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A Pharmaceutical Study on Quality Surveillance of Six Empagliflozin (10 mg) Tablet Generics in Pakistan

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Abstract: Sodium glucose co-transporters are a novel and potent class of anti-diabetic drugs. One of the members of this newest class of drugs is empagliflozin. It is considered as a favorable option for controlling type II diabetes mellitus. The objective of the current study is based on the quality surveillance of different empagliflozin brands in Pakistan. Six different empagliflozin counterparts (Emp-A to Emp-F) were collected and assessed for various pharmacopeial and non-pharmacopeial tests. The findings indicated good-quality features. In vitro kinetics was also evaluated by applying various dissolution models using DD-Solver software. All the six selected brands of empagliflozin generics satisfied the compendial requirement. Moreover, the percentage content obtained was within specifications (95%-105%). The applied method was validated. The released kinetic model was found to be the Korsmeyer-Peppas as the best fit at pH 6.8. The statistical evaluation (ANOVA) of the dissolution test exhibited no significant difference in the release pattern of empagliflozin substitutes ($p > 1.00$, 95% C.I.). This in vitro comparative approach will highlight the significant prospect and its interchangeability. Among all, Emp-A was found superior on the basis of pharmaceutical properties, while this study concluded that all empagliflozin brands available in the commercial market exhibited similar release profiles and is safe to use.

Keywords: marketed brands, quality surveillance, empagliflozin.

巴基斯坦六种 恩格列净（10毫克）片剂仿制药的质量监督药学研究

摘要：钠葡萄糖协同转运蛋白是一种新型且有效的抗糖尿病药物。恩格列净 是这类最新药物的成员之一。它被认为是控制 II 型糖尿病的有利选择。本研究的目的是基于对巴基斯坦不同恩格列净品牌的质量监督。收集了六种不同的恩格列净对应物（Emp-A 至 Emp-F),并针对各种药典和非药典测试进行了评估。调查结果表明具有良好的质量特征。还通过使用 双虚拟求解器软件应用各种溶解模型来评估体外动力学。所有六个选定品牌的恩格列净仿制药均满足药典要求。此外，获得的百分比含量在规格范围内(95%-105%)。所应用的方法得到验证

。发现发布的动力学模型是 科斯迈尔-百事可乐，因为它最适合 酸碱度 6.8。溶出度试验的统计评估显示恩格列净替代品的释放模式没有显着差异（p > 1.00，95%置信区间). 这种比较方法将突出显着前景及其互换性。在所有 Emp-A 中，根据药物特性发现其优越性，而该研究得出结论，商业市场上可用的所有 恩格列净 品牌都表现出相似的释放曲线，并且可以安全使用。

关键词：上市品牌，质量监督，恩格列净.

