MEDICAMENTOS DE REFERÊNCIA, GENÉRICO E SIMILAR: AVALIAÇÃO DA QUALIDADE DOS COMPRIMIDOS DE CAPTOPRIL E ENALAPRIL

REFERENCE, GENERIC AND SIMILAR DRUGS: QUALITY ASSESSMENT OF CAPTOPRIL AND ENALAPRIL TABLETS

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RESUMO

Este trabalho objetivou analisar a qualidade dos comprimidos e a relação entre os medicamentos de referência, genéricos e similares. Para estudo e coleta de dados, foram realizados testes físicos e físico-químicos de acordo com a Farmacopéia Brasileira, 5º edição, 2010. Os produtos analisados apresentaram resultados satisfatórios quanto aos aspectos visuais, teste de vazamento, determinação de peso médio em formas farmacêuticas sólidas e determinação de resistência mecânica através dos testes de dureza e friabilidade e teste de desintegração, demonstrando qualidade conforme as devidas especificações e estando adequados para o consumo.

Descritores: Controle de qualidade; Captopril; Enalapril; Genéricos; Similares.

ABSTRACT

This research asesses tablet quality and the relations between reference, generic and similar drugs. For the study and data collection, physical and chemical-physical tests were performed according to the official Brazilian Pharmacopoeia, 5th edition, 2010. The analyzed products showed satisfactory results regarding visual aspects, leakage test, determination of average weight in solid pharmaceutical forms, determination of mechanical strength through hardness and friability tests, and disintegration test. They demonstrated quality according to the mentioned specifications, and proved to be suitable for consumption.

Keywords: Quality control; Captopril; Enalapril; Generic products; Similar products.

REVISA

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INTRODUCTION

Circulatory system diseases prevail considerably among the causes of hospital morbidity and mortality in the Municipality of Valparaíso de Goiás, according to 2008 data by the Information Technology Department of the National Health System (DATASUS).[1] Among such diseases, one can highlight systemic arterial hypertension (SAH), a multifactorial clinical condition characterized by high and sustained blood pressure (BP) levels.[1-3]

According to the definition by the Brazilian Hypertension Society (SBH),[2,3] systemic arterial hypertension (SAH) is characterized by increased systolic blood pressure (SBP) and increased diastolic blood pressure (DBP), showing values greater than 140mm Hg and 90mm Hg, respectively. Data from the Basic Care Information System (SIAB) indicate that in Valparaíso de Goiás the number of hypertensive individuals increased from 3,533 to 4,131 between December 2007 and December 2015.[2-4]

Age is emphasized as one of the risk factors, showing a direct or linear relationship that interferes with the onset or worsening of arterial hypertension.[2-4] Nevertheless, antihypertensive drugs are within the three classes of drugs most used by the elderly, namely, psychotropic, antihypertensive and antiulcer drugs, according to a research conducted in the city of Cascavel in the State of Paraná, Brazil.[3,4]

The first drug belonging to the antihypertensive class to be developed was captopril and, building on it, other agents were developed for AH treatment, such as enalapril. Captopril and enalapril are in the same pharmacophore group – with the difference that enalapril does not contain a sulfhydryl terminal group (SH) -, belonging to the class of ACE inhibitors, and are administered orally and excreted by the kidneys.[5-8]

In Brazil, Captopril and Enalapril are marketed in the form of tablets, under the names of Renitec (MSD) and Captosen (Pharlab) as, which are the reference products for Enalapril and Captopril, respectively. And they are also available in the market as Similar and Generic products.[5-11]

Medications can be classified under three categories: reference, similar and generic.[5-10] The term "reference drug" generally refers to the novel drug, whose bioavailability, efficacy and safety have been determined by clinical trials during product development, prior to obtaining the official registration for marketing. After the expiry of the patent period, it is considered as a reference drug.[7.11] In this case, the manufacturer developed the formulation and pharmaceutical form appropriate to the drug's route of administration and therapeutic purpose, establishing and validating the manufacturing processes, as well as the specifications that must be reproduced later, batch by batch.[5-12]

The pharmaceutical equivalence of two medicinal products relates to the evidence that both contain the same drug (same base, salt or ester of the same therapeutically active molecule), in the same dosage and pharmaceutical form, which can be evaluated by means of *in vitro* tests.[5,6,9-13] Therefore, it can be considered as an indication of bioequivalence between the drugs under study, but it cannot guarantee it.

