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BIOEQUIVALENCE STUDY OF GENERIC SALBUTAMOL TABLETS WITH LOGO AND BRANDED GENERIC

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ABSTRACT

Salbutamol is a medication that stimulates beta receptors, particularly beta agonists, which are widely used as a remedy for sudden asthma attacks and those triggered by physical exercise due to its potent and rapid bronchodilating properties. These medications are known as short-acting beta-agonists (SABA). The purpose of this study was to examine in detail the significant differences in dissolution and absorption rates associated with the active ingredient in two pharmaceutically equivalent drug products, and to compare them to determine their bioequivalence. The research methodology involved experimental studies using a quantitative approach, including tests of physical quality, content determination, and dissolution testing. The results of the physical quality test for the uniformity of salbutamol tablet sizes showed that generic branded tablets, brand A, brand C, and brand D had a thickness of 0.10 cm ± 0 and a diameter of 0.50 cm ± 0, brand B had a thickness of 0.20 cm ± 0 and a diameter of 0.60 cm ± 0, and brand E had a thickness of 0.10 cm ± 0 and a diameter of 0.40 cm ± 0. The weight uniformity test results indicated that none of the generic branded tablets, brand B, or brand D deviated from columns A (7.5%) and B (15%), whereas none of the tablets from brands A, C, or E deviated from columns A (10%) and B (20%). The hardness test results showed that generic branded salbutamol tablets had a hardness of 6.05 kg/cm² ± 0.69, brand A had 4.93 kg/cm² ± 0.66, brand B had 5.08 kg/cm² ± 0.56, brand C had 4.76 kg/cm² ± 0.74, brand D had 7.91 kg/cm² ± 1.54, and brand E had 7.93 kg/cm² ± 1.09. The friability test results were 0.39% ± 0.22 for generic branded tablets, 0.61% ± 0.24 for brand A, 0.36% ± 0.27 for brand B, 0.37% ± 0.25 for brand C, 0.49% ± 0.27 for brand D, and 0.64% ± 0.25 for brand E. The disintegration time test results were 3 minutes ± for generic branded tablets, 1 minute ± 0 for brand A, 1 minute ± 0 for brand B, 0.2 minutes ± 0 for brand C, 3 minutes ± 0 for brand D, and 1 minute ± 0 for brand E. The results of this study indicate that both generic and branded salbutamol tablets met established standards. The dissolution rates for generic tablets were 103.38% ± 0, brand A 109.74% ± 0, brand B 106.93% ± 0, brand C 104.38% ± 0, brand D 98.89% ± 0, and brand E 95.03 ± 0. The similarity factor results were greater than 50, indicating that all six medications were identical.

Keywords : Bioequivalence, Similarity Factor (*f2*), Generic, Salbutamol

INTRODUCTION

Salbutamol is a medication that stimulates beta receptors, specifically beta agonists, which are widely used as a remedy for sudden asthma attacks and those triggered by physical exercise owing to their potent and rapid bronchodilating properties. These medications are known as short-acting beta-agonists (SABA). Examples of drugs in the SABA class include salbutamol, terbutaline, and fenoterol

(Sutrisna, 2014). Salbutamol tablets are formulated using excipients, such as fillers, binders, dispersants, disintegrants, lubricants, glidants, colorants, and flavorings. These excipients can affect the quality attributes of the tablets. Therefore, differences in bioavailability between tablets can be caused by variations in the concentrations of excipients used by different manufacturers (Pratiwi *et al*., 2023). To determine the bioavailability of a drug, it is necessary to measure its release parameters and dissolution rates using physicochemical methods in product development. Bioequivalence was used to compare two different drug products for solid dosage forms.

In Indonesia, salbutamol is the most widely used drug among the short-acting beta-agonists. Salbutamol can alleviate asthma symptoms by relaxing the smooth muscles of the airways (Akib *et al*., 2021). Salbutamol, the first selective SABA widely used in clinical practice, was introduced in 1968. Salbutamol acts as an acute selective beta-2 adrenergic receptor bronchodilator in asthma and other chronic bronchopulmonary disorders. It is indicated for the relief and prevention of bronchospasm owing to its strong smooth muscle relaxant properties (Sutrisna, 2014).

