University of Aden Journal of Natural and Applied Sciences., Vol.28(2) (2024), 75-85

University of Aden Journal of Natural and Applied Sciences

Journal homepage: https://uajnas.adenuniv.com

Research Article

Pharmaceutical Study to Assess the Equivalence of the Commercial Brands of Losartan Potassium Tablets Available in Aden Governorate, Yemen

Sana Saleh Al-Kubati[1]* and Fairoz Adel Hammed[1]

[1]Department of Pharmaceutics, Faculty of Pharmacy, Aden University, Aden, Yemen

https://doi.org/10.47372/uajnas.n2.a07

ARTICLE INFO

Received: 08 Nov 2024

Accepted: 14 Feb 2024

Keywords:

Losartan potassium, Quality control, Brands, dependent drug modeling, independent drug modeling.

Abstract

Losartan potassium, a non-peptide angiotensin II receptor antagonist, is prescribed by the physicians for hypertension treatment. In Aden governorate, Yemen, losartan is available as oral tablets and tablets combining losartan potassium and hydrochlorothiazide. A study comparing generic brands of 50 mg Losartan potassium tablets to their reference brand was conducted to determine their pharmaceutical equivalency. The study involved quality control parameters and *in vitro* dissolution studies using the USP method. The results showed that the seven brands of losartan potassium tablets met the specified criteria for immediate-release tablets, with the drug content ranging from 95.69% ±1.97 to 99.62% ±1.57. The reference brand LC-1 and the generic brands LC-2 and LC-3 achieved fast drug dissolution of about 80% within 30 minutes, while the generic brands from LC-4 to LC-7 gave drug dissolution in the range of 76.09–78.07. The dissolution kinetics of the seven brands followed the Weibull model, with similarity factors exceeding 50%, differences in dissolution efficiencies less than 10%, and a mean dissolution time between 10.93 and 13.57 minutes. In conclusion, the commercially generic brands of Losartan potassium tablets were pharmaceutically equivalent and could be used interchangeably with the reference brand.

1. Introduction

One unexpected and potentially dangerous adverse drug event that could go unnoticed or unreported is drug ineffectiveness (DI). Since DI represents the performance of a medicine in a real-life population, unexpected or inexplicable ineffectiveness may be a crucial event to report in pharmacovigilance and pharmacoepidemiological investigations. Pharmacovigilance, which focuses on medicine efficacy, quality, and safety, helps regulate the pharmaceutical sector. Post-marketing surveillance monitors a medication's safety following approval for sale [1]. The existence of multisource generic medicines, either clinically prescribed or over-the-counter dispensed, requires monitoring their equivalency to the innovator medicine to guarantee effectiveness and safety upon administration. The World Health Organization (WHO) has identified the prevalence of unregistered or counterfeit medications, which may have low levels of the active component, no active ingredient at all, counterfeit packaging, and substandard quality. It is thought that counterfeit pharmaceuticals pose a higher risk to health than substandard ones. The use of inferior and counterfeit drugs is a major source of morbidity and mortality, as well as a loss of public trust in pharmaceuticals and healthcare institutions. Substandard and counterfeit medications are substantially more prevalent in underdeveloped nations [2, 3].

To determine if multi-source medications are bioequivalent, in vitro dissolution studies can be used instead of in vivo bioavailability and bioequivalence studies, saving both resources and time. The Biopharmaceutical Classification System (BCS) demonstrates the bioequivalence of class 1 (high solubility-high permeability) and class 3 (high solubility-low permeability) drugs through in vitro studies. The biopharmaceutical stage of the tablets can be evaluated

* Correspondence to: Department of pharmaceutics, Faculty of pharmacy, Aden University, Aden, Yemen

E-mail address: ss.alkubati@pharm.adenuniv.com , : https://orcid.org/0000-0003-3355-7705

using in vitro pharmaceutical equivalency studies. The pharmaceutical equivalency and interchangeability of multisource medications with the innovator can be proven by quality control tests such as weight uniformity, hardness, disintegration, and friability, as well as the drugs' dissolution profile performance [4, 5]. The USP-NF outlines the official dissolution apparatus and provides instructions for performing dissolution tests on a variety of drug products, including tablets, capsules, and other distinctive products such as transdermal products. The Food and Drug Administration (FDA) may recommend a specific dissolution procedure for a medicine or specify one in the USP-NF monograph for that product [6].

Yemen has been unable to avoid the numerous chronic illnesses, such as hypertension, that have also affected other Arab nations and the developing world in other areas. The disease is complicated and multifaceted, including a number of risk factors, environmental variables, and physiological systems, and it is a precursor factor for the occurring cardiovascular (CV) diseases. Equally complex is the management and treatment of hypertension [7]. Drug selection for hypertension is influenced by age, comorbidities, ethnicity, pregnancy, and other factors, requiring individualized treatment strategies. Antihypertensive pharmacological classes that include β-adrenergic blockers, calcium-channel blockers, angiotensin-converting enzyme inhibitors (ACE inhibitors), and diuretics are employed. Potassium-sparing diuretics, loop diuretics, thiazide, and thiazide-like diuretics are the four subgroups that make up the diuretics group [8]. The cornerstone of managing hypertension is maintaining a healthy lifestyle, regardless of blood pressure level. It reduces total CV risk and enhances antihypertensive medications' effectiveness in decreasing blood pressure [9].