Similar medicinal products have the same active ingredient as the reference medicine, as well as the same concentration, pharmaceutical form, route of administration, dosage, and same therapeutic indication; they may differ in characteristics related to excipients and vehicles, size, product form, expiry, labeling and packaging. This medicinal product must always be identified by a commercial name or brand.[7-13]

Until March 2003, similar drugs did not need to submit comparative studies with the novel drug, such as pharmaceutical equivalence, dissolution profile and relative bioequivalence / bioavailability. However, in 2003, the

National Health Regulatory Agency (ANVISA) published two Resolutions of its Collegiate Board of Directors - RDC nº 133/2003 and RDC nº 134/2003 – determining that registration holders of similar drugs must submit the above-cited comparative studies. The purpose of these rules is to ensure a proof of therapeutic equivalence between similar drugs and their respective (innovative) reference drug.[5,7,10-14]

Generic drugs are similar to and interchangeable with the novel product, and are produced after the expiry of the period of protection by a patent or other exclusive right.[11] Interchangeability with the reference drug is recognized through pharmaceutical equivalence and bioequivalence tests, which are performed by ANVISA-accredited laboratories.[9,10,12]

The pharmaceutical equivalence between two drugs is determined by *in vitro* tests*,* that is, comparative quality studies aimed at proving that both have the same active ingredient (same base, salt or ester of the same therapeutically active molecule), in the same dosage and pharmaceutical form.[5,7,11-16] However, it is accepted that the formulation and manufacturing process are not identical, which usually occurs due to the different equipment and suppliers of raw materials of different manufacturers, as long as these differences do not jeopardize the bioequivalence between the products.[5,6,13-16]

Due to the diversity of products offered in the national market, there has been growing discussion about the performance of these products,[10-13] because the formulations and techniques used in the manufacturing process are not identical to those adopted by the manufacturers of the reference medicine, which may result in physical and physicochemical variations of the drug, which may, in turn, lead to changes in the dissolution, and consequently changes occur in bioavailability.[12-14]

The evaluation of tablet quality represents an essential step for market release of medicinal products, in such a way as to guarantee therapeutic safety and efficacy throughout products' shelf-life.[13-15]

In this regard, it is important to emphasize that differences in physical and physicochemical characteristics of the drug and other components of the formulation, as well as in the manufacturing processes, can generate differences in bioavailability that, in the case of generic products, may compromise bioequivalence and, consequently, interchangeability. Yet, such possibility can be avoided by appropriate pharmacotechnical product development.[5,13-16]

Thus, in addition to manufacturing methods, special attention should be paid to those pharmaceutical forms in which a drug is present in solid form, especially tablets whose dissolution can be significantly affected by the drug's inherent characteristics, and by the presence of excipients that can either favor or hinder its dissolution.[5,6,17-19]

In regard to tablet quality, tests are held to verify their dissolution and bioavailability. This stage is extremely important, because tablets obtained by direct compression, dry or humid granulation, may behave differently *in vitro* and *in vivo.* Aspects such as the manner and conditions of drying granules, mixing or agitation time, speed and compression strength can also significantly alter the performance of a pharmaceutical form in the body.[5,7,17-22]

It is important to point out that in-process controls carried out during batch production are essential to guarantee the quality and equivalence of generic and similar drugs vis-à-vis their reference products. In-process control tests are performed periodically and intensively during the manufacturing process. They aim at ensuring homogeneity of the units produced as regards the specifications defined in the monograph, while assuring the attainment of the standards established in the pharmacopoeia.[5-6,17-22]

To that effect, the objective is to determine and conduct quality control tests for two drugs already available in the market. The drugs Enalapril and

Captopril were chosen from three laboratories: reference, generic and similar. The tests performed in the evaluation of the tablets are: individual weight, average weight, hardness, friability and disintegration of the three types of Enalapril and Captopril tablets.

METHOD

Reagents and solvents

- Milli-Q Millipore® direct Q UV-3 Water
- Quantitative filter paper
- Non-sterile Millex® 0.45µm x 30mm PTFE membrane filter;
- 0.45µm nylon filter membrane, 47mm diameter Milipore®;
- Qhemis® hydrochloric acid 37%.

