance of the aliquots was observed at their respective wavelength, which gave the drug availability at a specified time [3], [20].

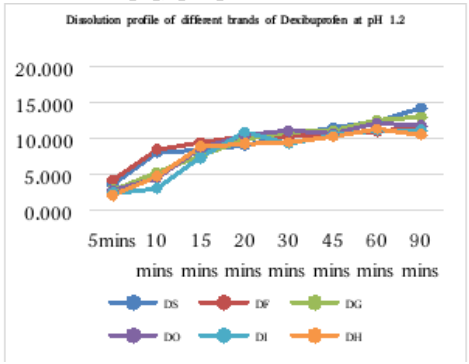

Fig. 9 Dissolution profile of different brands of Dexibuprofen at pH 1.2

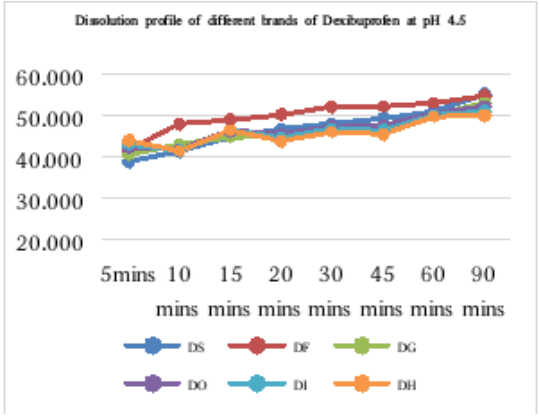

Fig. 10 Dissolution profile of different brands of Dexibuprofen at pH 4.5

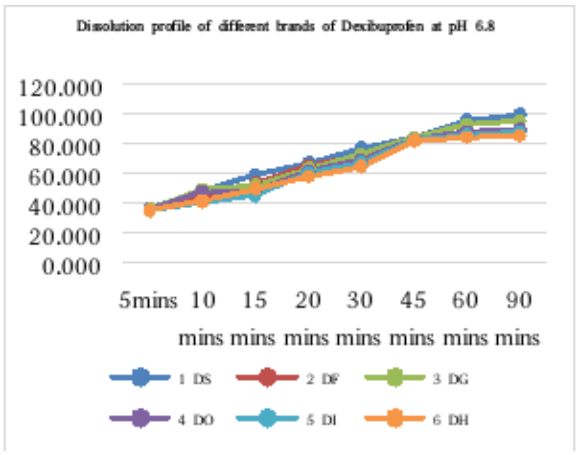

Fig. 11 Dissolution profile of different brands of Dexibuprofen at pH 6.8

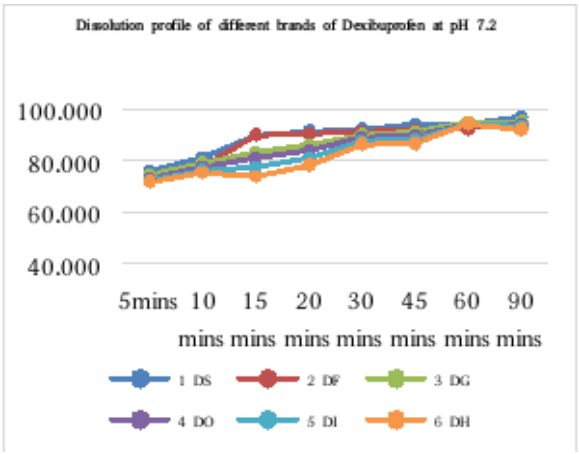

Fig. 12 Dissolution profile of different brands of Dexibuprofen at pH 7.2

The bioequivalence of two brands was considered to have the same in-vivo bioavailability which can be reflected through performing in-vitro dissolution; specifically, for drugs belonging to category of BCS-II drugs. It is necessary to consider multiple point dissolution studies. The dissolution studies performed on Dexibuprofen are conducted in four different media at pH 1.2, 4.5, 6.8 and 7.2. The figures 9-12 show the multiple point dissolution profiles of all six selected brands. The commercial brands were compared with reference to DS brand, the results showed that the reference DS brand showed the highest dissolution in all media, while DH brand showed the lowest dissolution in all media. While evaluation of all observed profiles revealed that all brands dissolved in all media in the acceptable range. The in-vitro dissolution profile is very helpful in predication of drug in-vivo performance and develops a correlation [21].

3.2. Model-Dependent Techniques

Dissolution profile comparison is an important tool to assess the products quality, stability, and batch to batch consistency. In this study, dissolution profiles were compared in buffer of pH 1.2, and pH 4.5, phosphate buffer in pH 6.8 and pH 7.2, for all six marketed brands of Dexibuprofen. Results were fitted

to model-independent and model dependent processes. These approaches were used frequently by numerous investigators. Different models were applied to analyze the data, i.e, *First Order*, *Higuchi model*, *Hixson – Crowell cube root law* and *Weibull model*, as shown in table [22]-[23].