Introduction

The quality of pharmaceutical drug products is a major concern across many developing countries [1]. Pakistan has been identified as a third-world country where the majority of the population suffers from financial crises. The prevalence of substandard and counterfeit drugs is growing increasingly now days. However, literature pertaining of ineffective and falsified products produces an alarming quality-related signal [2, 3]. It is a wide accepted fact that multiple brands of many generics are circulating in local markets and questions the safety, quality, and efficacy of such drug products. It is therefore imperative to substitute the brand with the drug generic counterparts in the prescription to save the economy [4]. This often becomes a matter of immense difficulty for physicians to prescribe an appropriate, reliable, safe, and cost-effective medicine that augments its commercial and customer worth. It is to be noted that the number of drug products manufactured in various countries lack physical and chemical standards resulting in therapeutic failure [5–7]. According to a study conducted on quality inspection of norfloxacin brands. Two of ten brands failed to meet the USP in vitro dissolution testing [8]. Pakistan is one of the Asian countries where the circulation of substandard drugs in the market poses difficulties for patients. Hence, the literature accounts for 40 to 50% consumption of low-quality medicines in Pakistan [9]. Moreover, Ali et al. investigated the presence of a higher level of impurity content in three active ingredient samples procured from India, Italy, and Jordan [10]. In the same vein a survey conducted on Ofloxacin where three out of thirty-four manufacturers failed to produce the desired antimicrobial effect [11]. In another study, 28.5% of the medicines were not meeting the criteria of pharmaceutical quality acceptance and were declared as substandard and counterfeit [3], [10]. These findings have evidenced the varieties of substandard medicinal products. To further this conversation, Pakistan has been criticized for poor quality medication therefore there is a severe dearth of drug regulatory controls to address the highlighted quality issues. To protect public health and retain the physician's confidence, it is needed to undergo the process of quality evaluation using in vitro and in vivo assessment. However, emphasis is being laid on in-vitro Pharmacotechnical testing because it saves time, money, and avoids humans as the subject [12], [13]. Diabetes mellitus (DM) is a progressive endocrine disorder that is a growing epidemic. The proportion of its widespread prevalence produces a global burden on public health worldwide [14], [15]. There is a number of anti-hyperglycemic agents that have been claimed to provide benefits in the management of diabetes. Among them, the gliflozin class of anti-diabetic medications ranks the top [16]. Empagliflozin was approved by USFDA in 2014 to be used for treating type II DM in adults (Fig. 1). The drug belongs to the newer class of selective and competitive inhibitors of sodium-glucose transporters. It is clinically effective for glycemic control [17], [18]. As anti-diabetic drugs are among the highly prescribed category of medications, massive production of empagliflozin tablets by numerous pharmaceutical companies triggers questions on the quality of the generic substitutes. Our weakened regulatory policies and lack of human and financial resources have resulted in the delivery of non-efficacious and unsafe medicines to the population. For these reasons, this study was undertaken to assess the quality of pharmaceutical brands of empagliflozin (10 mg) tablets available in drug stores in Karachi, Pakistan.

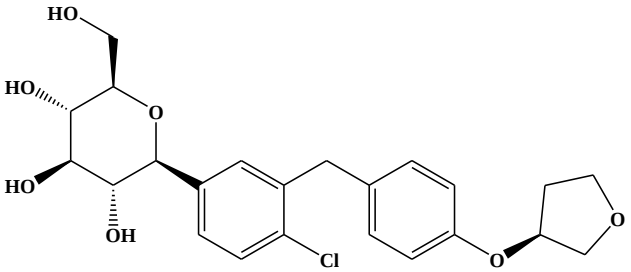

Fig. 1 Structure of empagliflozin

1. Materials and Methods

1.1. Chemicals

Empagliflozin was kindly supplied as a gift sample by Sami Pharma (Pvt.) Ltd. Pakistan. The reagents Potassium dihydrogen phosphate (KH2PO4) and sodium hydroxide (NaOH) were purchased from

(Sigma-Aldrich, Hamburg, Germany). Other chemicals acetonitrile, and orthophosphoric acid, were of suitable analytical grade and purchased from FMC Corporation, USA, and Dow Chemical, USA).

1.2. Chromatography

Analytical balance (GR-200 A& B Company), Electronic digital caliper (Seiko, China), pH meter (VSI-01ATC, VSI Electronics PVT. Ltd), hardness tester (MH-1Galvano Scientific), Tablet disintegrator (121-LGalvano Scientific) dissolution apparatus II (VDA-6DR Veego Instruments), single beam UV-visible spectrophotometer (UVmini-1240v, Shimadzu Corporation). The Shimadzu HPLC system comprised of an LC-20ATVP Pump, anSPD-M20AUV-programmable detector with a sample volume of 10µL. The software was controlled by Shimadzu chemical station LC software. The Mobile phase is constituted a mixture of 0.1% orthophosphoric acid and acetonitrile (70:30%). The experiment was performed by choosing the isocratic mode with a flow rate set at 1 mL/minute. The elution of the peak was carried out at Thermo Hypersil GOLD C18 column (150 × 4.6 mm, 5 µm pore size). The detection was performed at 225 nm with UV-detection. The run time of 10 min was programmed during the analysis.