Equipment and utensils

- Dr. Schleuniger Pharmatron® Durometer 3D Model Tablet tester;
- *Nova Ética*® Friabilimiter Mod. 300;
- Erweka® Disintegrator®;
- Agatec® vacuum desiccator®;
- Metter® H51 analytical scales;
- Fanem® Stirrer - Heater Mod. 258;

METHOD

For analysis and data collection in this study, physical and physical-chemical tests were performed according to the Brazilian Pharmacopoeia, 5th edition, 2010,[23] assessing the visual aspects, leakage test, average weight in solid pharmaceutical forms, mechanical resistance through hardness and friability tests, and disintegration test. The procedures were performed in the three forms of each drug, in accordance with the Pharmacopoeia's general methods.[23]

Evaluation of the visual aspect: The evaluation of the visual aspect of the samples analyzed the original state of the packages by friction of a metal piece on the place indicated in the secondary packaging (cartridge); in addition, it analyzed if they were within the validity period, uniformity of coloring among tablets, missing tablets in blisters, broken or cracked tablets, readability of batch records and validity markings on primary and secondary packaging, and any other apparent change.

Leakage test: The leakage test was performed to evaluate the characteristics of moisture permeability in blisters. For determining leakage in the primary packaging, two blisters of each sample were dipped into a desiccator containing 0.1% methylene blue dye solution under vacuum pressure of -0.300mmHg for four minutes, with a rest of one minute without vacuum. After removing the samples from the desiccator, a visual inspection was performed to check for dye infiltration into the blisters. The test was evaluated by the percentage of chambers without infiltration in the blisters, considering the minimum of 95% chambers without leakage.

Average weight: According to the Brazilian Pharmacopoeia,[23] obtaining the average weight consists of individually weighing 20 tablets in an analytical balance and dividing the total weight by the amount of units weighed. One can

tolerate no more than two units outside the specified limits and none of these two may be above or below the stated percentage.

Hardness: The hardness test is performed with 10 tablets individually to determine the resistance of each tablet upon crushing or rupture under radial pressure. The test applies only to uncoated tablets. The analysis was performed as described in the Pharmacopoeia.[23] Each tablet was subject to the action of a device that measures the force - applied diametrically - necessary to crush it, always following the same direction, i.e., the tablets were equally positioned in the equipment. The result was expressed as the average of the values obtained, in Newton (N). This test, according to the aforementioned specification, is for information purposes only.

Friability: The friability test allows determining the resistance of the tablets to abrasion, when subjected to the mechanical action of a device called Friabilimiter; this test applies only to uncoated tablets. The device comprises a rotating cylinder, which revolves around its axis at a speed of 25 revolutions per minute.

Disintegration: The disintegration test aims to check if tablets and capsules disintegrate within the specified time limit. The test consists in subjecting six tablets to an equipment called Disintegrator, which contains a system of baskets and tubes, a container suitable for the immersion liquid, resistors and thermostats to maintain the liquid at 37°C ± 1°C, to produce the same effects suffered by the tablet after being ingested and in the path between the mouth, stomach and intestine. For the purposes of this test, disintegration is defined as the state in which no residue of the tested units remains on the metal screen of the equipment.

RESULTS AND DISCUSSION

The target products of this research were uncoated tablets of Renitec® 20mg, Captosen® 25 mg, and their respective generic and similar products. All samples were purchased at a drugstore located in the city of Valparaíso de Goiás, Brazil. The choice of generic and similar manufacturers was made at random. The choice of the reference drug followed the specifications of ANVISA's list of reference drugs. For all samples, sufficient amounts were obtained for all pharmacopoeia tests.

The pharmaceutical products analyzed were identified according to their classifications, and the reference, generic and similar products are identified as product R, product G and product S, respectively. Table 1 shows relevant information on Captopril samples, such as batch, manufacturing and validity dates for the three selected types. Also the appearance of their three packages can be visualized. Table 1 also refers to Enalapril.

