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Short Communication

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Comparative Study of Three Brands of Antidiabetic Drug, Empagliflozin Available in Karachi, Pakistan

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ABSTRACT

Empagliflozin is a newer oral antidiabetic drug that treats people who have type-II Diabetes Mellitus. Empagliflozin reduces the reabsorption of filtered glucose and increases urine glucose excretion. The objective of the study is to analyze the physiochemical equivalence of different brands of Empagliflozin available in Pakistan. Three different brands of Empagliflozin were evaluated for their physicochemical properties and cost-effectiveness. These brands were analyzed for different physicochemical tests for weight variation, hardness, friability, disintegration, and dissolution. All the brands had an average hardness of ≥2kg, which was suitable for an immediate-release tablet. All three brands had shown their friability variation within ±1% range specified by United State Pharmacopoeia (USP). The standard deviation was also calculated. All three brands showed good disintegration and dissolution profile which would aid in maximizing bioavailability and satisfying patient needs. The present findings suggest that almost all three brands of Empagliflozin that are available in Karachi meet the USP specification for quality control analysis.

KEYWORDS: Empagliflozin, Physicochemical testing, Hardness, Thickness, Friability, Dissolution, Disintegration.

INTRODUCTION

Pharmaceuticals are essential for preserving human health. However, in order to provide the intended pharmacological effect, it is important to determine the medications' safety, efficacy, and quality. However, in order to make the claim that a drug is of high quality, pharmaceuticals must adhere to regulatory regulations according to USP [1]. Additionally, the quality of pharmaceuticals must be trustworthy in order to guarantee the safety and effectiveness of pharmaceutical products. Therefore, routine laboratory testing at various points throughout and after the production process of the drugs should be conducted in order to achieve the requisite quality medications [2].

Comparative studies are executed to check, evaluate and compare the quality standards of commercially available pharmaceutical brands of different Multinational and National Pharmaceutical companies of Pakistan. Along with the availability of pharmaceuticals from multiple sources came the widespread circulation of fake and low-quality drug items [3]. This critical public health issue is far more prevalent in developing and underdeveloped countries. In addition, taking low-quality medications has a number of negative effects, such as treatment failure, drug resistance, and increased morbidity and death. Similarly, the availability of low-quality pharmaceuticals is a result of some countries' weak drug regulatory agencies and lax quality control procedures [4].

These factors prompted all researchers involved to conduct quality assessment studies on the pharmaceutical products that were currently on the market in order to identify subpar drug products [5,6]. Thus, the goal of the current study was to compare the physicochemical composition of Empagliflozin tablets produced locally and imported for Karachi Pakistan.

Empagliflozin chemical name is D-Glucitol 1,5-anhydro-1-C-[4-chloro-3-[[4-[[(3S)-tetrahydro-3furanyl[oxy]phenyl]

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methylphenyl]-,(1S). Empagliflozin chemical formula is C23H27CLO7, with a molecular weight of 450.91[7].

It is a more recent medication that was approved in Europe and the United States of America and is used to treat patients of type-II Diabetes Mellitus. These oral drug agents inhibit sodium glucose cotransporter-2 (SGLT-2) by reducing the reabsorption of filtered glucose and increasing urine glucose excretion[8-11]. Therefore, the aim of this study was to evaluate the different physicochemical properties and cost-effectiveness of Empagliflozin antidiabetic drug brands available in Karachi (Pakistan). This study will be beneficial for the choice of the best brand by doctors and pharmacists [12-17].

METHODOLOGY

Sample collection: There are many brands of Empagliflozin 10mg tablets available in the market of Karachi, Pakistan which makes it challenging to choose a brand that can be used and determine whether it will be as effective as an ethical brand; as a result, the current study has been created to assess the quality control parameters of several chosen brands of empagliflozin. Therefore, three brands of empagliflozin with price ranges from 275 to 350 PKR were purchased and analysed for the following parameters.

Weight variation:

Weight variation of a tablet is a physical test and is used to ensure the content uniformity of dosage form. It was done by using FX-400A.N. D Electronic Balance. It must be within a limited range as stated in U.S.P. In this, randomly, 20 tablets were selected from each brand. The acceptable limit range was selected according to USP, i.e. Less variate from±10%. After performing the test, upper and lower limits were calculated by the following formula.

UCL= Mean+3 X S.D

LCL= Mean-3 X S.D

Minimum and Maximum variation in percent limits are calculated by the given formula.

Min. weight variation % =(avg. Wt–Min. wt)/ avg. wt x 100

Max. Weight variation %=(Max. wt–avg. wt.)/ age wt. x 100

Whereas,

UCL=upper control limit, LCL=lower control limits'=standard deviation, in=Minimum

Mix=Maximum, Avg wt. =Average weight.

Diameter and Thickness: Thickness and diameter are important parameters of the Quality control test; Thickness may variate from 2-4mm, and diameter is to be 4-13mm. The Compaction degree is measured via randomly selected 20 tablets by means of Vernier Caliper [18].

Hardness: A hardness test is performed by taking 10 tablets from each brand respectively to check a tablet's structural integrity and breaking point when mechanical force applies to it. In our research laboratory, we use MH-1 Hardness tester of Galvano scientific. Hardness must be 4-6 kg but not less than 3kg [19].

Friability: Ten tablets from each of three brands of antidiabetic drugs were randomly selected and subjected in a uniform manner in FB-1004 CURIO COMPANY fraibilator for the specified time period of 4 minutes, at 25 rotations per minute. Initial and final readings of tablets were recorded and compared to evaluate the weight loss. A friability test is performed to estimate the abrades of tablets during packaging and shipment [20].