DuPont-Merck laboratories developed losartan potassium (LP), a BCS class 1 drug, which was approved by the FDA on April 14, 1995, as a therapy for hypertension. It is well tolerated in heart failure patients and has a license for the prevention of strokes [10, 11]. It functions as an alternative to the frequently used treatment for chronic diseases by selectively blocking angiotensin II receptors, which has a slow and long-lasting antihypertensive effect [12]. It is available as tablets that are sold under different commercial brands, both on their own and in combination with hydrochlorothiazide.

The study aimed to employ the in vitro dissolution specification in the USP monograph for losartan potassium tablets to determine the pharmaceutical equivalency of seven commercial brands of losartan potassium film-coated tablets that contain 50 mg of losartan and are prescribed in the Yemeni governorate of Aden. Statistical equivalency indicators include the mean dissolution time, efficiency, and similarity factor dissolution.

2. Materials and Methods

2.1 Materials

The Losartan potassium standard was received as a gift sample (Modern Pharmaceutical Company, Yemen). We purchased seven commercial brands of 50 mg film-coated losartan potassium tablets from local pharmacies in Aden governorate, Yemen. Brand LC-1 was considered a reference brand, and the six others were generic brands (LC-2 – LC-7) from six countries of origin.

2.2 Samples collection

An investigation of the commercial brands of 50 mg LP film-coated tablets was conducted in the local pharmacies in Aden governorate, Yemen. The inquiry includes a search for the brand names, the nation of origin, the batch number, the dates of manufacturing and expiration, the price, and whether or not the product package leaflets or Google provide information about the excipient.

2.3 Evaluation of the commercial brands LP film-coated tablet

2.3.1 Physical evaluation

The seven commercial products of LP film-coated tablets included in this study were assessed physically in terms of appearance, shape, and color.

2.3.2 Weight uniformity, and thickness

A digital weighing balance (AND HR-250, Japan) was used to measure the weight of each of the seven brands' ten tablets, both individually and collectively, to ensure weight uniformity. A micrometer screw gauge was used for measuring the thickness of ten tablets of each brand [13].

$$\text{Deviation}=\frac{\text{Average Weight}}{100}\times\%\ \text{of Deviation} \quad \ldots\ldots\ldots\ 1$$

2.3.3 Hardness

Hardness plays a crucial role in determining how resistant a tablet is to breaking, abrasion, and chipping during handling, shipping, and storage prior to use. The weight of the material used, the pressure applied for compression, and the distance between the two punches of the tableting machine at the time of compression all have

an impact on the tablet's hardness [14, 15]. By using the hardness tester (Monsanto, India), the hardness of the ten tablets individually of each brand was assessed to determine the force needed to break the tablet.

2.3.4 Friability

The randomly selected ten tablets of each product were first weighed and placed inside the friability tester (Thermonik, India) at a speed of 25 rpm for 4 minutes (100 rounds), after which they were dusted and weighed. The weight reduction percentage was obtained using the equation below [16]:

$$\% \textbf{ Friability} = \frac{\textbf{Initial Weight} - \textbf{ Final Weight}}{\textbf{Initial Weight}} \times \% \textbf{ 100} \ldots . \textbf{2}$$

2.3.5 Drug Content

One tablet from each brand was dissolved in an appropriate amount of distilled water, and the volume was finished to the mark with the same solvent in a 100-ml volumetric flask. This solution was diluted with distilled water in a 25-ml volumetric flask. The solution was diluted with distilled water to a concentration of 15 µg/ml before centrifugation at 3000 rpm for 30 minutes. The absorbance was measured at wavelength 254 nm using a UV spectrophotometer (Lasany UV-VIS-L1-295, India). The concentration of LP was calculated using a calibration curve equation. Following that, the LP percentages contained in one tablet of the seven brands were determined and compared to the LP standard [4].

2.3.6 Disintegration time

Six tablets from each brand were randomly selected and examined using the disintegration instrument (Erweka ZT41, Germany). One tablet was placed in each tube of the apparatus basket and submerged in one liter of distilled water. The temperature was previously set to 37 ±2 ˚C. The time required for complete disintegration of the six tablets was determined [16].

2.3.7 *In vitro* dissolution studies

The *in vitro* dissolution tests were conducted using the USP dissolution equipment type II, paddle method, to determine the dissolving rate of LP from the seven brands. The dissolving media was 900 ml of distilled water, with the temperature set to 37 ±0.5 °C and the paddle rotating at 50 rpm [17]. One tablet was placed in each vessel. At intervals of 5, 10, 15, 20, 25, 30, 45, and 60 minutes, a 5 ml volume of sample was removed from each vessel and replaced with equal volumes of dissolving media kept at the same temperature. A spectrophotometer was used to detect absorbance at 254 nm. The concentrations were determined with the linear equation of the calibration curve of LP, and the amount dissolved was expressed as a percentage. Then dissolution rate curves were plotted based on the amount dissolved (%) versus time (minutes).