1.3. Software

DD-Solver as an Adds-Inn menu in Microsoft Excel® software was used to predict the in vitro drug dissolution behavior. Drug-release data of EMP-A to Emp-F were compared and analyzed by IBM SPSS (Statistical Package for the Social Sciences software) (Version 20).

1.4. Sampling of Brands

This study was a laboratory-based cross-sectional survey undertaken in Karachi, Pakistan. The reason for selecting this city was as it is a metropolitan city and holds a huge number of Pharma companies, retail pharmacies, and medical stores. Most of the drug stores are segmented with low- quality and sub-standard products that compromise the therapeutic outcomes of the patient. To perform this study, a random sampling technique was adopted. The six brands containing 10 mg empagliflozin were purchased from licensed drug stores, and local and retail pharmacies in Karachi, City Pakistan. The brands were coded as A, B, C, D, E, and F. All the brands were ensured for their shelf-life period. The selected brands undergo analytical testing. About, 100 tablets were procured for each marketed brand. All the detailed label information including the manufacturing date, a manufacturing company, and batch no. with expiry date was thoroughly checked and is presented in Table 1.

1.5. Study Design

The experimental in vitro part was undertaken at Jinnah Sindh Medical University, Located in Karachi, Pakistan. All the available and commonly prescribed brands available during the study period were examined in this study.

2. Evaluation of Physicochemical Parameters of Empagliflozin Brands

2.1. Identification Test

To confirm the presence of the active ingredient, a high-performance liquid chromatographic procedure was adopted. Six replicates of the standard and five samples were injected to determine the average peak retention time.

2.2. Uniformity of Weight

The weight variation was performed by randomly selecting 20 coated tablets from each brand using an analytical balance. Finally, the average weight, standard deviation (SD), and percentage deviation were computed [19].

2.3. Thickness and Diameter Variation

For each brand, 20 tablets were sampled for thickness and diameter using a vernier caliper and readings were recorded as triplicate in millimeters [20].

2.4. Hardness

The mechanical property known as hardness (n=20) was measured using a hardness tester. The tablets were placed, and the force required to crush the diametrically placed tablet was noted [19].

2.5. Disintegration Time

Measurement of disintegration time was recorded using a basket rack assembly filled with distilled water and temperature maintained at 37 °C. Tablets (n=6) from each brand were placed in each of the six tubes covered by the disc. The timer was set and the time when no was fragment left behind in the basket was noted down [19, 20].

2.6. Dissolution Testing

Empagliflozin- marketed brands were evaluated for in vitro dissolution testing using USP dissolution apparatus (paddle type) at 75 rpm. Six units of each brand were placed in a 900 ml buffer solution of pH 6.8 keeping the temperature at 37°C. After 5, 10, 15, 30, and 45 minutes, 10 ml of the sample was drawn, filtered, and diluted immediately by an equal volume of the dissolution medium, thus maintaining the sink conditions. Finally, the release rate of the active compound was determined by measuring the drug concentrations on HPLC [21].

2.7. Investigation of Release Kinetics

Several model-dependent methods were applied to assess the dissolution behavior of the drug. In model-

dependent approaches, release data were analyzed through six kinetic models including the zero-order, [22] first-order, [23] Higuchi matrix, [24] Hixson–Crowell, [25] Korsmeyer-Peppas [26]and the Weibull model [27] using DD-Solver Adds-Inn software. Equations are summarized in Table 2.

2.8. Quantitative Assay

2.8.1. Standard Preparation

Drug assay was estimated as per the reported and validated method by Shymala et al. [28]; Twenty tablets from each brand were weighed individually and powdered in a mortar and pestle. The amount equivalent to the mean weight was calculated and placed in a 20 mL volumetric flask with a volume made up to the mark with diluent. The sample was kept in a sonicator and filtered. From the filtrate, 1 mL was pipette in another volumetric flask to acquire the final concentration.

2.8.2. Sample Preparation

The stock solution was prepared by carefully weighing the 10-mg empagliflozin and transferring it to a 10 mL volumetric flask containing 5 mL of buffer solution. The solution was thoroughly shaken to dissolve the contents. Later, it was sonicated and finally made up to the mark with the mobile phase.