Table 6 Different models for dissolution profile at different pH (1.2, 4.5, 6.8 and 7.2)

pH	Formulations Codes	First Order		Higuchi		Hixson Crowell		Weibull model		
		r^2	K1(h–1)	r^2	KH(h1/2)	r^2	KHC(h1/3)	r^2	α	β
pH 1.2	DS	-0.679	0.002	0.862	1.504	0.799	0.000	0.990	19.156	0.234
	DF	-3.653	0.002	0.563	1.130	0.515	0.000	0.990	13.060	0.108
	DG	-0.217	0.002	0.809	1.543	0.704	0.000	0.950	23.121	0.275
	DO	-0.608	0.002	0.640	1.433	0.539	0.000	0.859	20.162	0.230
	DI	-0.246	0.002	0.640	1.398	0.532	0.000	0.794	25.145	0.268
	DH	-0.703	0.002	0.606	1.306	0.506	0.000	0.888	19.888	0.203
pH 4.5	DS	-14.977	0.018	0.900	4.130	0.893	0.001	0.978	2.715	0.168
	DF	-34.822	0.021	0.682	3.426	0.677	0.001	0.991	1.732	0.069
	DG	-30.425	0.017	0.951	3.569	0.948	0.001	0.970	3.492	0.205
	DO	-38.418	0.018	0.872	3.350	0.868	0.001	0.914	2.745	0.153
	DI	-50.468	0.017	0.826	3.092	0.824	0.001	0.841	3.720	0.205
	DH	-63.565	0.017	0.717	2.820	0.716	0.000	0.719	13.264	0.416
pH 6.8	DS	0.930	0.058	0.921	10.851	0.988	0.009	0.978	22.746	0.983
	DF	0.802	0.049	0.864	9.614	0.930	0.007	0.984	6.500	0.614
	DG	0.889	0.051	0.926	10.408	0.986	0.008	0.993	28.611	0.995
	DO	0.819	0.047	0.904	9.854	0.959	0.007	0.979	14.638	0.805
	DI	0.841	0.042	0.899	9.842	0.949	0.006	0.969	19.488	0.860
	DH	0.783	0.042	0.896	9.506	0.941	0.006	0.974	11.537	0.723
pH 7.2	DS	-0.009	0.221	0.610	6.034	0.775	0.007	0.951	0.936	0.263
	DF	-0.065	0.193	0.502	5.974	0.622	0.005	0.893	0.866	0.216
	DG	-0.810	0.190	0.801	6.440	0.915	0.005	0.991	1.630	0.363
	DO	-1.051	0.171	0.812	6.540	0.912	0.004	0.981	1.854	0.377
	DI	-1.319	0.156	0.839	6.714	0.922	0.004	0.958	3.697	0.516
	DH	-1.478	0.142	0.836	6.874	0.903	0.004	0.921	11.298	0.732

The selected brands were manufactured on the multi-national and national level; the application of pharmacokinetic drug release evaluated the quality profile of six selected brands. The drug release was observed at four different pH level 1.2, 4.5, 6.8, and 7.2. The data were analyzed through Model-dependent kinetics (First order, Higuchi, Hixson Crowell and Weibull model) by the DD solver which revealed that Weibull is the best fit model among all the selected kinetics models for comparison of Dexibuprofen drug release profile. It was observed that [21] followed the similar pattern of model dependent approach in mefenamic acid and Weibull model fits the best in commercial tablets. Considering commercial tablets of Dexibuprofen brands different studies had stated the satisfactory results obtained for Dexibuprofen [24].

3.3. In Vitro Measurement of Therapeutic Equivalence

The procedure conducted was multipoint time release profile, on all six marketed brands of Dexibuprofen at 5, 10, 15, 20, 25, 30, 45, 60, and 90 minutes. The reference product, i.e., brand 01 (DS), was compared with test products of brand 02 (DF), brand 03 (DG), brand 04 (DO), brand 05 (DI) and brand 06 (DH). The in-vitro measurement of poorly water-soluble compound Dexibuprofen tablet was conducted in four different pH values (1.2, 4.5, 6.8, and 7.2) as the drug belongs to BCS-II. Pair Wise techniques were applied as a mathematical approach to calculate the products similarity, such as similarity factor (f_2) and difference factor (f_1) [17].

Table 7 Difference factor (f1) and Similarity factor (f2) at different dissolution media with reference a1 as a reference brand

Standard vs. Brands	pH 1.2	pH 4.5	pH 6.8	pH 7.2
f_1				
DS vs DF	10.21	7.08	6.99	2.26
DS vs DG	9.45	3.20	4.42	3.15
DS vs DO	12.76	3.43	7.87	4.82
DS vs DI	19.86	4.77	11.17	6.35
DS vs DH	15.82	6.10	11.78	7.91
f_2				
DS vs DF	90.36	70.61	60.04	80.01
DS vs DG	90.44	85.88	70.60	71.89
DS vs DO	85.62	83.06	58.20	64.37
DS vs DI	79.86	77.52	52.22	58.13
DS vs DH	82.99	72.77	51.18	53.25

The commercial brands were compared with respect to reference DS in terms of in vitro dissolution profile

by dissimilarity factor (f_1) and similarity factor (f_2). The values were evaluated in terms of DS vs DF, DS vs DG, DS vs DO, DS vs DI and DS vs DH. When DF, DG, DO, DI and DH brands were compared with the value of f_1, DI brand showed more difference with the reference product of DS brand and maximum difference was observed in pH 1.2. All the values fitted in the range with USP specifications except 19.86 of DI and 15.82 of DH in pH 1.2. When DF, DG DO, DI and DH brands were compared with value of f_2, DG brand showed better similarity with the reference product of DS brand and maximum similarity was observed in pH 1.2. All the values fitted in the range with USP specifications.