2.3.8 The statistical analysis of the evaluation parameters

The data of the assessment parameters were calculated and presented as the mean values with the standard deviations (±S.D.) for seven brands of LP.

2.3.9 Dissolution data modeling

2.3.9.1. Dependent drug modeling

The dependent drug modeling was used for comparison the in vitro dissolution rate data of the seven brands of LP film-coated tablets. The following models' equations were used to determine the best model that describe the dissolution kinetics of LP based on the values of R^2 [18, 19]:

- Zero-order model: $M_t = k_\circ\, t + b$ 3
- First-order model: $\ln M = k_1\, t$ 4
- Higuchi-model: $M_\circ - M = k_H\, t^{0.5}$ 5
- Hixson-Crowell-model: $M_\circ^{1/3} - M^{1/3} = k_{HC}\, t$ 6
- Korsmeyer-Peppass-model: $\log(M_\circ - M) = n \log t + \log k_{KP}$ 7
- Weibull model: $Mt = M\infty\,(1 - \exp(-k_w\,.\,t^{\beta}))$ 8

Where (M°) is the initial drug content at time (t°), (M) is the remaining drug content at time (t). The zero-order model is the drug dissolved (%) versus time (t), the first-order model is the amount remaining of the drug against time, the Higuchi model is the drug dissolved (%) against square root of time (t^2), and the Hixson-Crowell model is the cubic root of the undissolved drug (%) against time (t). The Korsmeyer-Peppass model is the log of the dissolved drug (%) versus log time (log t); for Weibull, the drug amount dissolved (Mt) in the time (t); (M∞) is the maximum drug amount dissolved in an infinite time; and (β) is the exponential curve shape.

2.3.9.2. Independent drug modeling

An independent drug modeling uses the similarity factor (f2), the dissolution efficiency (DE%) and mean dissolution time (MDT) to statistically compare the in vitro dissolution data of the seven brands of LP [2, 18].

$$f2 = 50\log\left[\sqrt{\left\{1 + \frac{1}{n}\sum_{t=1}^{n}\left(Rt - Tt\right)^2\right\}} \times 100\right] \quad \ldots\ldots\ldots 9$$

Where (n) are the time points, (Rt) and (Tt) are the percentages of the dissolution of the reference and test drug products, respectively. The acceptable range of f2 is between 50 and 100. For the dissolution efficiency, the dissolution of the test brand is similar to the reference brand when the drug dissolved percentage at each time point does not differ by more than 10%.

$$\mathbf{DE}\ (\%) = \frac{AUC_0^t}{Q^{\infty}\ t^{\infty}} \times 100 \quad \ldots\ldots\ldots 10$$

Where (AUC) is the area under the dissolution-time curve from zero time (t0) to the last time (t∞), and (Q∞) is the mean of the drug dissolved (%).

$$MDT = \frac{\Sigma\ (ti - \Delta Qi)}{Q\infty} \quad \ldots\ldots\ldots 11$$

Where ∑(ti - ΔQi) is the of the subtracting of the time and the drug dissolved (%), and (Q∞) is the drug dissolved at the last time.

3. Results and discussion

3.1 Samples collection

Table 1 displays the findings of the investigation for the commercial brands of LP film-coated tablets. According to the survey, seven different commercial products were available for purchase at private pharmacies in the Aden governorate of Yemen. In the product package leaflets, the excipients used in the tablet's manufacturing were listed only for the reference brand L-1 and three generic brands (LC-3, LC-6, and LC-7). However, generic brands LC-2, LC-4, and LC-5 were not listed in the leaflets of the product or on Google. The information regarding the excipients should be provided so that the patient is aware of any potential health risks, such as sensitivity or the existence of any disease. As well as, a variation in the excipient employed could have an impact on the ability of the drug to dissolve in the recommended dissolving medium, which could have an impact on the bioavailability of the drug from the viewpoints of quality control and quality assurance.

3.2. Physical evaluation

As shown in Table 2, all the brand tablets of LP have an elegant appearance, are round in shape, and scored from the middle, except for the generic brands LC-4 and LC-6. All the brands had a white color except the generic brand, LC-5, which had a rose color.

3.3. Weight uniformity, diameter, and thickness

The weight uniformity of the seven different LP products was measured and found to be between 156.22 and 280.96 mg. Each medication product had uniform weights that fell within the permissible range as indicated by USP requirements, with no tablets deviated from 7.5% [20], which is a reliable indicator of drug content consistency. The thickness and diameter measurements ranged from 2.48 ±.0.12 mm to 5.32 ±0.321 mm and 7.06 ±0.007 mm to 9.02 ±0.011 mm, respectively (Table 3).