Table 1- Data for identifying the analyzed samples of Captopril 25mg and Enalapril 20mg: batch, date of manufacture, validity date and visual appearance. The letters R, G and S are used, respectively, referring to reference, generic or similar product. Goiás, 2018

Drug	**Captopril**			**Enalapril**		
Type	Product R	Product G	Product S	Product R	Product G	Product S
Batch	021152	426229	1708618	*N022713*	*2627230*	*HD5522*
Date of	02/2017	02/2017	06/2017	03/2017	05/2017	04/2017

Manufacture Validity date	02/2019	02/2019	06/2019	03/2019	05/2019	04/2019
Appearance of Packaging						

Due to technological advances and high-performance machines, most laboratories produce the drugs in a fast-paced manner. This increases the risk of occurrences of out-of-specification tablets reaching the market, in case the human monitoring performed through quality control tests is not adequately and effectively carried out. [12-17, 21.22]

It is important to point out that one and the same drug produced in the same concentration and in the same pharmaceutical form may have different bioequivalence and bioavailability profiles, depending on the brand or even on the batch produced by the same company. This is attributed to many factors inherent to manufacturing, such as:[5-7] (a) the quality of raw materials; (b) quality of manufacturing practices; (c) particle size of its components and; (d) production methods.[7, 19-25]

It is for this reason that quality control tests are so important, as they serve to ensure homogeneity among the produced units, in accordance with previously defined specifications. The first tests to be carried out are those referring to products' physical-chemical properties.[6-7]

Thus, the quality of Captopril and Enalapril was initially assessed by visual inspection, that is, by observing and evaluating the characteristics of each product (tablet), as well as their packaging. All inspected tablets showed superficial appearance according to the expected, shiny and uniform surfaces. According to Banker and Anderson (2001), [24] the tablets must have a uniform, homogeneous surface, with a characteristic color, smoothness and brightness, being free from defects such as flaws, cracks and contamination. The packages are original and are within the validity period. The tablets should show their characteristics repeatedly and uniformly in each batch, and this was found for the selected samples.

Qualitative inspections constitute the initial steps in quality testing, and must be performed to control production. [14-17, 21-25] Thus, the evaluation of the visual aspect is quite important, since it serves as a way to control qualitative characteristics such as: the verification of the engraving of the batch number and validity, information that enables tracing products, and the verification of whether packages are original, guaranteeing the legitimacy of the product.[19-25]

After this preliminary test, the packaging of the samples went through the leakage test, carried out according to a simple and non-destructive method. The importance of this test should be highlighted, as packaging integrity is vital to ensure drug stability against humidity, air and bacteria.

The leakage test was performed using 0.1% Methylene Blue dye; if a dye infiltration occurs, it shows that blisters are not properly sealed. 100% of the blisters were adequately sealed, that is, there was no infiltration of 0.1% Methylene Blue dye in the tested samples. Thus, the results demonstrated compliance with the specifications as regards a minimum limit of units without leakage of 95%.

Again, the importance of the leakage test is emphasized, since the performance of the equipment and operator can affect the container (blister) sealing and allow the penetration of humidity.[23] Depending on the conditions in which the blisters are packed, external influences may occur, such as: light, humidity, air and microorganisms, which may lead to hydrolysis and oxidation reactions, microbial contamination and changes in the product's appearance, leading to a loss of stability and therapeutic action of the drug in the body.[17-25]

The next test to be carried out was the identification of the average sample weight. To that effect, it was necessary to obtain the individual weights of 20 tablets for each tablet type. The weight of the tablets is determined by the amount of powder or granulate introduced into the matrix and by the adjustment of the lower punches of the compressors.[22-25] The individual weight values obtained were used to calculate the average weight and, based on them, the variation limit was determined.

For uncoated tablets containing an average weight of 80mg or less, the acceptable variation is ± 10,0%; for tablets containing an average weight of 80 to 250 mg, the allowed variation is ± 7.5%; for those with an average weight greater than or equal to 250mg, the variation limit allowed is ± 5.0%. The analysis was performed according to the Pharmacopoeia's description.[17.23] The average weight analysis was performed for the three drug types of Captopril and Enalapril, and the obtained data are shown in Table 2.