3.4. Statistical Analysis

Statistical estimation was conducted by IBM Statistics 19.0 software for Microsoft Excel 2013, (Microsoft Corporation, USA). One-way ANOVA was also used to evaluate the drug release performance of Dexibuprofen commercial brands available in market at four different pH including: pH 1.2, pH 4.5, phosphate buffer 6.8 and buffer pH 7.2 solution as dissolution media. The statistical evaluation of different formulations and brands is given in Table 8. The statistical approaches taken in consideration were one-way ANOVA; the approaches clarify the significant differences in the performance of different brand if present to demonstrate various level of pH and time relation on efficacy of formulation [17], [25].

Table 8 Multiple comparison of different brands of Dexibuprofen by Dennett's test

Dunnett t (2-sided)							
Dependent Variables	**(I) Media**	**(J) Mediua**	**Mean Difference (I-J)**	**Std. Error**	**Sig.**	**95% Confidence Interval**	
						Lower Bound	**Upper Bound**
% of drug dissolved in 5 min	ph1.2	ph7.2	-70.19200*	.74534	.000	-72.0854	-68.2986
	ph4.5	ph7.2	-31.42033*	.74534	.000	-33.3138	-29.5269
	ph6.8	ph7.2	-37.59033*	.74534	.000	-39.4838	-35.6969
% of drug dissolved in 10 min	ph1.2	ph7.2	-72.02825*	1.52464	.000	-75.9014	-68.1551
	ph4.5	ph7.2	-34.92333*	1.52464	.000	-38.7965	-31.0502
	ph6.8	ph7.2	-32.50383*	1.52464	.000	-36.3770	-28.6307
% of drug dissolved in 15 min	ph1.2	ph7.2	-73.98117*	2.39561	.000	-80.0669	-67.8954
	ph4.5	ph7.2	-36.13350*	2.39561	.000	-42.2192	-30.0478
	ph6.8	ph7.2	-31.40150*	2.39561	.000	-37.4872	-25.3158
% of drug dissolved in 20 min	ph1.2	ph7.2	-75.21883*	1.91303	.000	-80.0786	-70.3590
	ph4.5	ph7.2	-39.22117*	1.91303	.000	-44.0810	-34.3614
	ph6.8	ph7.2	-22.76050*	1.91303	.000	-27.6203	-17.9007
% of drug dissolved in 30 min	ph1.2	ph7.2	-79.02333*	1.56096	.000	-82.9887	-75.0579
	ph4.5	ph7.2	-41.54133*	1.56096	.000	-45.5067	-37.5759
	ph6.8	ph7.2	-18.94483*	1.56096	.000	-22.9102	-14.9794
% of drug dissolved in 45 min	ph1.2	ph7.2	-79.32883*	1.07664	.000	-82.0639	-76.5938
	ph4.5	ph7.2	-42.11067*	1.07664	.000	-44.8457	-39.3756
	ph6.8	ph7.2	-7.47700*	1.07664	.000	-10.2121	-4.7419
% of drug dissolved in 60 min	ph1.2	ph7.2	-82.34467*	1.41128	.000	-85.9298	-78.7595
	ph4.5	ph7.2	-43.28450*	1.41128	.000	-46.8697	-39.6993
	ph6.8	ph7.2	-5.66700*	1.41128	.002	-9.2522	-2.0818
% of drug dissolved in 90 min	ph1.2	ph7.2	-82.11367*	1.76759	.000	-86.6040	-77.6233
	ph4.5	ph7.2	-41.49133*	1.76759	.000	-45.9817	-37.0010
	ph6.8	ph7.2	-3.49983	1.76759	.148	-7.9902	0.9905

*. The mean difference is significant at the 0.05 level.

a. Dennett-tests treat one group as a control, and compare all other groups against it.

It is necessary to perform in vitro studies through different statistical profiles as they are a necessary key that mimics performance of drug in in-vivo conditions. The dissolution of all selected brands in different dissolution media was compared through multiple comparison Dennett's t-test. The results were evaluated according to the FDA guidelines on different dissolution media with pH 1.2, 4.5, 6.8 and 7.2. The evaluated results suggest that all the brands of Dexibuprofen have appropriate drug release in all selected pH media, waiver studies may be also recommended, as drug is well absorbed and bioavailable in different physiological pH of the body. Dennett's test shows the significant values in all media while interaction between pH 6.8 and 7.2 depicting non-significant values means no significant variations in release of Dexibuprofen occurring in both media [16].