According to the World Health Organization (WHO), salbutamol is a safe and highly effective medication. In the market, salbutamol consists of generic and branded drugs. According to RISKESDAS 2018, generic drugs have a smaller market share than branded generic drugs. This reality is linked to the public perception that generic drugs have lower quality standards than branded products (Rissa and Puspita, 2023). Negative perceptions regarding the quality of generic drugs can be a barrier to the healing process and can reduce public interest in consuming generic drugs (Puspita and Rissa, 2022). To ensure that the quality of generic drugs is not inferior to that of branded drugs, understanding drug quality standards is essential (Kartikaningtum *et al*., 2022). Comprehensive laboratory research is often necessary to convince the public about the quality of generic drugs. Various studies can provide insights into drug efficacy, including bioequivalence testing (Ulfa and Nuryanto, 2021).

Previous research by Mutaharah *et al* (2023) on the bioequivalence study of generic and non-generic paracetamol tablets in vitro stated that both generic and non-generic paracetamol tablets met the dissolution test requirements. Sari (2023) conducted a dissolution test of generic and branded chloroquine tablets in the Heram District, Jayapura City, and reported that the generic chloroquine content was 98.25%, ribokuin branded content was 97.41%, malarex branded content was 96.16%, and mexaquine branded content was 97.33%. There was no difference in the dissolution test results for generic and branded chloroquine tablets. Another study by Noorjannah and Noval (2020) on a comparative dissolution test between generic and branded ramipril tablets stated that there was a difference in the dissolution profiles of generic and branded drugs, although other parameters met the requirements.

This research methodology is experimental and involves physical quality testing, content determination, and dissolution testing. The aim of this study was to examine in detail the significant differences in dissolution and absorption rates associated with the active ingredient in two pharmaceutically equivalent drug products, and to compare them to determine their bioequivalence. If it is proven that the dissolution rate of branded tablets is equivalent to that of generic products and bioequivalence is achieved, it is hoped that this will promote the successful use of salbutamol tablets in healthcare practice.

RESEARCH METHOD

Tools and Materials

The equipment used in this research included a caliper, Ohaus Adventure™ analytical balance, Erweka TBH 28 tablet hardness tester, Erweka TAR tablet friability tester, Erweka ZT 502 disintegration tester, Pyrex glassware, volumetric pipettes, pipette pump, Genesys 10S UV-Vis spectrophotometer (Thermo Scientific), Erweka DT 700 dissolution tester (7 Type 1 apparatus), and Mettler Toledo S-20 pH meter. This study utilized a 4 mg generic branded salbutamol tablet and five 4 mg branded salbutamol tablets, salbutamol standard, NaOH solution, potassium dihydrogen phosphate, and distilled water.

Research Procedure

1. Sample Preparation

This study utilized 4 mg salbutamol tablets, which were categorized under the Biopharmaceutical Classification System (BCS) class 1, available in the market. The subjects included one generic Salbutamol tablet and five branded salbutamol tablets, each containing an equivalent active ingredient of 4 mg. Approximately 100 tablets from each uniform batch were used for each sample.

2. Physical Quality Testing of Tablets

a. Organoleptic Testing

Organoleptic examination involves the assessment of the uniformity of color, surface condition, aroma, and taste (Gusnadi *et al*., 2021).

b. Size Uniformity Testing

Size uniformity was examined by selecting 20 tablets from each formulation and measuring their thickness and diameter using a caliper. The diameter must not exceed three times or be less than one-third of the thickness of the tablet, as established (Ulfa *et al*., 2018).

c. Weight Uniformity Testing

Weight consistency testing was performed by weighing 20 tablets of each formulation and calculating the mean weight. No two individual tablets should exceed the mean weight by more than the deviation specified in column A, and the number of tablets deviating from the mean weight should comply with column B according to the standards in the Indonesian Pharmacopoeia V (Ulfa *et al*., 2018).