3.4. Hardness

Except for generic brand LC-3, which had a tablet hardness of 11.94 ±4.11 kg/cm^2, the six brands' LP hardness measurement findings, ranging from 5.40 ±0.25 to 8.72 ±0.34 kg/cm^2, were within the allowable ranges of 4-10 kg/cm^2 [21].

3.5. Friability

The friability determination yielded findings ranging from 0.03% to 0.61%, which were less than 1%, showing that the tablets had superior mechanical resistance to abrasion or breaking. Brand LC-3 had a slightly higher hardness rating (11.94 ±4.11 kg/cm^2) and passed the friability test by less than 1% (0.04%). As a result, tablets with a hardness of more than 10 kg/cm^2 are acceptable [21].

3.6. Drug content

Table 4 shows that the drug content of all tested products ranged from 95.06 ± 0.28 to 99.62% ± 1.57%, indicating uniformity. It was determined to be within the USP's 95% to 105% limit [17]. Figure 1 depicts the calibration curve of LP in distilled water at a wavelength of 254 nm; it shows linearity over the concentration range from 5 to 25 µg/ml and the regression equation where y = 0.0367x - 0.0021 and R^2 = 0.9996.

Table 1: Information on the reference brand and the generic brands of 50 mg losartan potassium tablets available in Aden governorate pharmacies, Yemen

Brand code	Mgf./B. NO. Exp. Date	Excipient Involved In The Tablets	Price/ packet ($)
LC-1	5/2022/ 26464 5/2025	hydroxypropylcellulose, hyprolose, hypromellose, microcrystalline cellulose, lactose monohydrate, titanium dioxide, pregelatinized starch, magnesium stearate	10.5
LC-2	01/2023/ 23A034 01/2026	NA	2
LC-3	12/2022/ 106 12/2025	crospovidone, anhydrouslactose, manesium stearate, colloidal silicon dioxide, hydroxypropylcellulose, methylcellulose, microcrystalline cellulose, polyethyleneglycol, titanium dioxide	5
LC-4	11/2022/ L401 11/2025	NA	5
LC-5	5/2022/pmx22002 4/2025	NA	2
LC-6	11/2022/ 0281122 11/2025	lactose monohydrate, pregelatinized starch, magnesium stearate, hyprolose, hypromellose, microcrystalline cellulose	5
LC-7	/41471 02/2025	microcrystalline cellulose, lactose monohydrate, pregelatinized starch, magnesium stearate, hyprolose, hypromellose, titanium dioxide	3

*Mfg.: Manufacturing date, B. No.: Batch Number, Exp.: Expiration, NA: Not available

Table 2: The physical evaluation of the seven brands of losartan potassium tablets

Evaluation parameter	Brand code						
	LC-1	**LC-2**	**LC-3**	**LC-4**	**LC-5**	**LC-6**	**LC-7**
Shape	round, scored	round, scored	round, scored	round	round, scored	round	round, scored
Color	white	white	white	white	rose	white	white
							

Table 3: The diameter, thickness and weight uniformity of the seven brands of losartan potassium tablets

Evaluation parameter		Brand code						
		LC-1	LC-2	LC-3	LC-4	LC-5	LC-6	LC-7
Diameter (mm ±SD)		8.16 ± 0.0	7.12 ± 0.012	9.02 ± 0.011	7.06 ± 0.007	8.03 ± 0.003	7.16 ± 0.021	7.13 ± 0.031
Thickness (mm ±SD)		4.40 ± 0.007	4.23 ± 0.013	5.32 ± 0.321	4.31 ± 0.017	2.48 ±.012	4.16 ± 0.034	4.35 ± 0.009
Weight uniformity (mg)	max. limit	224.70	167.94	302.03	174.10	171.57	170.50	168.29
	average	209.02 ± 3.70	156.22 ± 3.06	280.96 ± 2.78	161.96 ± 1.76	159.60 ± 2.03	158.60 ± 1.98	156.55 ± 1.93
	min. limit	193.34	144.51	259.88	149.81	147.63	146.71	144.81

Table 4: The hardness, friability and drug content and disintegration time of the seven brands of losartan potassium tablets

Evaluation Parameter	Brand code						
	LC-1	LC-2	LC-3	LC-4	LC-5	LC-6	LC-7
Hardness (kg/cm^2 ±SD)	7.32 ± 0.58	6.18 ± 0.08	11.94 ± 4.11	7.02 ± 0.50	6.97 ± 0.10	8.72 ± 0.34	5.40 ± 0.25
Friability (%)	0.61	0.03	0.04	0.08	0.49	0.40	0.60
Drug Content (% ±SD)	96.59 ±1.97	99.62 ±1.57	97.51 ±1.37	97.55 ± 0.70	96.18 ± 0.54	95.69 ± 0.68	95.06 ± 0.28
Disintegration Time (minutes) ±SD	8.46 ±1.03	6.87 ± 0.53	14.84 ± 0.60	13.21 ± 0.05	12.55 ± 0.47	13.66 ± 0.38	13.76 ± 0.54