It is observed that, in general, there were no large fluctuations in the mass values obtained for all tested samples. For Captopril, an average weight of 0.129 ± 0.002 was obtained for the R variant; 0.11613 ± 0.004 was obtained for G, and 0.079 ± 0.001 for S. With the obtained standard deviation value, one can observe a weak dispersion of the values measured in the three types of Captopril variants. It was also found that the average weight values for the Enalapril samples are satisfactory and the masses of the samples tested show weak variability. The average weight values obtained for R, G and S were respectively 0.199 ± 0.001, 0.277 ± 0.004, and 0.166 ± 0.001.

Table 2- Individual weight, average weight, standard deviation and relative standard deviation of Captopril 25mg (R, G and S tablets) and Enalapril 20mg (R, G and S tablets). Goiás, 2018

Drug	**Captopril**			**Enalapril**		
Type	**Product R (g)**	**Product G (g)**	**Product S (g)**	**Product R (g)**	**Product G (g)**	**Product S (g)**
1	0.130	0.163	0.079	0.199	0.279	0.166
2	0.128	0.168	0.079	0.200	0.272	0.166
3	0.128	1.156	0.080	0.202	0.281	0.166
4	0.127	0.166	0.076	0.198	0.278	0.166
5	0.127	0.162	0.081	0.196	0.267	0.169
6	0.129	0.155	0.079	0.199	0.280	0.166
7	0.130	0.157	0.078	0.199	0.277	0.166
8	0.130	0.161	0.079	0.198	0.279	0.168
9	0.128	0.163	0.079	0.198	0.271	0.164
10	0.129	0.154	0.078	0.201	0.281	0.165
11	0.131	0.162	0.081	0.199	0.275	0.168
12	0.128	0.162	0.079	0.200	0.277	0.165
13	0.130	0.163	0.081	0.198	0.284	0.167
14	0.130	0.158	0.080	0.200	0.279	0.166
15	0.131	0.166	0.078	0.199	0.281	0.164
16	0.129	0.164	0.080	0.202	0.278	0.166
17	0.130	0.160	0.079	0.196	0.278	0.166
18	0.125	0.163	0.076	0.201	0.280	0.168
19	0.129	0.164	0.077	0.196	0.271	0.165

20	0.126	0.158	0.079	0.199	0.278	0.166
Average Weight	0.129	0.161	0.079	0.199	0.277	0.166
Standard Deviation	0.002	0.004	0.001	0.001	0.004	0.001
Relative Standard deviation (%)	1.160	2.360	1.770	0.900	1.510	0.780

For improved visualization of average weight results, please see the graphs of weight (g) *versus* tablets. The Captopril results graph is available in Figure 1, where one can see that all three drugs are within the 7.5% limit. According to the results, none of the tablets was outside the established variation limit, thus showing a uniformity of weight among samples, which is in compliance with the specifications established by the Pharmacopoeia.[23]