d. Tablet Hardness Testing

Tablet hardness was tested using 20 tablets, each placed vertically in a hardness tester. The compression tool was rotated until the tablet broke and the hardness level was read on a scale in kilograms (Ulfa *et al*., 2018).

e. Friability Testing

Friability testing was conducted on 20 tablets, after they were freed from any powder and weighed. The tablets were then rotated in a friability tester for 5 minutes at 25 rpm. The tablets were weighed periodically and the friability percentage was determined (Ulfa *et al*., 2018).

f. Disintegration Time Testing

Disintegration time testing was performed on six tablets, each placed in the basket of the disintegration tester. The medium used was water at a temperature close to the human body temperature of approximately 37 °C. The water level should not be less than 15 cm to ensure that the basket can move properly with an agreed-upon vertical distance of 7.5 cm (Ulfa *et al*., 2018).

3. Determination of Salbutamol Content/Content Uniformity in Tablets

a. Preparation of Phosphate Buffer Solution pH 6

Prepare 1000 mL of phosphate buffer solution at pH 6.8 by weighing 6.8005 grams of KH_2PO_4 and 0.896 grams of NaOH, and dissolve them in 1000 mL of water. The pH to 6.8 (Depkes RI, 2020).

b. Preparation of Salbutamol Stock Solution

A 1000 ppm salbutamol stock solution was prepared by adding 50 mg of salbutamol standard to a 50 mL volumetric flask and diluting it with phosphate buffer solution pH 6.8. The stock solution (1000 ppm) was diluted to 100 ppm by transferring 5 mL of the stock solution into a 10 mL volumetric flask and adding phosphate buffer solution pH 6.8 up to the mark (Depkes RI, 2020).

c. Determination of Maximum Absorption Wavelength and Preparation of Standard Curve

A salbutamol sulfate standard curve was created by diluting the 100 ppm stock solution with phosphate buffer pH 6.8 in 10 mL volumetric flasks to obtain standard solutions at concentrations of 10, 20, 30, 40, and 50 ppm. A UV spectrophotometer was used to measure the absorbance of the solutions at wavelengths between 200 nm and 400 nm to determine the wavelength with the highest absorbance. Once the maximum wavelength was identified, the absorbance of all standard solutions at this wavelength was measured using a UV-Vis spectrophotometer. The absorbance values were plotted to create a standard curve using linear regression analysis (Depkes RI, 2020).

d. Determination of Salbutamol Content in Generic and Branded Tablets

To determine the salbutamol content, 20 tablets of salbutamol from brands A, B, C, D, E, and generic tablets were used. Each tablet was weighed and the average weight was calculated to determine the content per tablet. Grind 4 tablets from each brand (A, B, C, D, E) and the generic tablets, weigh the resulting powder, and dissolve it in phosphate buffer pH 6.8 to a concentration of 300 ppm in a 10 mL volumetric flask. Further dilution was performed to achieve a concentration of 45 ppm in a 10 mL volumetric flask by taking 1.5 mL of 300 ppm solution with phosphate buffer pH 6.8. The weighing and dilution processes were repeated thrice. The absorbance of each diluted solution was measured using a UV-Vis spectrophotometer at the maximum absorption wavelength of salbutamol. The absorbance values were inserted into the standard curve equation to determine the salbutamol content and calculate the % recovery (Depkes RI, 2020).

4. Uji Disolusi Tablet Salbutamol

a. Preparation of Dissolution Media

According to the Indonesian Pharmacopoeia Edition VI, the preparation of phosphate buffer solution at pH 6.8 involves mixing 250 mL of 0.2 M potassium dihydrogen phosphate and 18 mL of 0.1 N sodium hydroxide solution. The mixture was diluted with CO2-free water. The pH was adjusted to 6.8 with 0.2 N NaOH, and the volume was brought up to 1000 mL (Depkes RI, 2020).