Table 9 Application of one-way ANOVA descriptive method on different brands of Dexibuprofen in different media

		N	**Mean**	**Std. Deviation**	**Std. Error**	**95% Confidence Interval for Mean**	
						Lower Bound	**Upper Bound**
% of drug dissolved in 5 min	ph1.2	6	2.9818	.78232	.31938	2.1608	3.8028
	ph4.5	6	41.7535	1.87352	.76486	39.7874	43.7196

		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
						Lower Bound	Upper Bound
	ph6.8	6	35.5835	.52305	.21353	35.0346	36.1324
	ph7.2	6	73.1738	1.50688	.61518	71.5925	74.7552
	Total	24	38.3732	25.47836	5.20075	27.6146	49.1317
% of drug dissolved in 10 min	ph1.2	6	5.6433	2.11984	.86542	3.4186	7.8679
	ph4.5	6	42.7482	2.59361	1.05884	40.0263	45.4700
	ph6.8	6	45.1677	3.51217	1.43384	41.4819	48.8535
	ph7.2	6	77.6715	2.08289	.85034	75.4856	79.8574
	Total	24	42.8076	26.17084	5.34210	31.7567	53.8586
% of drug dissolved in 15 min	ph1.2	6	8.3795	.77355	.31580	7.5677	9.1913
	ph4.5	6	46.2272	1.56063	.63712	44.5894	47.8649
	ph6.8	6	50.9592	4.76703	1.94613	45.9565	55.9619
	ph7.2	6	82.3607	6.56574	2.68045	75.4703	89.2510
	Total	24	46.9816	27.10165	5.53210	35.5376	58.4256
% of drug dissolved in 20 min	ph1.2	6	9.9767	.69612	.28419	9.2461	10.7072
	ph4.5	6	45.9743	2.27612	.92922	43.5857	48.3630
	ph6.8	6	62.4350	3.42988	1.40024	58.8356	66.0344
	ph7.2	6	85.1955	5.14655	2.10107	79.7945	90.5965
	Total	24	50.8954	28.18332	5.75290	38.9946	62.7961
% of drug dissolved in 30 min	ph1.2	6	10.2083	.74365	.30360	9.4279	10.9887
	ph4.5	6	47.6903	2.21984	.90624	45.3608	50.0199
	ph6.8	6	70.2868	4.34995	1.77586	65.7218	74.8518
	ph7.2	6	89.2317	2.19914	.89780	86.9238	91.5395
	Total	24	54.3543	30.16441	6.15728	41.6170	67.0916
% of drug dissolved in 45 min	ph1.2	6	10.7868	.44120	.18012	10.3238	11.2498
	ph4.5	6	48.0050	2.40606	.98227	45.4800	50.5300
	ph6.8	6	82.6387	.89638	.36594	81.6980	83.5794
	ph7.2	6	90.1157	2.66883	1.08955	87.3149	92.9164
	Total	24	57.8865	32.21802	6.57648	44.2821	71.4910
% of drug dissolved in 60 min	ph1.2	6	11.6832	.64974	.26525	11.0013	12.3650
	ph4.5	6	50.7433	1.16394	.47518	49.5219	51.9648
	ph6.8	6	88.3608	4.62601	1.88856	83.5061	93.2155
	ph7.2	6	94.0278	.85061	.34726	93.1352	94.9205
	Total	24	61.2038	33.86631	6.91293	46.9033	75.5043
% of drug dissolved in 90 min	ph1.2	6	12.0530	1.33372	.54449	10.6533	13.4527
	ph4.5	6	52.6753	2.08056	.84939	50.4919	54.8587
	ph6.8	6	90.6668	5.37557	2.19457	85.0255	96.3081
	ph7.2	6	94.1667	1.57736	.64396	92.5113	95.8220
	Total	24	62.3905	34.14331	6.96947	47.9730	76.8079

Table 10 Application of one-way ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
% of drug dissolved in 5 min	Between Groups	14897.051	3	4965.684	2979.543	.000
	Within Groups	33.332	20	1.667		
	Total	14930.382	23			
% of drug dissolved in 10 min	Between Groups	15613.523	3	5204.508	746.318	.000
	Within Groups	139.472	20	6.974		
	Total	15752.995	23			
% of drug dissolved in 15 min	Between Groups	16549.144	3	5516.381	320.406	.000
	Within Groups	344.337	20	17.217		
	Total	16893.481	23			
% of drug dissolved in 20 min	Between Groups	18049.313	3	6016.438	547.991	.000
	Within Groups	219.582	20	10.979		
	Total	18268.895	23			
% of drug dissolved in 30 min	Between Groups	20781.307	3	6927.102	947.652	.000
	Within Groups	146.195	20	7.310		
	Total	20927.502	23			
% of drug dissolved in 45 min	Between Groups	23804.469	3	7934.823	2281.771	.000
	Within Groups	69.550	20	3.477		
	Total	23874.019	23			
% of drug dissolved in 60 min	Between Groups	26259.817	3	8753.272	1464.959	.000
	Within Groups	119.502	20	5.975		
	Total	26379.319	23			

		Sum of Squares	df	Mean Square	F	Sig.
% of drug dissolved in 90 min	Between Groups	26625.145	3	8875.048	946.865	.000
	Within Groups	187.462	20	9.373		
	Total	26812.607	23			

One-way ANOVA descriptive method was applied on dissolution profile obtained to compare mean percentage of drug release with respect to reference DS brands in all dissolution media (pH 1.2, 4.5, 6.7, and 7.2). It has been evaluated through obtained results that show the significant values in comparison of all variables group at different time interval. No significant difference was observed in the performance of all selected brands of Dexibuprofen.