2.8.3. Validation of the Analytical Method

The validation of the HPLC method was conducted as per ICH (2005) and Food and Drug Administration (FDA) (2001) guidelines.

2.8.4. Preparation of Stock Solution

The Stock solution of 100µg/mL was prepared by dissolving accurately 0.1-mg empagliflozin (pure) in 100 mL of mobile phase with sonication of 15 minutes. The Mobile phase was constituted by mixing 70mL of 0.1%orthophosphoric acid and 30-mL acetonitrile (70:30). Working solutions of various strengths were prepared using the stock solution with appropriate dilution.

2.8.5. Linearity and Specificity

The linearity of the underlying method was observed at nine standard solutions ranging from 0.1 to 100 µg/mL strength (0.1, 0.5, 1.56, 3.125, 6.25, 12.5, 25, 50, and 100 µg/mL). The linearity plot was constructed by taking the peak area against the drug concentration in Microsoft Excel software. Specificity is one of the significant parameters to analyze the interference in the peak of the API, which was observed with the blank (mobile phase) and the placebo mixture. Common excipients required for tablet preparation such as microcrystalline cellulose, lactose, talc, silicon dioxide, and magnesium stearate were added.

2.8.6. Precision and Accuracy

The known strength of standard solutions prepared, and their concentration were then analyzed on the same and three different days. Precision and accuracy of the analytical method were calculated through recovery analysis of samples using three different concentration levels (6.25, 12.5, and 25 µg/mL) with three replicate analyses (n =6). Obtained data were expressed as % accuracy and % coefficient variation of analytes respectively. According to the official procedure, the percent coefficient of variation (CV) and % mean accuracy should be ≤5% and ≥90% respectively.

2.8.7. Robustness

It was assessed through deliberate changes in the temperature of the column (30ºC ± 2ºC), rate of flow (± 0.2 mL/min) and detection wavelength (± 2 nm) using a standard solution of drug having 2.5 µg/mL strength.

2.8.8. System Suitability

In this study, system suitability was determined by assessing the peak area, tailing factor, theoretical plates, and retention time of the empagliflozin (100 µg/mL) solution. Five samples of said strength was injected into the system (n=5). It is officially recommended that the % RSD (relative standard deviation) and tailing factor of peak area must be <2%. Moreover, theoretical plates >2000 and retention time >2.0 are also essential requirements of a suitable HPLC system (USP, 2014).

2.8.9. Statistical Analysis

The data reported in the current study were expressed as means, standard deviations, and graphically in Microsoft Excel 2010. However, the statistical evaluation of the experiment was analyzed using SPSS software (version 23). To compare the significant differences among the dissolution pattern of the marketed brands, a One-way analysis of variance test (ANOVA) with a 95% confidence interval was applied showing (p>1.00, 95% C.I.).

3. Results

Results are displayed in Tables 1-9.

Table 1 General characteristics of empagliflozin (10 mg) brand tablets

Code	Manufacturer	Batch No.	Mfg. Date	Exp. Date	Price per pack in PKR (10 tablets)
Emp-A	Getz Pharma	026FB5	11-2021	11-2023	200
Emp-B	Hilton Pharma	141836	12-2021	12-2023	200
Emp-C	Horizon Pharma	938	02-2021	02-2023	250
Emp-D	Macter Pharma	1010	10-2021	09-2023	270

Continuation of Table 1

Emp-E	Searle Pharma	00027	12-2021	12-2023	280
Emp-F	Genix Pharma	016T220	13-10-2021	12-10-2023	230

Table 2 Applied models for drug dissolution pattern

Kinetic Models	**Equations**
Zero–order release	$Qt = K0t$
First–order model	$\text{Log } Q = \text{Log}Q_0 - \frac{kt}{2.303}$
Higuchi kinetics	$Q = kt^{\frac{1}{2}}$
Korsmeyer–Peppas Model	$\frac{M_t/M_\infty}{t^n}$
The Weibull model	$\text{Log}[-\ln(1-m)] = b\log(t-Ti) - \log\alpha$
Hixon-Crowell model	$Q_0^{1/3} - Q_t^{1/3} = K_{HC} \times t$