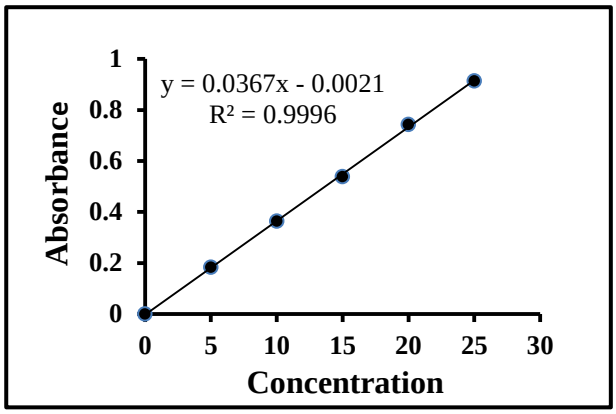

Figure 1: Calibration curve of losartan potassium in distilled water at wavelength of 254 nm

3.7. Disintegration time

Table 4 shows that all seven brands of LP tablets had disintegration times ranging from 6.87 ±0.53 to 14.84 ±0.60, which were within the USP time limit. The disintegration test is an important step for immediate-release dosage forms since the rate of disintegration influences solubility in the dissolution medium and biological fluids and, as a result, the bioavailability of the medicine. The US Pharmacopoeia (USP) requires that the uncoated and film-coated tablets dissolve within 30 minutes [17].

3.8. Dissolution Studies

Replacement with generic products is only possible when a generic product's bioequivalence to a reference product typically the innovator product is equivalent. The World Health Organization (WHO) has suggested using a well-known pharmaceutical product as the comparator pharmaceutical product in case the innovator products are unavailable, particularly in developing nations [22]. The dissolution studied was performed using the USP dissolution apparatus, type II, as recommended by USP, and brand LC-1 as the reference product. Figure 2 and Table 5 summarizes the mean percent dissolved at each time point. The dissolution percentages of brands LC-1, LC-2, and LC-3 were 80.13% ±0.48, 80.39% ±5.30, and 83.97% ±4.70, respectively, within 30 minutes, while for brands LC-4, LC-5, LC-6, and LC-7, the dissolution percentages were 76.13 ±1.54, 76.56 ±5.25, 76.09 ±1.81, and 78.07 ±3.23, respectively, within 30 minutes. Only the

reference brand LC-1 and the generic brands LC-2 and LC-3 met the criteria for immediate release tablets: 80% of the drug must dissolve in 30 minutes [23]. In the other generic products, the percentages of drug dissolution were slightly lower, which could be attributed to differences in formulation, type and amount of excipients, and manufacturing processes. The immediate-release tablet coating has no substantial effect on the drug's dissolution in its dosage form. The coating components protect the coated material, make swallowing easier, and hide undesirable tastes [24].

3.9 Dissolution data modeling

3.9.1. Dependent drug modeling

The dissolution curves of the seven LP brands were assessed by fitting the data to zero and first-order models, as well as the Higuchi, Krosmeyer-Peppas, Hixson-Crowell, and Weibull models. Based on the linear regression analysis, the Weibull model determination constant (R^2) was the highest among the others (Table 6). The Ti represents the time intervals required to dissolve or release 63.2% of the medication contained in the pharmaceutical dosage form. The LP values ranged from 4.726 to 3.090, with β values smaller than one. The Weibull model showed the best fit for describing the dissolution kinetics of LP. This result was consistent with Simionato et al.'s findings for meloxicam [25].

3.9.2. Independent drug modeling

Table 5 shows the results of analyzing dissolution data to evaluate the equivalence of generic products (LC-2-LC-7) to the reference product (LC-1) using the similarity factor (f2), dissolve efficiency (%DE), and mean dissolving time (MDT). The f2 values of the six generic products were larger than 50% (between 50 and 100%), the DE was greater than 50% and ranged from 56.28% to 62.66%, and the MDT ranged from 10.93 to 13.57 minutes. The FDA recommends applying the f2 as a statistical tool to compare the dissolving profiles of generic and reference products [26]. The difference in DE between the reference and generic brands was less than 10%, showing that the seven LP brands are interchangeable [4]. As a result, the generic brands of LP film-coated tablets on the market (LC-2-LC-7) had statistically comparable *in vitro* dissolving properties to the reference brand (LC-1).

