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Evaluation of Pharmaco-equivalence Properties of Oral Lisinopril Dihydrate Tablets

Maram Tobeili, Faten Mulla, Doaa R. Adam, Aiman Y. Alwadi, and Omar Z. Ameer
College of Pharmacy, Alfaisal University, Riyadh, Saudi Arabia

Background

- Lisinopril dihydrate (**Figure-1**) is one of the first line antihypertensive drugs that has various oral tablet brands in the Saudi market.
- It was first approved in 1987 and sold under the name Zestril®, manufactured by AstraZeneca Pharmaceuticals; available as 5, 10, and 20 mg strengths (**Figure-2**).

Objectives

- The aim of this study is to evaluate quality control and pharmaceutical equivalence criteria of generic brands of lisinopril dihydrate tablets in comparison to the innovator brand (Zestril®).
- To ensure compliance with tablet quality parameters, product suitability following marketing, provide feedback to regulatory bodies, and ensure user's safety, satisfaction and protection.

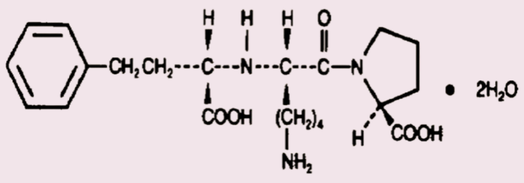
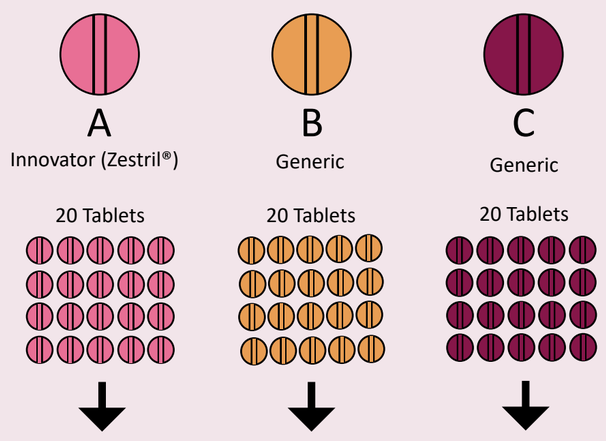


Figure-1: Chemical structure of lisinopril dihydrate (Zestril's API).

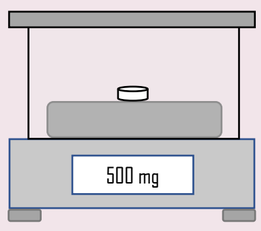
Figure-2: Lisinopril dihydrate innovator brand.

Methods

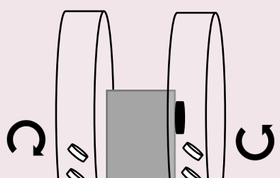
- Tested brands were coded **A-C** and investigated for conformity with the United States Pharmacopoeia (USP) standards.



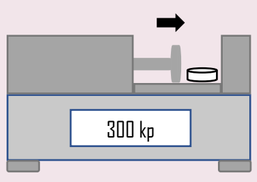
- **Uniformity of dosage unit test:** To test for weight variation across units, 20 tablets from each brand were randomly selected and weighed individually, then percent deviation from average weight was calculated.

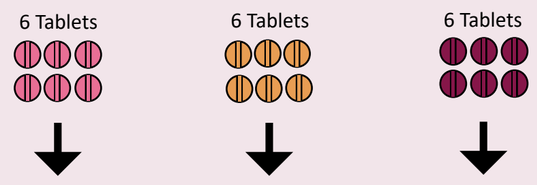


- **Friability test:** To test whether tablets can withstand chipping, abrasion, and breakage, 20 tablets were randomly selected, weighed and placed into a friabilator chamber. After the run, tablets were weighed again and the differences in weight were calculated as percentage friability.

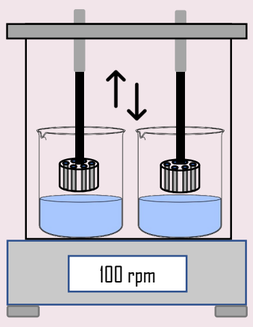


- **Hardness test:** The degree of force required to break a tablet across the diameter was measured by placing a sample of 20 tablets from each brand one by one in a tablet hardness tester.





- **Disintegration:** The breakdown of tablets into smaller particles is tested by placing 6 tablets from each brand individually inside each of the 6 tubes of the disintegration apparatus baskets. The time when no particles remain in the system's basket is the disintegration time.



Results

- The tablet weight of brand B at strengths of 5 mg and 10 mg, and brand C at 5mg were heavier than those of brand A, while the weight of brand B 20 mg, and brand C 10 mg and 20 mg were lighter than the innovator A tablet (**Table-1**).
- Tablet weight loss of 3.61 and 1.08 % for the 5 mg and 10 mg of brand B and C, respectively were higher than all other tested tablets (**Table-1**).