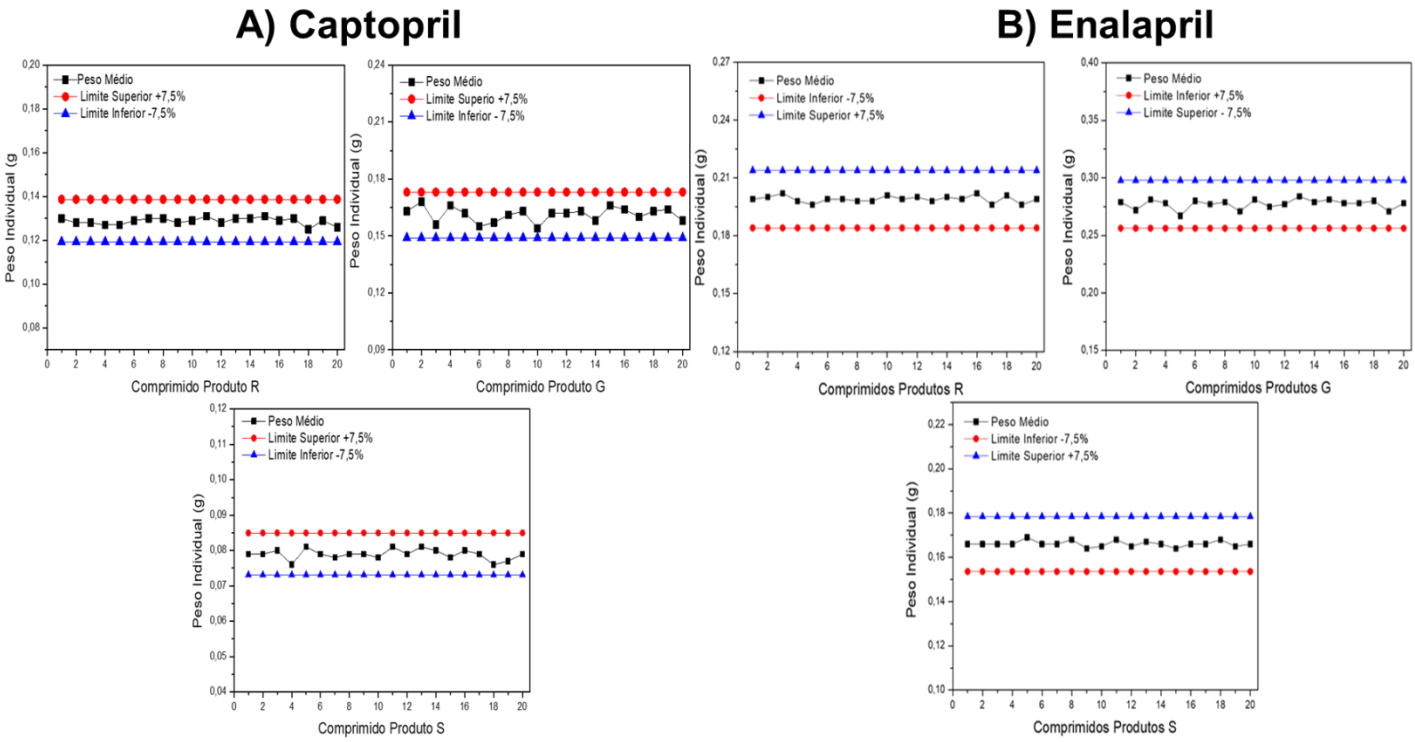

Figure 1: A) Average weight (per tablet) of each of the three Captopril drug types, identified as R, S and G, compared to the ± 7.5% limit values. B) Average weight analyses of Enalapril, identified as R, S, and G. Goiás, 2018

According to the results shown by Figure 1, none of the analyzed tablets was outside the variation limit. Therefore, the samples' uniformity of weight is compliant with the specifications established by the Pharmacopoeia.[17,23-25] It is worth mentioning that the formula of solid drugs is based on the weight of the pharmaceutical form, i.e., on the average weight. For this reason, the process control that determines tablet weight is of great importance, since, ultimately, it directly influences the concentration of active ingredient in each unit.[14-17]

Mechanical strength tests were then performed on the tablets. Tablet resistance depends on a number of factors that include component cohesion, types of granulation, binders, tablet size and shape, and the state of units.[14-17] The first performed test

was a tablet hardness test. Hardness may reflect in the disintegration of tablets at different disintegration rates and, consequently, cause variations in the dissolution and bioavailability profiles of units.[13-15,17-25]

For the hardness test, all tablets were placed in the same direction, so their grooves would remain at a 90°-angle in relation to the crushing-direction. The results for the Captopril and Enalapril samples are shown in Table 3.

Table 3- Results of hardness test performed on Captopril and Enalapril tablets for their R, G and S variants. Goiás, 2018

Drugs	**Captopril**			**Enalapril**		
Type	Product R	Product G	Product S	Product R	Product G	Product S
1	45	68	59	179	49	135
2	43	58	69	193	56	168
3	47	79	60	178	65	149
4	46	75	72	168	48	205
5	46	71	61	64	52	153
6	40	100	46	75	34	168
7	44	112	66	62	53	118
8	46	102	59	67	44	132
9	43	94	63	77	49	145
10	42	87	66	112	56	82
Minimum hardness	40	58	46	62	34	82
Maximum hardness	47	112	72	193	65	205
Maximum - Minimum	7	54	26	131	31	123
Average	44.20	84.60	62.10	117.50	50.60	145.50
Standard Deviation	2.20	17.24	7.16	55.44	8.19	32.83
Relative standard deviation (%)	**4.98**	**20.38**	**11.52**	**47.18**	**16.20**	**22.57**

The results indicate that the average hardness of Captopril tablets was 42 ± 2.2 for product R, 84 ± 17 for G, and 62 ± 7 for S. The generic product showed greater variability with respect to tablet hardness; nevertheless, all results were all within the maximum and minimum hardness reference values. As for Enalapril samples, results show that the reference product presented greater variability with respect to tablet hardness; nevertheless, all variations were within maximum and minimum hardness reference values. Values for types R, G and S were 118 ± 55; 51 ± 8 and 146 ± 3, respectively.