3.5. Pricing of the Brands

The selected marketed brands were evaluated on the basis of their monetary value and pack price were compared and represented.

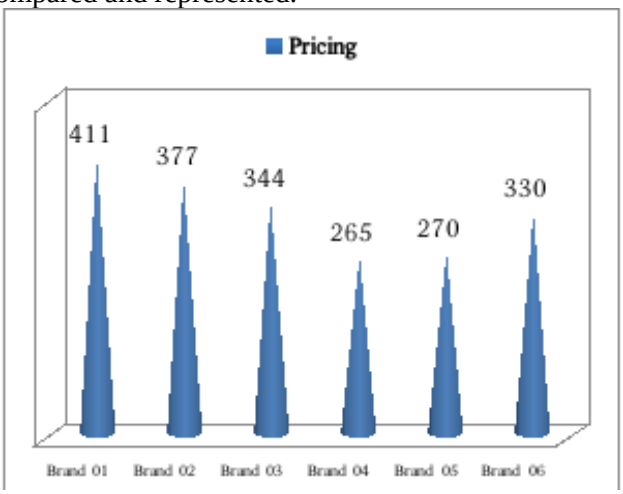

Fig. 13 Price of Dexibuprofen brands

Figure 13 represents the pricing of available marketed brands of Dexibuprofen, this figure shows that brand 01 (DS) is available with the highest market price in Pakistani rupees of Rs. 411 and only brand 04 is sold in the market comparatively cheaper than others. In terms of price brand 04 (DO) is the most pocket-friendly brand available in market. Although there are no fix criteria regarding pricing strategies of any pharmaceutical medicine, but still layman preference is always inclined toward the cheapest and safest drug. Most people in our society rely on a physician to provide them a medicine which is efficacious, safe and pocket-friendly, they are not concerned with how a medicine works. Therefore, it is necessary that pricing policies should be introduced by health authorities to control pricing of pharmaceutical products, and doctors should consider writing generic name of drug in bracket along with the drug brand name, so that it will be easier for any consumer to find that particular drug if that brand is not available [26]-[27].

After performing all the necessary analytical testing on six available commercial brands of Dexibuprofen along with analyzing it through monetary values, the data reports that all brands have fulfilled all specifications criteria of updated guidelines of USP/BP [28]-[30]. Therefore, all these six brands are reliable and safe to use, which will provide appropriate pharmacological effect.

The findings of the study showed comparison of reference innovator DS brand of Dexibuprofen to other available brands; it has been evaluated through the study that all brands in term of pharmacopeial perspective are similar in performance as all the obtained results are in acceptable range according to USP/BP 2009 [31] but they do differ in monetary values.

4. Conclusion

Although the price of DS is comparatively the highest, the reference brand outperformed in all drug release pattern in all dissolution media. The model dependent approach showed that all brands have no significant difference in their drug release pattern and Dexibuprofen mainly follows Weibull model which suggests homogeneity in profile. While, model independent approaches exclaimed that similarity between reference DS brand to other available brands.

Brand 01 (DS) showed outstanding performance is all categories of analytical test and showed best results, while other Brands showed comparatively lowest performance in major categories, the brand fulfilled all specification limits and is considered as safe and reliable to use.

It has been concluded that brand 04 (DO) can be most suitable choice for many consumers as this brand not only performed great in all categories, it had advantage over other brands in terms of monetary values as this brand cost lowest.

It is safe to consider through this study that all these brands are considered pharmaceutical equivalent and can be used as each other alternatives to get the Dexibuprofen NSAID effect. These brands are very safe, efficacious and reliable to use and fulfill all parameter requirements within specified limits.

In the current study presented the effectiveness of Dexibuprofen alternatives available in the market; the qualitative and quantitative analysis provide therapeutic equivalence, cost effective dosage form for consumers and interchangeable in clinical practice and prescription writing.

However, this study does not cover IVIVC (in vivo - in vitro comparison) studies but presents bio waiver studies conducted using different dissolution media and results of all brands shown within the specified limit, being equivalent biopharmaceutically and chemically. It shows little variations in drug performance in all

brands and, therefore, can provide cost effective alternative for the consumers.

References

[1] BINDU S, MAZUMDER S, and BANDYOPADHYAY U. Non-steroidal anti-inflammatory drugs (NSAIDs) and organ damage: A current perspective. *Biochemical Pharmacology*, 2020, 180: 114147. https://doi.org/10.1016/j.bcp.2020.114147

[2] DAVIS A, & ROBSON J. The dangers of NSAIDs: look both ways. *British Journal of General Practice*, 2016, 66(645): 172-173.