Table 3 Systems suitability parameters (n = 5)

Parameters	**Findings**	**Remarks**
USP Tailing factor	0.975	Compliant
Peak Area (mean)	1826329 ± 29222	Compliant
% RSD	1.60	Compliant
Retention time (min)	9.118 ± 0.004	Compliant
% RSD	0.05	Compliant
Theoretical plates	51895	Compliant
Resolution (Rs)	1.27	Compliant
Capacity factor (K')	1.47	Compliant

Table 4 Retention time of empagliflozin tablets

Test sample	**Peak Retention Time (Rt) min**	**Identification test**
Empagliflozin RS	9.11	Pass
Empa-A	9.11	Pass
Empa-B	9.11	Pass
Empa-C	9.12	Pass
Empa-D	9.11	Pass
Empa-E	9.12	Pass
Empa-F	9.12	Pass

Table 5 Physico-chemical evaluation of the empagliflozin (10 mg) brand tablets

Code	**Weight variation (mg) n = 20 (Mean ± SD)**	**Thickness (mm) n = 20 (Mean ± SD)**	**Diameter (mm) n = 20 (Mean ± SD)**	**Hardness (kg) n = 20 (Mean ± SD)**	**Disintegration Time n = 6**	**Assay (%) n = 3 (Mean ± SD)**
Emp-A	252.12 ± 1.48	2.94±0.02	7.49 ± 0.03	5.19 ± 0.21	4 min 34 sec	94.37
Emp-B	263.53 ± 1.99	3.45±0.05	7.07 ± 0.04	4.76 ± 0.58	6 min 39 sec	94.40
Emp-C	255.75 ± 1.19	3.48±0.04	8.14 ± 0.04	4.48 ± 0.49	5 min 33 sec	100.97
Emp-D	245.98 ± 2.20	3.11±0.28	8.12 ± 0.05	4.65 ± 0.98	4 min 01 sec	96.60
Emp-E	251.92 ± 1.90	3.47±0.04	8.20 ± 0.23	5.07 ± 0.43	5 min	94.40
Emp-F	256.12 ± 2.85	3.26±0.27	8.14 ± 0.04	6.01 ± 0.40	5 min	93.91

Table 6 Drug's linearity profile

Parameter	**Findings**
Concentration Range	50-2.5 µg/mL
Coefficient of correlation	0.9998
Expression	Y = 18745x + 54385
Slope	18745
Y intercept	54385

Table 7 Reproducibility (inter and intra-day precision and accuracy = 3)

Reproducibility	**Added Concentration (µgmL^{-1})**	**Concentration found(µgmL^{-1}) (Mean ± SD)**	**Percent Mean Accuracy (%)**	**%CV for precision (< 2%)**
Precision	25	24.86 ± 0.11	99.44	0.47
Interday	12.5	12.41 ± 0.03	99.33	0.24
	6.25	6.17 ± 0.05	98.72	0.85
Precision	25	24.98 ± 0.10	99.94	0.41
Intraday	12.5	12.41 ± 0.05	99.33	0.46
	6.25	6.19 ± 0.03	99.14	0.50

Table 8 Robustness of the analytical method (n = 3)

Variations in Chromatographic conditions (2.5 µgmL^{-1})		**Concentration obtained (µgmL^{-1}) (Mean ± SD)**	**CV (%)**	**Mean Accuracy (%)**
Flowrate (mLmin^{-1})	0.8	2.46 ± 0.04	1.06	98.64
	1.0	2.50 ± 0.008	0.34	100.03
	1.2	2.48 ± 0.001	0.74	99.25

Continuation of Table 8				
Column Temperature(℃)	32	2.47 ± 0.02	1.13	99.16
	30	2.47 ± 0.03	1.29	99.06
	28	2.49 ± 0.02	1.00	99.78
Detection wavelength(nm)	235	2.47 ± 0.01	0.60	98.94
	233	2.50 ± 0.01	0.63	100.32
	237	2.49 ± 0.03	1.22	99.73