b. Determination of Dissolved Salbutamol Content

To prepare the salbutamol stock solution, 100 mg of the standard salbutamol was weighed and dissolved in distilled water in a beaker. The solution was transferred to a 100 mL volumetric flask, and phosphate buffer (pH 6.8) was added to the mark. This stock solution was diluted to obtain a concentration of 100 ppm in a 50 mL volumetric flask by pipetting 5 mL of the 1000 ppm solution into the flask and adding phosphate buffer pH 6.8 up to the mark. The maximum absorption wavelength was determined by diluting the 100 ppm stock solution to concentrations of 10, 20, 30, 40, and 50 ppm, each in a 10 mL volumetric flask. Once the maximum absorption wavelength was identified, the dissolved salbutamol content in 5 mL aliquots from each tablet at dissolution intervals of 5, 10, 15, 20, 25, and 30 minutes. Transfer each 5 mL aliquot to a 10 mL volumetric flask and diluted with phosphate buffer pH 6.8 to the mark. The absorbance was measured using a UV-Vis spectrophotometer at the maximum absorption wavelength of salbutamol. Dissolution performance parameters, such as Dissolution Efficiency (DE) and Similarity Factor (*f2*), were evaluated (Depkes RI, 2020).

Data Analysis

The collected data were analyzed using SPSS version 21. The Shapiro-Wilk test was used to evaluate homogeneity and normality. One-way ANOVA was used to analyze the variation in one direction. However, if the data were not normally distributed, ANOVA could not be applied. In such cases, the Kruskal-Wallis test was used as an alternative to ANOVA, especially when the data distribution did not meet the normality criteria.

RESULTS AND DISCUSSION

1. Physical Quality Testing of Tablets

Physical quality testing of the tablets was conducted to ensure the quality of the tested preparations and confirm the quality and efficacy of the evaluated salbutamol tablets. The results of the physical tests are as follows:

a. Organoleptic Testing of Generic and Branded Salbutamol Tablets

Organoleptic testing is the preliminary stage of all the tablet tests. This test involves visual observation using human senses to assess the uniformity of color, surface condition, aroma, and taste of salbutamol tablets (Ansel, 2005). The results of organoleptic testing are summarized in Table I, which presents the observations.

Table I. Results of Organoleptic Testing for Branded Generic Salbutamol Tablets

Spesification	Generic
Form	Tablet
Color	Green
Odor	Odorless
Taste	Bitter

Based on Table I, the organoleptic test results for the branded generic salbutamol tablets indicated that the tablets were green in color, odorless, and had a bitter taste.

Table II. Results of Organoleptic Testing for Branded Salbutamol Tablets

Brand A	Brand B	Brand C	Brand D	Brand E
Tablet	Tablet	Tablet	Tablet	Tablet
Pink	Green	Pink	White	Pink
Odorless	Odorless	Odorless	Odorless	Odorless
Bitter	Bitter	Bitter	Bitter	Bitter

Based on Table I and Table II, all six tablets have the same form, odor, and taste but differ in color. The differences in tablet color may be attributed to the addition of small amounts of colorants to mask the less attractive color of the drug and enhance the aesthetic appeal of the tablet. Furthermore, the addition of color helps distinguish the product from the others. Color also aids in product monitoring, as fading colors can indicate that the tablets are no longer usable or damaged (Fendri *et al.*, 2023).

b. Tablet Size Uniformity Testing for Generic and Branded Salbutamol Tablets

Size consistency is a crucial aspect in determining the tablet quality. Consistency in tablet thickness and diameter is essential because it can affect the quality and efficiency of the packaging process. Inconsistent thickness and diameter can complicate the packaging process and make it less efficient. The findings from the comparative calculation of the size uniformity test between the branded generic and branded salbutamol tablets are summarized in Table III.