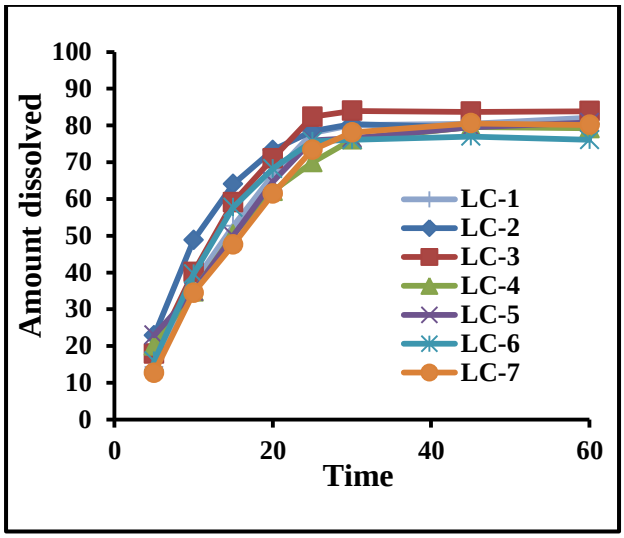

Figure 2: Comparison of the *in vitro* dissolution profile of losartan potassium from reference brand (LC-1) and generic brands (LC-2 - LC-7)

4. Conclusion

This study was an attempt to compare the seven commercial brands of LP film-coated tablets available in the Aden governorate for pharmaceutical equivalence through in vitro dissolution evaluations and other quality control parameters. The results showed that all LP brands matched the standards outlined in the official monograph, except dissolution. The generic brands LC-4, LC-5, LC-6, and LC-7 showed lower dissolution at 30 minutes (less than 80%). However, the statistical analysis of the dissolution data by using the dependent model revealed that all seven brands exhibited dissolution kinetics following the Weibull model. According to f2, the generic brands were pharmaceutically equivalent to the reference brand and could be interchangeable.

Acknowledgments

The authors would like to thank Modern Pharmaceutical Company, Yemen, for donating the losartan potassium standard.

Table 5: *In vitro* dissolution of losartan potassium the tablets of the seven brands, similarity factor, dissolution efficiency and mean dissolution time.

Time (minutes)	**Amount of the drug dissolved (%± SD)**						
	LC-1	**LC-2**	**LC-3**	**LC-4**	**LC-5**	**LC-6**	**L-7**
5	14.28 ±3.58	22.84 ±5.21	17.91 ±1.97	20.10 ±5.15	22.92 ±7.29	15. 86 ±5.84	12.69 ±4.01
10	37.06 ±4.32	48.81 ±8.74	40.06 ±2.58	34.83 ±5.60	34.79 ±1.29	39.56 ±4.07	34.45 ±4.70
15	52.63 ±1.57	64.00 ±8.98	59.10 ±3.71	50.27 ±4.47	49.95 ±2.26	57.71 ±2.99	47.58 ±3.47
20	66.57 ±4.25	73.30 ±1.21	71.03 ±7.11	62.14 ±4.70	64.66 ±1.76	68.23 ±5.06	61.43 ±5.11
25	77.94 ±4.51	78.47 ±5.30	82.38 ±5.66	69.96 ±3.09	75.90 ±1.91	75.66 ±4.91	73.36 ±8.13
30	80.13 ±0.48	80.39 ±5.30	83.97 ±4.70	76.13 ±1.54	76.56 ±5.25	76.09 ±1.81	78.07 ±3.23
45	80.46 ±1.88	79.51 ±2.01	83.70 ±4.34	79.59 ±0.69	79.48 ±1.42	76.99 ±2.16	80.58 ±0.37
60	82.37 ±8.09	80.35 ±1.57	83.90 ±3.41	79.24 ±0.43	80.77 ±1.34	76.09 ±3.20	80.15 ±1.25
f_2 (%)	**-**	**57.57**	**68.92**	**67.43**	**70.76**	**71.07**	**72.77**
DE (%)	**58.83**	**63.05**	**62.66**	**56.55**	**57.84**	**58.30**	**56.28**
MDT (minutes)	**12.10**	**9.31**	**11.31**	**13.03**	**12.25**	**10.93**	**13.57**

f_2: similarity factor, DE: dissolution efficiency and MDT: mean dissolution time

Table 6: The kinetic models and the statistic parameters for the *in vitro* dissolution data of the seven brands of losartan potassium tablets

Model	**parameter**	**Brand code**						
		LC-1	**LC-2**	**LC-3**	**LC-4**	**LC-5**	**LC-6**	**LC-7**
Zero-order	**R^2**	0.7987	0.7324	0.7736	0.8448	0.8306	0.7442	0.826
	k_0	1.957	2.000	2.048	1.875	1.914	1.887	1.894
First order	**R^2**	0.9604	0.9460	0.9618	0.9735	0.9666	0.9314	0.965
	k_1	0.049	0.059	0.056	0.044	0.046	0.048	0.044
Higuchi	**R^2**	0.8878	0.8361	0.8686	0.9217	0.9084	0.8460	0.908
	k_H	12.643	13.188	13.316	12.106	12.388	12.334	12.15
Krosmeyer-Peppas	**R^2**	0.8980	0.8704	0.8857	0.9310	0.9196	0.8691	0.913
	k_{KP}	15.730	24.099	18.697	15.475	16.620	18.722	13.44
	n	0.437	0.326	0.402	0.429	0.415	0.380	0.471
Hixson-Crowell	**R^2**	0.9529	0.9448	0.9618	0.9648	0.9604	0.9208	0.955
	k_{HC}	0.014	0.017	0.016	0.012	0.013	0.014	0.012
Weibull	**R^2**	0.9781	0.9787	0.9756	0.9812	0.9697	0.9707	0.980
	β	0.617	0.396	0.630	0.618	0.647	0.451	0.652
	Ti	4.356	4.685	4.151	3.527	3.090	4.726	4.276