Table 9 In vitro release kinetics of various brands of empagliflozin (10 mg) tablets at pH 6.8

Code	Zero Order		First Order		Higuchi		Korsmeyer-Peppas			Hixon-Crowell		Weibull		
	r^2	K0 (hr-1)	r^2	K (hr-1)	r^2	KH (hr-1/2)	r^2	KKP (hr-n)	n	r^2	KHC (hr-1/3)	r^2	α	β
Emp-A	0.627	0.012	0.628	0.000	0.698	0.151	0.996	0.642	0.125	0.628	0.000	0.791	300.118	0.310
Emp-B	0.704	0.011	0.704	0.000	0.771	0.133	0.909	0.457	0.190	0.704	0.000	0.842	347.783	0.315
Emp-C	0.749	0.009	0.749	0.000	0.791	0.121	0.912	0.504	0.162	0.749	0.000	0.873	272.542	0248
Emp-D	0.651	0.013	0.651	0.000	0.738	0.147	0.934	0.491	0.179	0.651	0.000	0.795	398.808	0.364
Emp-E	0.718	0.010	0.719	0.000	0.775	0.128	0.941	0.500	0.161	0.719	0.000	0.857	319.775	0.290
Emp-F	0.635	0.011	0.635	0.000	0.806	0.139	0.976	0.593	0.158	0.635	0.000	0.803	304.679	0.296

4. Discussion

4.1. A Sampling of Marketed Brands of Empagliflozin

We performed a blind study on six available samples of empagliflozin manufactured by national pharma companies. Upon thorough visual inspection, none of the coded brands were found to be defective. Brand A-F displayed a coated appearance with a smooth texture and round shape. The data of the general characteristics with unit retail price of the available marketed brands are shown in Table 1. Analyses of price variation among the brands disclosed no significant difference with promising outcomes.

4.2. Identification Study

HPLC is a versatile, accurate, and reliable technique widely employed in analysis to achieve separation of the components [29]. Here, the average retention times varied from 9.12 min (Empa-F) to 9.11 min (Empa-D), and the peak retention times of the empagliflozin reference standard was found to be 9.11 min as presented in Table4 and Figure 2 (A-G). All the generic counterparts of empagliflozin exhibited retention times corresponding to the standard. Hence, it proves the validity of the test.

4.3. Uniformity of Weight

The uniformity of the weight test assesses the incorporation of the right proportion of active and inactive ingredients. Two important factors such as die feeding and the applied lower and upper punch forces greatly influence the weight variation [30]. Here, the official method of British pharmacopeia was adopted to conduct the test. As endowed in Table 5, the maximum and minimum average weights of the brands were recorded to be 263.53±1.99 and 251.92 ±1.90mg, respectively. As per the passing criteria, all the brands fulfill the pharmacopeia standards of weight variation [19]. Concerning a previous study undertaken to investigate multiple local and five multi-national brands of paracetamol, similar satisfactory results in weight variation were found [31].

4.4. Thickness and Diameter Test

Dimensional measurement is a rapid in-process test. The tablets of six brands maintained their thickness and diameter within their stipulated range of ±5% as shown in Table 5. The results suggest the fact that uniformity in the size of the tablets was maintained during production.

4.5. Hardness Test

A Hardness test was conducted on the brands of Empagliflozin. The mean hardness ranges between 4-7 kg. A breaking force of 4-6 Kg is sufficient to prevent damage during transportation [32], [33]. Hence, based on the results of Table 5, all the brands displayed adequate hardness with sufficient mechanical integrity.

4.6. Disintegration Time

All the examined brands are immediate- release formulations that are designed in a way to disintegrate in less than about 30 minutes [34]. A disintegration time of fewer than 30 minutes was observed in all empagliflozin-marketed brands (Table 5). The one possible reason for the quick disintegrating effect is the powerful action of the super disintegrant [35]. The higher compression forces during tableting produce harder tablets with prolonged disintegration time and compromise the consistency of the manufactured batch. Therefore, adequate disintegration time is a necessary requisite for maintaining pharmaceutical quality standards. In this study, Empa-B showed the highest disintegration time and Empa-A and D as slow.