The results show that all tablets were broken with a force higher than 30N, compliant with the parameter established by the Pharmacopoeia,[23] which states that the minimum force acceptable for analysis is 30N.

It is known that the a tablet's hardness is proportional to the logarithm of compressive force and inversely proportional to its porosity, which implies that tablets must have adequate mechanical resistance, since they are subject to friction, mechanical shocks during production processes, storage, packaging, transportation, distribution and handling by users.[17, 21-25]

In this context, one should include product friability, which is defined as tablet's lack of resistance to abrasion when

submitted to mechanical action. The evaluated tablets had friability levels compatible with the specifications. Before weighing the tablets again, all dust residues were removed from their surface, and based on their initial and final weights the percentage of loss was calculated.[13-15.17]

The results obtained in the friability analysis for the two drugs appear in Table 4, showing that the percentage of weight loss of all samples was lower than 1% of their initial value, i.e., an extremely small value in the difference of sample weights.

According to the results shown in Table 4, all tested samples obtained satisfactory results in the friability test, since there was no weight loss higher than the 1.5% of the limit established by the Pharmacopoeia. Thus, there was no need to repeat the test. Such practice would be necessary in case of analytical error.[23-25]

Table 4: Data obtained by Friability (variation between initial and final weight) and Disintegration Time analyses for the three types of Captopril and Enalapril investigated: R, G and S. Goiás, 2018

Drug	Type	Weight			Disintegration
		Initial (g)	Final (g)	Loss (%)	Time (s)
Captopril	R	2.58	2.58	0.23	27
	G	3.22	3.22	0.09	109
	S	1.58	1.58	0.32	29
Enalapril	R	3.98	3.98	0.05	290
	G	5.55	5.54	0.18	45
	S	3.33	3.33	0.06	152

Friability represents the resistance of tablets to wear. The importance of the friability test lies in the verification of tablet resistance to weight loss when subjected to mechanical shocks inherent to industrial processes and everyday actions, e.g. storage, transportation, distribution, and users' handling.[17, 21-25]

High friability can cause a loss of active ingredients, compromising the drug's therapeutic efficacy, in addition to causing poor appearance on account of breaks, cracks and fragmented edges, sometimes leading to patient rejection and discontinuation of treatment.[13-15,17, 21-25]

Finally, the disintegration-time of the six samples was determined. The time was measured until there was no palpable tablet core attached to the metal screen of the acrylic tube, or to the cylindrical disc placed above the samples. The results of the analysis are shown by Table 4, where it is observed that all tested samples showed satisfactory results, since no sample presented a disintegration time higher than the limit of 30 minutes established by the Brazilian Pharmacopoeia.[23]

Several factors could significantly affect the value of disintegration time, such as: granular physical and chemical properties and pharmaceutical form's porosity, as well as the effect of the disintegrating compound of a formula. For these reasons, assessing disintegration time is relevant, as it impacts directly on drugs' pharmacological action. This is so because for the active ingredient to be available for absorption, tablet

disintegration needs to occur, thus the amount of smaller particles is increased and the surface of contact with the dissolution medium is increased, favoring absorption and the bioavailability of the drug in the body.[17-19-25]

FINAL REMARKS

The objectives of this study were to evaluate the quality of Captopril 25mg and Enalapril 20mg tablets marketed in the city of Valparaíso de Goiás, Brazil, and to compare the quality of the medicines according to their classification as a reference, generic and similar drug.

Based on the obtained results, this study concludes that all samples of the tested batches achieved satisfactory results and are in compliance with the specifications of average weight in solid dosage forms, mechanical resistance via hardness and friability tests, permeability percentage, and disintegration time. These specifications are established in the Brazilian Pharmacopoeia, 5th ed. 2010.

With the compliance conferred by these results, one can conclude that the reference, generic and similar product samples of Captopril 25 mg and Enalapril 20 mg were compatible, and that they are suitable for consumption.

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