Table III. Results of Size Uniformity Testing for Salbutamol Tablets

Product	Thickness (cm) ± SD	Diameter (cm) ± SD	Remarks
Generic	0,10 cm ± 0	0,50 cm ± 0	Tablet diameter should not exceed 3 times or be less than 1/3 of the tablet thickness (Depkes RI, 2020)
Brand A	0 ,10 cm ± 0	0,50 cm ± 0	
Brand B	0,20 cm ± 0	0,60 cm ± 0	
Brand C	0,10 cm ± 0	0,50 cm ± 0	
Brand D	0,10 cm ± 0	0,50 cm ± 0	
Brand E	0,10 cm ± 0	0,40 cm ± 0	

Based on the results in Table III, all six tablets met the requirements, with the diameter not exceeding 3 times and not being less than 1/3 of the tablet thickness (Depkes RI, 2020). The uniformity of tablet size is influenced by factors such as flow properties, uniform density, and stability of the punch in tablet compression equipment.

c. Weight Uniformity Testing for Generic and Branded Salbutamol Tablets

Weight uniformity of tablets is a critical aspect in determining the consistency of the active ingredients contained within a tablet. A uniform weight ensures the safety of a tablet, as it relates to the consistency of the drug dose administered to the body. The results of weight uniformity testing for branded generic and branded salbutamol tablets are presented in Table IV and Table V.

Table IV. Weight Uniformity Testing Results for Salbutamol Tablets with Average Weight 151 mg–300 mg

Product	Average Tablet Weight (mg) ± SD	Deviation of Column A (7,5%)		Deviation of Column B (15%)	
		Maximum Limit (mg)	Minimum Limit (mg)	Maximum Limit (mg)	Minimum Limit (mg)
Generic	211,94 ± 2,3	227,84	196,05	243,74	180,16
Brand B	211,22 ± 2,89	227,07	195,39	242,91	179,54
Brand D	158,34 + 2,92	170,22	146,47	182,09	134,59
Conclusion		**Passed**		**Passed**	

Based on Table IV, it can be concluded that the weight uniformity of the salbutamol tablets for the generic and brands B and D met the specifications, with no deviations exceeding 7.5% (Column A) or 15% (Column B).

Table V. Weight Uniformity Testing Results for Salbutamol Tablets with Average Weight 26 mg–150 mg

Products	Average Tablet Weight (mg) ± SD	Deviation of Column A (10%)		Deviation of Column B (20%)	
		Maximum Limit (mg)	Minimum Limit (mg)	Maximum Limit (mg)	Minimum Limit (mg)
Brand A	135,14 ± 1,09	148,65	121,62	162,17	108,11
Brand C	124,95	137,44	112,46	149,94	99,96

Brand E	± 1,48 90,66 ± 6,63	99,73	81,59	108,79	72,53
Conclusion		**Passed**		**Passed**	

Based on the results presented in Table IV and Table V, the weight uniformity tests for the salbutamol tablets indicated that all six tablets met the weight uniformity requirements. For tablets with an average weight of 26–150 mg, no more than two tablets deviated by 10% from the average weight and none deviated by more than 20%. For tablets with an average weight of 151–300 mg, no more than two tablets deviated by 7.5% from the average weight, and none deviated by more than 15%. Based on the results of the study it can be concluded that the six tablets meet the requirements Despite meeting the weight uniformity test requirements, there are variations in the weights of individual tablets. These variations can be attributed to the inconsistent distribution of the drug during the mixing or granulation process, separation of the mixture or granules during manufacturing, or storage of tablets (Fadhilah and Saryanti, 2019).

d. Hardness Test of Generic and Branded Salbutamol Tablets

The hardness of a tablet reflects its ability to withstand mechanical pressure, such as shocks, and prevents the formation of cracks during manufacturing, packaging, and distribution processes. This ensures that the tablet reaches consumers under safe conditions. One of the critical requirements for a tablet is adequate hardness. The results of the hardness tests for the generic branded salbutamol tablets are presented in Table VI.