References

1. Khabbaz HJAl, Talal AA and Rayan IA. (2023). "Assessment of the Post-Marketing "Drug Ineffective" Reports Received by the Saudi Vigilance System." *Journal of Pharmaceutical Research International*; 35 (30): 54-65.
2. Alvarado AT, Muñoz AM, Bendezú MR, Palomino-Jhong JJ, García JA, Alvarado CA, Alvarado EA, Ochoa-Pachas G, Pineda-Pérez M and Bolarte M. (2021). In vitro biopharmaceutical equivalence of carbamazepine sodium tablets available in Lima, Peru. Dissolut. Technol; 28 (2): 1-10.
3. Uddin, M. S., Mamun, A. A., Hossain, M. S., Asaduzzaman, M., Sarwar, M. S., Rashid, M., & Herrera-Calderon, O. (2017). In vitro quality evaluation of leading brands of ciprofloxacin tablets available in Bangladesh. BMC research notes, 10, 1-9.
4. Al-Kubati SSF, Al-Hariri FM and Ibraheem GK. (2020). Comparison of in vitro dissolution of Bisoprolol Fumarate tablets of five Brands marketed in Aden, Yemen. University of Aden Journal of Natural and Applied Sciences; 24 (1): 265-273.
5. Shuma, M. L., & Halder, S. (2021). Statistical assessment of in vitro drug release kinetics and quality evaluation of desloratadine orally disintegrating generic tablets available in Bangladesh. Journal of Generic Medicines, 17(1), 10-16.
6. Abbirami V, Sainithya P, Shobana A, Devi DR and Hari BV. (2013). A review on in-vitro bioequivalence studies and its methodologies. Int J Chem Tech Res; 5 (5): 2295-2302.
7. Leimena, C and Qiu, H. (2018). Non-coding RNA in the pathogenesis, progression and treatment of hypertension. International journal of molecular sciences; *19* (4): 927.6.
8. Zisaki A, Miskovic L and Hatzimanikatis V. (2015). Antihypertensive drugs metabolism: an update to pharmacokinetic profiles and computational approaches. Current pharmaceutical design; 21 (6): 806-822.
9. Schellack N and Naicker P. (2015). Hypertension: a review of antihypertensive medication, past and present. SA Pharmaceutical Journal; 82 (2): 17-25.
10. Aniñon ADA, Binos RSR, Brizuela KMM, de Luna WJC, del Rosario RPS, Dimalala JJC, Dueñas TJP, Linatoc IIB, Recto JD, Salinas MV and Paraiso WKD. (2014). Spectrophotometric determination of losartan potassium in tablets. Science Diliman; 26 (1): 41-52.
11. Varillas MA, Brevedan MIV and González Vidal NL. (2022). Pharmaceutical Equivalence of Losartan Potassium Tablets in Argentina. Dissolution Technology.
12. Raju DB, Venkanna B, Darsini YSP and Prakash VJ. (2020). Evaluation of Different Marketed Brands of Losartan Potassium Tablets: A Comparative Study with Generic Shop Products. International Journal of Research in Pharmacy and Science; 10 (2): 27-39.
13. Singh, R., Saxena, M., Sahay, D., & Singh, S. (2017). In-vitro study of quality control parameters of three different brands of azithromycin tablets. Int J Basic Clin Pharmacol, *6*(7), 1572.
14. Osei, Y. A., Oppong Boakye, E., Bayor, M. T., & Akuffo Owusu, F. W. (2022). Physicochemical Equivalence and Quality Assessment of Various Brands of Gastro-Resistant Omeprazole Capsules in the Kumasi Metropolis. The Scientific World Journal, 2022 (1), 7924600.
15. Pande, V., Karale, P., Goje, P., & Mahanavar, S. (2016). An overview on emerging trends in immediate release tablet technologies. Austin Therapeutics, 3(1), 1026.
16. Dhakal, B., Thakur, J. K., Mahato, R. K., Rawat, I., Rabin, D. C., Chhetri, R. R., ... & Pandey, J. (2022). Formulation of Ebastine Fast-Disintegrating Tablet Using Coprocessed Superdisintegrants and Evaluation of Quality Control Parameters. The Scientific World Journal, 2022.
17. United States Pharmacopeia 35/ National Formulary 29. Monograph of losartan potassium, Pp: 3723 (2011) Rockville, the United States Pharmacopeial Convention, Inc.
18. Muselík, J., Komersová, A., Kubová, K., Matzick, K., & Skalická, B. (2021). A critical overview of FDA and EMA statistical methods to compare in vitro drug dissolution profiles of pharmaceutical products. Pharmaceutics, 13(10), 1703.
19. Paarakh, M. P., Jose, P. A., Setty, C. M., & Christoper, G. P. (2018). Release kinetics–concepts and applications. Int. J. Pharm. Res. Technol, 8 (1), 12-20.
20. Chaturvedi, H., Garg, A., & Rathore, U. S. (2017). Post-compression evaluation parameters for tablets-an overview. Eur J Pharm Med Res [Internet], 4 (11), 526-30.
21. Yulianita, R., Sopyan, I., Gazzali, A. M., & Muchtaridi, M. (2021). A Novel Stability Study of Simvastatin Generic Tablet in Public Pharmacy Facilities of Purwakarta, Indonesia. Indonesian Journal of Pharmacy/Majalah Farmasi Indonesia, *32*(4).
22. Reddy, N. H., Patnala, S., Löbenberg, R., & Kanfer, I. (2014). In vitro dissolution of generic immediate-release solid oral dosage forms containing BCS class I drugs: comparative assessment of metronidazole, zidovudine, and amoxicillin versus relevant comparator pharmaceutical products in South Africa and India. AAPS PharmSciTech, 15, 1076-1086.
23. REDC/ADF. (2018). Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances Guidance for Industry". Food and Drug Administration, 1-8,.
24. Santos, A. D. F., Barbosa, I. S., Santos, V. L. D., Silva, R. L., & Caetite, E. (2014). Test of dissolution and comparison of in vitro dissolution profiles of coated ranitidine tablets marketed in Bahia, Brazil. Brazilian Journal of Pharmaceutical Sciences, 50 (1), 83-89.