[3] ALI FR, SHOAIB MH, YOUSUF RI, et al. Design, development, and optimization of Dexibuprofen microemulsion based transdermal reservoir patches for controlled drug delivery. *BioMed Research International*. 2017. https://doi.org/10.1155/2017/4654958

[4] GLISZCZYŃSKA A, and SÁNCHEZ-LÓPEZ E. Dexibuprofen Therapeutic Advances: Prodrugs and Nanotechnological Formulations. *Pharmaceutics*, 2021, 13(3): 414. https://doi.org/10.3390/pharmaceutics13030414

[5] MAGUIRE J A, JIANG W, and YU L X. Modern Pharmaceutical Regulations: Quality Assessment for Drug Products. In *Developing Solid Oral Dosage Forms*, pp. 1095-1126. Academic Press, 2017. https://doi.org/10.1016/B978-0-12-802447-8.00040-6

[6] ABDUL-HASAN M T, Al-SHAIBANI A J N, WANNAS A N, & HASAN AL-GBURI K M. Quality control testing of conventional clopidogrel bisulfate tablets marketed in Iraq. *International Journal of Applied Pharmaceutics*, 2022: 221-225. https://doi.org/10.22159/ijap.2022v14i1.43331

[7] HAMEED A, SHARIF N, ASHRAF M, et al. Pharmaceutical Equivalent Analysis Work for Fexofenadine Preparations Accessible in Pakistan. *SAJ Pharmacy and Pharmacology*, 2018, 5: 203. http://article.scholarena.com/Pharmaceutical-Equivalent-Analysis-Work-for-Fexofenadine-Preparations-Accessible-in-Pakistan.pdf

[8] LOMBARDO L, PALONE M, LONGO M, et al. MicroCT X-ray comparison of aligner gap and thickness of six brands of aligners: an in-vitro study. *Progress in Orthodontics*, 2020, 21(1): 1-12. https://progressinorthodontics.springeropen.com/articles/10.1186/s40510-020-00312-w

[9] HAMBISA S, BELEW S, and SULEMAN S. In vitro comparative quality assessment of different brands of norfloxacin tablets available in Jimma, Southwest Ethiopia. *Drug Design, Development and Therapy*, 2019, 13: 1241. https://doi.org/10.2147/DDDT.S189524

[10] ALSAIFI A, and ALYAHAWI A. Quality assessment of different brands of paracetamol tablets in Yemeni market. *Universal Journal of Pharmaceutical Research*, 2018, 3(4): 39-43. https://doi.org/10.22270/UJPR.V3I4.182

[11] ALSAIFI A. Comparative evaluation quality of different brands of ibuprofen 400 mg tablets available in Yemeni's Market. *Chronicles of Pharmaceutical Science*, 2018, 3: 730-742.

[12] WEBER A, STEINER W J, and LANG S. A comparison of semiparametric and heterogeneous store sales models for optimal category pricing. *OR Spectrum*, 2017, 39(2): 403-445.

[13] MURRAY L, ARIAS A, LI J, et al. Innovative in vitro methodologies for establishing therapeutic equivalence. *Revista Panamericana de Salud Publica*, 2016, 40: 23-28. https://www.scielosp.org/article/rpsp/2016.v40n1/23-28/

[14] CRISTOFOLETTI R, ROWLAND M, LESKO LJ, et al. Past, present, and future of bioequivalence: improving assessment and extrapolation of therapeutic equivalence for oral drug products. *Journal of Pharmaceutical Sciences*, 2018, 107(10): 2519-2530.

[15] SANTORO A, GENOV G, SPOONER A, et al. Promoting and protecting public health: how the European Union pharmacovigilance system works. *Drug Safety*, 2017, 40(10): 855-69.

[16] HANIF AM, SIAL AA, ALI H, et al. Dexibuprofen: Statistical assessment of drug release kinetics and investigative quality perspective. *Pakistan Journal of Pharmaceutical Sciences*, 2018, 31(5): 2157-2162

[17] MUSHTAQ M, FAZAL N, and NIAZ A. Formulation and evaluation of fast-disintegrating tablets of flurbiprofen and metoclopramide. *Journal of Pharmaceutical Innovation*, 2021, 16(3): 419-438.

[18] LAI J, LIN W, SCHOLES P, and LI M. Investigating the effects of loading factors on the in vitro pharmaceutical performance of mesoporous materials as drug carriers for ibuprofen. *Materials*, 2017, 10(2): 150.

[19] SHAHID MA. Development of analytical method of Dexibuprofen in different pharmaceutical dosage forms available in the market by HPLC method 2017. https://scholar.google.com.pk/scholar?hl=en&as_sdt=0%2C5&as_ylo=2017&as_yhi=2022&as_vis=1&q=Shahid+MA.+Development+of+analytical+method+of+dexibuprofen+in+different+pharmaceutical+dosage+forms+available+in+the+market+by+HPLC+method+2017.&btnG=

[20] MOHAMED H R S A K, CHUNGATH T T, SRIDHAR K, et al. Development and Validation of a Discriminative Dissolution Medium for a Poorly Soluble Nutraceutical Tetrahydrocurcumin. *Turkish Journal of Pharmaceutical Sciences*, 2021, 18(5): 565. https://doi.org/10.4274/tjps.galenos.2021.91145

[21] PESTIEAU A, and EVRARD B. In vitro biphasic dissolution tests and their suitability for establishing in vitro-in vivo correlations: A historical review. *European Journal of Pharmaceutical Sciences*, 2017, 102: 203-219. https://doi.org/10.1016/j.ejps.2017.03.019

[22] HAMED R, ALNADI S H, and AWADALLAH A. The effect of enzymes and sodium lauryl sulfate on the surface tension of dissolution media: toward understanding the solubility and dissolution of carvedilol. *AAPS PharmSciTech*, 2020, 21(5): 1-11.