4.7. In Vitro Dissolution and Release Mechanism

Fig. 2 illustrates the release profile of multiple empagliflozin brands. In this graph, the drug release is shown at pH 6.8. According to the scope of the study, a drug release of > 80% had to be observed in the respective media. The results suggested the complete

release of the drug content within 15 minutes in phosphate buffer. Out of the six brands, EMPA-A displayed the highest Q value of 100.8 ± 1.47%. The order of the in vitro release rate from different brands at a different time is as follows Empa-A > Empa F > Empa D > Empa C > Empa E > Empa B. The variation in the cumulative drug release is attributed to the different and/or the same kind(s) of excipients incorporated and to the employed manufacturing process adopted during processing [36]. The Dissolution profiling comparison is a valuable exercise to compare the test and reference brand at specified time intervals [37]. In this regard, SUPAC-IR has been focusing on establishing a comparative dissolution profiles using various methods [38]. A study based on bioequivalence and interchangeability in metformin brands was also conducted in Qatar previously [39]. Further, to elucidate the drug release mechanism, the dissolution data were fitted to various kinetic models (Table 6). The results were computed using DD-Solver Excel Sheet software. In this research, the mathematical treatment revealed Korsmeyer-Peppas to be the best-fit model with the release exponent values laid between 0.45-0.89, as shown in Table 6. Moreover, the ANOVA test confirms that the drug release pattern of all generic counter parts with *p* value > 1.0.

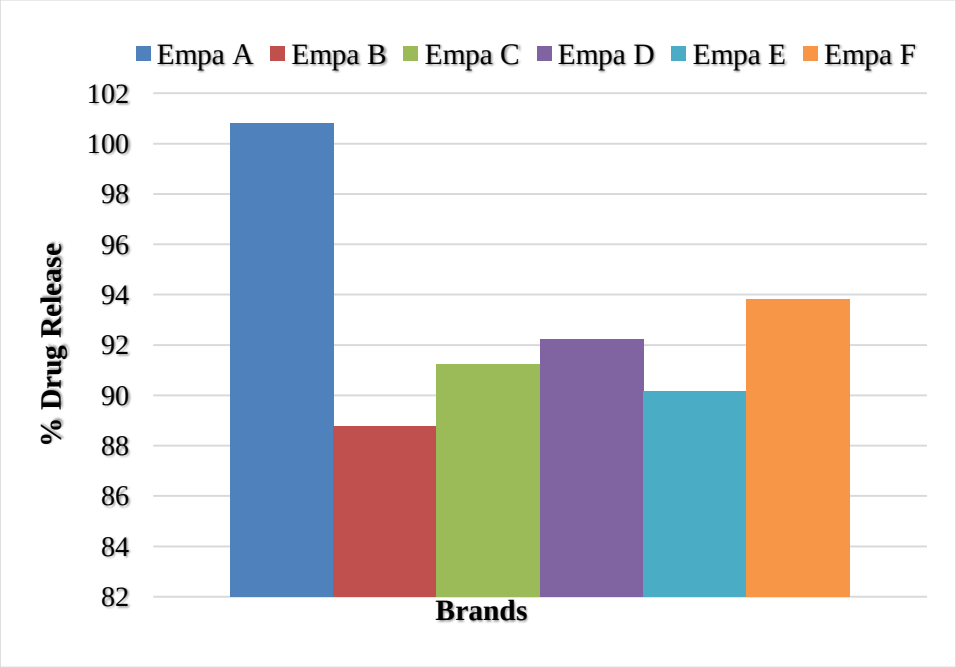

Fig. 2 Comparative dissolution profile of empagliflozin at pH 6.8

4.8. Drug Content

To ascertain the same amount of active content in the tablet, an assay should be performed. As an outlined, none of the empagliflozin brands exceeded the limit of not less than 95.0 % and not more than 105.0 % of the stated amount (Table 5). It is evident from this study that the correct strength of the active ingredient is present in all tested brands. Thus, they satisfied the quality control requirement of the assay test. In a study undertaken in Senegal concerning the market surveillance of individual and combined formulations the results of assay were found satisfactory [40].