25. Simionato, L. D., Petrone, L., Baldut, M., Bonafede, S. L., & Segall, A. I. (2018). Comparison between the dissolution profiles of nine meloxicam tablet brands commercially available in Buenos Aires, Argentina. Saudi pharmaceutical journal, 26 (4), 578-584.

26. Khalid, F., Hassan, S. M. F., Mushtaque, M., Noor, R., Ghayas, S., Muhamma, I. N., & Hassan, F. (2020). Comparative analysis of biopharmaceutic classification system (BCS) based biowaiver.

University of Aden Journal of Natural and Applied Sciences., vol.28(2) (2024), 75 - 85

مجلة جامعة عدن للعلوم الطبيعية والتطبيقية

Journal homepage: https://uajnas.adenuniv.com

بحث علمي

دراسة صيدلانية لتقييم تكافؤ العلامات التجارية لأقراص اللوسارتان بوتاسيوم المتوفرة في محافظة عدن، اليمن

سناء صالح القباطي[1]، فيروز عادل حميد[1]

[1]قسم الصيدلانيات - كلية الصيدلة - جامعة عدن

https://doi.org/10.47372/uajnas.2024.n2.a07

الملخص

يستخدم اللوسارتان بوتاسيوم، وهو مضاد لمستقبلات الأنجيوتنسين II غير الببتيدية، لعلاج ارتفاع ضغط الدم. في محافظة عدن، اليمن، يتوفر اللوسارتان على شكل أقراص عن طريق الفم وأقراص تجمع بين اللوسارتان بوتاسيوم وهيدروكلوروثيازيد. أجريت دراسة لمقارنة العلامات التجارية العامة لأقراص اللوسارتان بوتاسيوم 50 ملغ مع علامتها التجارية المرجعية لتحديد مكافئتها الصيدلانية. تضمنت الدراسة معايير مراقبة الجودة ودراسات الذوبان في المختبر باستخدام طريقة USP. أظهرت النتائج أن العلامات التجارية السبعة لأقراص اللوسارتان بوتاسيوم استوفت المعايير المحددة للأقراص ذات الإطلاق الفوري، حيث يتراوح محتوى الدواء من 95.69% ±1.97 إلى 99.62% ±1.57. حققت العلامة التجارية المرجعية LC-1 والعلامات التجارية العامة LC-2 وLC-3 ذوبانًا سريعًا للدواء بنسبة حوالي 80% خلال 30 دقيقة، بينما أعطت العلامات التجارية العامة LC-4 وLC-7 ذوبانًا دوائيًا في نطاق 76.09-78.07. اتبعت حركية الذوبان للعلامات التجارية السبع نموذج ويلبول، حيث تجاوزت عوامل التشابه 50%، والاختلافات في كفاءة الذوبان أقل من 10%، ومتوسط وقت الذوبان بين 10.93 و13.57 دقيقة. في الختام، كانت العلامات التجارية العامة لأقراص اللوسارتان بوتاسيوم مكافئة صيدلانياً ويمكن استخدامها بالتبادل مع منتج العلامة التجارية المرجعية.

مفاتيح البحث

التسليم : 08 نوفمبر 2024

القبول : 14 فبراير 2025

كلمات مفتاحية :

اللوسارتان بوتاسيوم، مراقبة الجودة، العلامات التجارية، المعتمد على النموذج، المستقل عن النموذج..