[23] SIMIONATO L D, PETRONE L, BALDUT M, et al. Comparison between the dissolution profiles of nine meloxicam tablet brands commercially available in Buenos Aires, Argentina. *Saudi Pharmaceutical Journal*, 2018, 26(4): 578-584.

[24] CASCONE S. Modeling and comparison of release profiles: Effect of the dissolution method. *European Journal of Pharmaceutical Sciences*, 2017, 106: 352-361.

[25] BUSHRA R, SHOAIB MH, ALI H, et al. In vitro drug analysis and stability studies of optimized formulations of Aceclofenac (100 mg) Tablets. *Latin American Journal of*

Pharmacy, 2016, 35(4): 695-704.
[26] WORLD HEALTH ORGANIZATION. *Systematic reviews for the update of the WHO guideline on country pharmaceutical pricing policies*. World Health Organization, 2020. https://apps.who.int/iris/bitstream/handle/10665/335704/9789240011892-eng.pdf
[27] WOUTERS O J, KANAVOS P G, and MCKEE M. Comparing generic drug markets in Europe and the United States: prices, volumes, and spending. *The Milbank Quarterly*, 2017, 95(3): 554-601. https://onlinelibrary.wiley.com/doi/pdfdirect/10.1111/1468-0009.12279
[28] VICENT M. *Assessment of quality of Metropolitan tablet brands sold in Ishaka town pharmacies*. Research Report. Kampala International School of Health Sciences Press, 2018.
[29] AREFIN P, AHMED R, HABIB M S, et al. Evaluation of Critical Quality Attributes of Immediate Release Ciprofloxacin Tablets of Different Pharmaceutical Companies in Bangladesh. *Biosciences Biotechnology Research Asia*, 2021, 17(4): 781.
[30] RAHMAN S. Comparative in vitro quality evaluation of different brands of Ebastine 10 mg tablets commercially available in Bangladesh. PhD Thesis, Bracu University, 2019. http://dspace.bracu.ac.bd/xmlui/bitstream/handle/10361/13923/15146048_PHR.pdf?sequence=2&isAllowed=y
[31] JAIN A, CHAUDHARY J, SAINI A, and MEHAN N. Quality assessment and comparative study of different marketed brands of metformin. *Research Journal of Pharmacy and Technology*, 2019, 12(3): 1357-1360. https://rjptonline.org/HTML_Papers/Research%20Journal%20of%20Pharmacy%20and%20Technology__PID__2019-12-3-67.html

参考文:

[1] BINDU S、MAZUMDER S 和 BANDYOPADHYAY U. 非甾体类抗炎药(非甾体抗炎药)和器官损伤：当前观点。生化药理学，2020，180：114147. https://doi.org/10.1016/j.bcp.2020.114147
[2] DAVIS A, 和 ROBSON J. NSAIDs 的危险：从两方面看。英国全科医学杂志，2016，66(645)：172-173。
[3] ALI FR、SHOAIB MH、YOUSUF RI 等。基于右布洛芬微乳液的透皮储库贴剂的设计、开发和优化，用于控制药物输送。国际生物医学研究。2017. https://doi.org/10.1155/2017/4654958
[4] GLISZCZYŃSKA A 和 SÁNCHEZ-LÓPEZ E. 右布洛芬治疗进展：前药和纳米技术制剂。药剂学，2021，13(3)：414。https://doi.org/10.3390/pharmaceutics13030414
[5] MAGUIRE J A, JIANG W, 和 YU L X. 现代制药法规：药品质量评估。在开发固体口服剂型中，第 1095-1126 页。学术出版社，2017。https://doi.org/10.1016/B978-0-12-802447-8.00040-6
[6] ABDUL-HASAN M T、Al-SHAIBANI A J N、WANNAS A N 和 HASAN AL-GBURI K M。在伊拉克销售的常规硫酸氢氯吡格雷片剂的质量控制测试。国际应用药剂学杂志，2022：221-225。https://doi.org/10.22159/ijap.2022v14i1.43331
[7] HAMEED A、SHARIF N、ASHRAF M 等。巴基斯坦可获得的非索非那定制剂的药物等效性分析工作。三杰药学与药理学，2018，5：203。http://article.scholarena.com/Pharmaceutical-Equivalent-Analysis-Work-for-Fexofenadine-Preparations-Accessible-in-Pakistan.pdf
[8] LOMBARDO L、PALONE M、LONGO M 等。六个品牌矫治器的矫治器间隙和厚度的微 CT X 射线比较：一项体外研究。正畸学进展，2020，21(1)：1-12. https://progressinorthodontics.springeropen.com/articles/10.1186/s40510-020-00312-w
[9] HAMBISA S、BELEW S 和 SULEMAN S. 埃塞俄比亚西南部吉马市不同品牌诺氟沙星片剂的体外质量比较评估。药物设计、开发和治疗，2019，13：1241。https://doi.org/10.2147/DDDT.S189524
[10] ALSAIFI A 和 ALYAHAWI A. 也门市场上不同品牌扑热息痛片的质量评估。万能药物研究杂志，2018，3(4)：39-43。https://doi.org/10.22270/UJPR.V3I4.182
[11] ALSAIFI A. 也门市场上不同品牌布洛芬 400 毫克片剂的质量比较评价。药学编年史，2018，3：730-742。
[12] WEBER A、STEINER W J 和 LANG S。半参数和异构商店销售模型的最佳类别定价比较。或光谱，2017，39(2)：403-445。
[13] MURRAY L、ARIAS A、LI J 等。建立治疗等效性的创新体外方法。泛美公共卫生杂志，2016，40：23-28. https://www.scielosp.org/article/rpsp/2016.v40n1/23-28/
[14] CRISTOFOLETTI R、ROWLAND M、LESKO LJ 等。生物等效性的过去、现在和未来：改进口服药物产品治疗等效性的评估和外推。药学杂志，2018，107(10)：2519-2530.
[15] SANTORO A、GENOV G、SPOONER A 等。促进和保护公众健康：欧盟药物警戒系统如何运作。药品安全，2017，40(10)：855-69.
[16] HANIF AM、SIAL AA、ALI H 等。右布洛芬：药物释放动力学的统计评估和调查质量的观点。巴基斯坦药学杂志，2018，31(5)：2157-2162
[17] MUSHTAQ M、FAZAL N 和 NIAZ A。氟比洛芬和甲氧氯普胺快速崩解片的配方和评价。药物创新杂志，2021，16(3)：419-438.
[18] LAI J、LIN W、SCHOLES P 和 LI M. 研究负载因子对作为布洛芬药物载体的介孔材料体外药学性能的影响。材料，2017，10(2)：150.
[19] 沙希德马。通过高效液相色谱方法开发市场上不同药物剂型中右布洛芬的分析方法 2017. https://scholar.google.com.pk/scholar?hl=en&as_sdt=0%2C5&as_ylo=2017&as_yhi=2022&as_vis=1&q=Shahid+MA.+Development+of+dexibuprofen+in+different+pharmaceutical+dosage+forms+available+in+the+market+by+HPLC+method+2017.&btnG=
[20] MOHAMED HRSAK、CHUNGATHTT、SRIDHARK 等。开发和验证难溶性营养保健品四氢姜黄素的鉴别溶出度介质。土耳其药学杂志，2021 年，18(5)：565。https://doi.org/10.4274/tjps.galenos.2021.91145
[21] PESTIEAU A 和 EVRARD B. 体外双相溶出试验及其建立体外-体内相关性的适用性：历史回顾。欧洲药学杂志，2017，102：203-219。https://doi.org/10.1016/j.ejps.2017.03.019
[22] HAMED R、ALNADI S H 和 AWADALLAH A. 酶和

十二烷基硫酸钠对溶解介质表面张力的影响：了解卡维地洛的溶解度和溶解度。AAPS 医药科技, 2020, 21(5): 1-11.
[23] SIMIONATO L D、PETRONE L、BALDUT M 等。阿根廷布宜诺斯艾利斯市售的九种美洛昔康片品牌的溶出曲线比较。沙特制药杂志，2018，26(4)：578-584。
[24] CASCONE S. 释放曲线的建模和比较：溶解方法的影响。欧洲药学杂志，2017，106：352-361。
[25] BUSHRA R、SHOAIB MH、ALI H 等。醋氯芬酸(100 毫克)片剂优化配方的体外药物分析和稳定性研究。拉丁美洲药学杂志，2016 年，35(4)：695-704。
[26] 世界卫生组织。更新世卫组织国家药品定价政策指南的系统审查。世界卫生组织，2020。https://apps.who.int/iris/bitstream/handle/10665/335704/9789240011892-eng.pdf
[27] WOUTERS OJ、KANAVOS PG 和 MCKEE M。比较欧洲和美国的仿制药市场：价格、数量和支出。米尔班克季刊，2017，95(3)：554-601。https://onlinelibrary.wiley.com/doi/pdfdirect/10.1111/1468-0009.12279
[28] VICENT M. 伊沙卡镇药店销售的大都会片剂品牌质量评估。研究报告。坎帕拉国际健康科学学院出版社，2018。
[29] AREFIN P、AHMED R、HABIB M S 等。孟加拉国不同制药公司速释环丙沙星片的关键质量属性评价。亚洲生物科学生物技术研究, 2021, 17(4): 781.
[30] RAHMAN S. 孟加拉国市售的不同品牌依巴斯汀 10 毫克片剂的体外质量比较评价。博士论文，布拉库大学，2019。http://dspace.bracu.ac.bd/xmlui/bitstream/handle/10361/13923/15146048_PHR.pdf?sequence=2&isAllowed=y
[31] JAIN A、CHAUDHARY J、SAINI A 和 MEHAN N. 不同市售品牌二甲双胍的质量评估和比较研究。药学与技术研究杂志，2019，12(3)：1357-1360. https://rjptonline.org/HTML_Papers/Research%20Journal%20of%20Pharmacy%20and%20Technology__PID__2019-12-3-67.html