Table 1: Weight variation and friability tests results of lisinopril dihydrate innovator and generics tablet dosage form.

Brand Code	Dosage strength (mg)	Weight Mean (mg) ± SD	Friability Loss (%)
A[a]	5	105.7 ± 0.7	0.24
	10	211.6 ± 1.4	0.27
	20	224.0 ± 1.3	0.23
B	5	110.3 ± 1.2*	**3.61**
	10	218.4 ± 1.0*	0.42
	20	217.4 ± 2.8*	0.71
C	5	201.2 ± 2.8*	0.14
	10	198.1 ± 2.3*	**1.08**
	20	199.7 ± 3.0*	0.25

[a] Innovator lisinopril dihydrate brand. Data were analyzed by one-way ANOVA followed by Dunnett *post-hoc* analysis. * Statistically significant difference ($p<0.05$) vs innovator (A).

- The hardness of brand B 5mg and all tested dosage strengths of brand C were significantly higher than those of tablets of brand A (**Figure-3**).

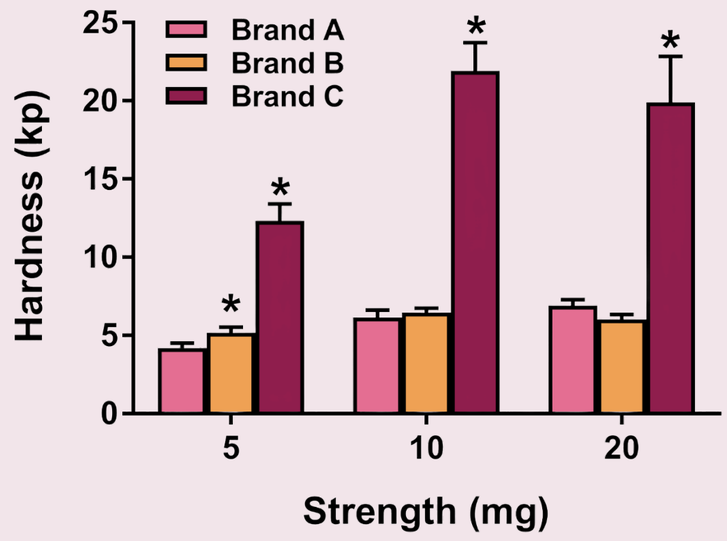


Figure-3: Hardness test results of lisinopril dihydrate innovator and generics tablet dosage form. [a] Innovator lisinopril dihydrate brand. Data were analyzed by one-way ANOVA followed by Dunnett *post-hoc* analysis. * Statistically significant difference ($p<0.05$) vs innovator (A).

- Tablet disintegration times for dosages 10 mg and 20 mg of brand B were faster than those of brand A. All tested tablet strengths of brand C took longer to disintegrate relative to their corresponding tablets of the innovator A (**Figure-4**).

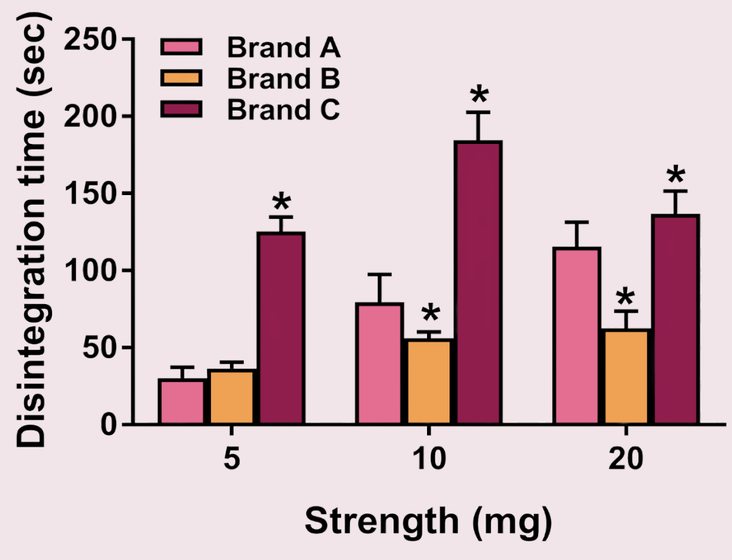


Figure-4: Disintegration test results of lisinopril dihydrate innovator and generics tablet dosage form. [a] Innovator lisinopril dihydrate brand. Data were analyzed by one-way ANOVA followed by Dunnett *post-hoc* analysis. * Statistically significant difference ($p<0.05$) vs innovator (A).

Conclusion

- There are inherent and baseline differences in the organoleptic and physical properties of the tested lisinopril dihydrate oral tablet dosage forms of the generic brands B and C relative to the innovator Zestril®.
- Brand B (5 mg) and brand C (10 mg) both failed the friability test.
- The hardness of brand B (5 mg) and all tested dosage strengths of brand C were significantly higher than those of brand A.
- All disintegration profiles were within the specified standards.

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References:

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