4.9. Validation of the Proposed Method

The proposed analytical method exhibited validity for the quantification of empagliflozin in commercially available oral formulations. The value of the correlation coefficient obtained through the generated calibration plot was 0.9998 (Figure 3). This suggests excellent linearity over the relevant concentration range. To establish reproducibility, both intra and inter-day precision were assessed and the results obtained are presented in Table 7. Additionally, the accuracy was calculated by the mean percent recovery against each set of prepared samples. The findings assure us that the method is accurate and precise. Here, the method was also challenged for robustness studies after modifying the chromatographic conditions. The results indicate robustness as the % RSD did not exceed 5% of its normal conditions. During the experiment, the method was also found to be suitable as the parameters listed in Table-aligned with the USP recommendations. Similarly, no significant peaks were observed at the elution time, thus elucidating the selectivity of the method for the intended purpose.

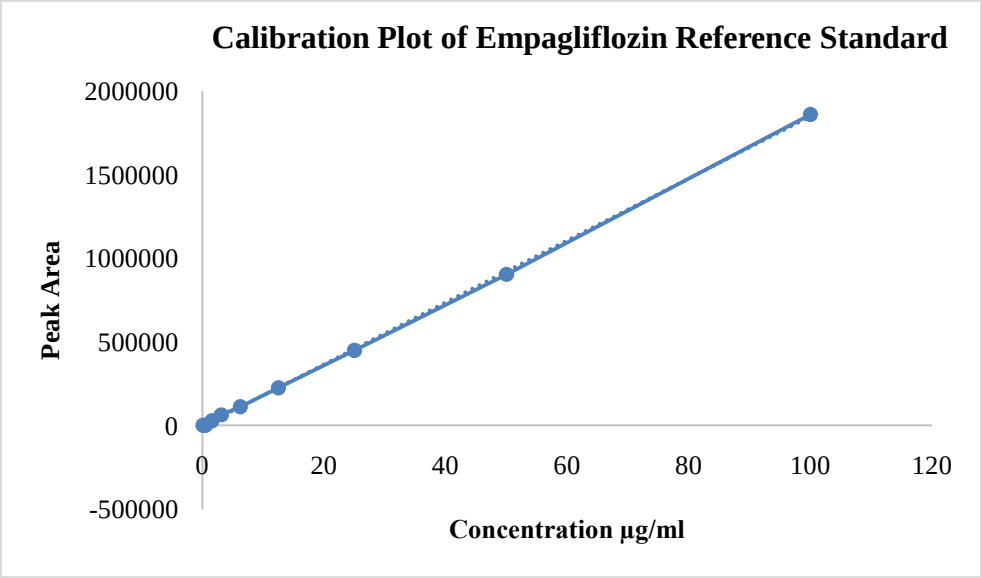

Fig. 3 Calibration plot of empagliflozin reference standard

5. Conclusion

The drug release revealed that all empagliflozin brands exhibited no significant difference in their release pattern and, Empagliflozin obeyed the Korsmeyer-Peppas model. Among all, Empa-Ashowed excellent physicochemical characteristics. All the brands available in the market met the pharmacopeial criteria and hence are considered suitable, effective, and reliable in prescribing. It has also been concluded that there is also no significant variation in the prices of all brands. Hence, all the empagliflozin brands are claimed to be bioequivalent and could be used interchangeably. The proposed study describes the quality standard of Empagliflozin-marketed brands, the quantitative and qualitative profile, and its replacement in clinical prescribing by physicians. It is further suggested to cover IVIVC (in vitro - in vivo correlation) studies as this type of study influences patient compliance by overcoming the chances of drug therapy failure related to substandard medications.

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