The friability of tablets is calculated by giving the formula;

$$\text{Friability \%} = \frac{(W1-W2)}{W1} \times 100$$

Whereas W1 and W2 is the initial and final weight of 10 tablets [21].

Disintegration: Disintegration was carried out by using CURRO MODEL NO DS-0702. For this 900ml beaker was filled with distilled water and set at a temperature of 370 C. Randomly 6 tablets of each Empagliflozin brand were selected and introduced into the basket rack assembly of the disintegration apparatus. The timing of disintegration was determined to be when there were no tablet granules left on the mesh [22].

Dissolution: Dissolution is performed to determine the release of API (Active pharmaceutical ingredient) from the dosage form, such as a tablet or capsule, when introduced to the medium. This test was carried out by using GDT-7L model, Galvano scientific Paddle Apparatus I in 900ml 0.1N HCL dissolution media at 100rpm for 60 minutes. The tablets were placed in the vessels for each test, and the stopwatch was started concurrently, vessels were enclosed during the cycle with plastic covers to reduce evaporation. The temperature in the vessels was maintained at 37+/-0.50C during every dissolution cycle. Samples are manually taken out using 5ml syringe fitted with stainless tubing to make certain reproducibility of the samples site. Absorbance was recorded at 274 nm by UV-Spectrophotometer for calculating percent drug release [23].

RESULTS & DISCUSSION

The physico-chemical parameters such as weight variation, hardness, thickness, friability, dissolution and disintegration have been performed invitro in order to analyze three different brands of Empagliflozin 10mg tablets, i.e., Emg-01, Emg-02, Emg-03. The results were compared with the limits given by USP. The price comparison of three different brands of Empagliflozin shows in figure-I.

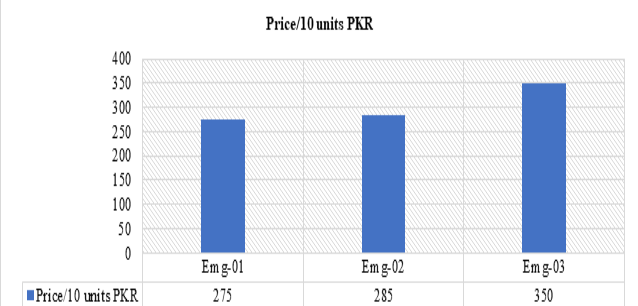

Figure-I: Price comparison of three brands.

A weight Variation test has been performed and found slight variation in weights of both brands, but in order to calculate whether this variation is within limits, the standard deviation was calculated. All the brands, i.e., Emg-0, Emg-02, and Emg-03, comply with the USP specifications, and none of the brands deviates by ±7.5 % of the mean value. Hardness is a non-official test to check the tablet's strength. USP specifies the range of stress between 4 to 6 Kg. Tablets were subjected to the stress applied by a hardness tester. The hardness and Thickness test of the three brands were found to be in acceptable ranges. The results were reported in average values that range between 3.91 to 7.85 kg for hardness and 0.20 to 0.34mm for thickness, respectively (Table-I).

The friability value should not be more than 1%. The results of all three brands lie within the limit. Emg-01 and 03 have minimum friability, i.e., 0.158, 0.231, and Emg-02 has shown maximum friability i.e., 0.332[24].

Disintegration time is the time taken by the tablets to break up into granules, and it should be within 3min. All given brands had been disintegrated within the time limit.

A dissolution test of brands has been found within the official specification of USP, which said that the amount of drug release (Active ingredient) in solution should not be less than 80% of the label claim amount at 30min (Table-II).

Table-I: Statistical weight variation, hardness and thickness test.

Brands	Mean±SD (gm)*	M±SD n(Kg)	Mean±SD (mm)
Emg -01	0.187 ± 0.001	3.755 ± 0.136	3.557 ±0.072
Emg -02	0.151 ± 0.002	3.773 ± 0.147	3.484 ±0.131
Emg-03	0.159 ± 0.002	3.763 ± 0.187	3.584 ±0.151

Deviation should be ±7.5%.

Table-II: Dissolution, Disintegration and Friability test.

Brands	Percent drug release in 45 min	Limit	Remarks	Disinteg-ration time	Limits	Remarks	Friability (%)	Limits	Result
Emg-01	88		Pass	1min		Pass	0.158		within limits
Emg-02	86	NLT 85%	Pass	10sec	NLT 85%	Pass	0.332	NLT 85%	within limits
Emg-03	89		Pass	20Sec		Pass	0.352		within limits

NLT: Not less than; NMT: Not more than.

CONCLUSION

Each tablet fulfilled USP requirements for friability and showed uniformity in hardness and weight variation. The disintegration and Dissolution test of brands has been found within the official specification of USP. As a result, it can be concluded that all of the brands of Empagliflozin tested have uniform weights, sufficient physical stability to maintain physical integrity over time, and the ability to withstand the rigours of mechanical shocks encountered during its production, packaging, shipping, and dispensing.

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Author's Contribution:

Khadija Aslam: Substantial contributions to the conception or design of the work.
Safila Naveed: Acquisition, analysis, or interpretation of data for the work
Fatima Qamar: Drafting the work or reviewing it critically for important intellectual content
Halima Sadia: Substantial contributions to the conception or design of the work.
Muhammad Ulusyar Khan: Interpretation of data for the work.
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