Table VI. Hardness Test Result of Salbutamol Tablet

Products	Tablet Hardness (kg/cm^2) ± SD	Remarks
Generic	6,05 ± 0,69	A good tablet hardness ranges from 4 to 8 kg/cm^2 (Rahmaningrum and Saputra, 2023)
Brand A	4,93 ± 0,66	
Brand B	5,08 ± 0,56	
Brand C	4,76 ± 0,74	
Brand D	7,91 ± 1,54	
Brand E	7,93 ± 1,09	

As shown in Table VI, all six tablets met the hardness test requirements with an acceptable range of 4-8 kg/cm^2. A tablet hardness below 4 kg/cm^2 is acceptable, as long as friability does not exceed the specified limit. However, tablets that are not sufficiently hard may become brittle during packaging and transportation. A tablet hardness greater than 10 kg/cm^2 is still acceptable if it meets the disintegration time requirements. Tablet hardness is influenced by the amount of pressure applied during compression, properties of the materials, type and concentration of binders used, and condition of the granules. The greater the pressure applied during compression, the harder is the tablet. Higher binder concentrations resulted in stronger inter-particle bonds within the tablet. Tablet hardness must be carefully monitored because it affects the disintegration time and dissolution rate. A higher tablet hardness means that the constituent particles are more difficult to release from the dosage form, leading to longer disintegration times and slower dissolution rates (Rahmaningrum and Saputra, 2023).

e. Friability Test of Generic and Branded Salbutamol Tablets

The friability test, also known as the friability test, is a process to assess how resistant the surface of a tablet is to abrasion during the production process. This test involves the use of a friability tester. A tablet is considered good if its friability does

not exceed 1% (Feladita and Hidayanti, 2020). The results of friability tests for various salbutamol tablets are presented in Table VII.

Table VII. Friability Test Results of Salbutamol Tablets

Products	Tablet Friability (%) ± SD	Conclusion
Generic	0,39% ± 0,22	Meets the friability test requirement of not exceeding 1% thickness (Depkes RI, 2020)
Brand A	0,61% ± 0,24	
Brand B	0,36% ± 0,27	
Brand C	0,370% ± 0,25	
Brand D	0,49% ± 0,27	
Brand E	0,64% ± 0,25	

From Table VII, the results of the friability test for salbutamol tablets indicate that all products, both generic and branded, meet the friability test standards, as the friability values of all six products are less than 1%. This test measures weight loss due to abrasion or erosion of the tablet surface. High friability levels can affect the concentration or amount of active ingredients in the tablet. Tablet hardness is a factor that influences friability, where higher tablet hardness corresponds to lower friability.

f. Disintegration Time Test for Generic and Branded Salbutamol Tablets

The disintegration time test measures the speed at which a tablet disintegrates in bodily fluid. A comparison of the disintegration time results between generic branded salbutamol tablets and branded tablets is presented in Table VIII.

Table VIII. Comparison of Disintegration Time for Salbutamol Tablets

Products	Disintegration Time (Minutes)
Generic	3 ± 0
Brand A	1 ± 0
Brand B	1 ± 0
Brand C	0,2 ± 0
Brand D	3 ± 0
Brand E	1 ± 0
Average	**1,53 ± 1,17**

Based on the data presented in Table VIII, it is evident that all types of salbutamol tablets, whether generic or branded (Brand A, Brand B, Brand C, Brand D, and Brand E), meet the established disintegration time requirement, which is less than 15 minutes thickness (Depkes RI, 2020). Nevertheless, among all the samples, Brand C stood out as the fastest to disintegrate. The disintegration rate of the tablet can contribute to an increase in the bioavailability of the active ingredient in the body. Variations in disintegration times among products may be attributed to differences in the formulation and manufacturing processes used by each pharmaceutical company. Factors such as the concentrations of binders and disintegrants also play a role. Binders are intended to enhance the cohesion of powder particles; therefore, a higher binder concentration results in a longer time required to break the bonds between particles and the tablet matrix, ultimately slowing the disintegration time of the tablet.

2. Determination of Salbutamol Content in Generic and Branded Tablets

a. Determination of Maximum Absorption Wavelength (λmax) for Salbutamol

The salbutamol content was determined using pure salbutamol standards and measured using a UV Spectrophotometer. In this study, a wavelength of 276 nm was chosen as the reference because it exhibited the highest absorption value, and this wavelength was used to measure the salbutamol content in the tablets.

b. Preparation of Salbutamol Calibration Curve

The stock solution at 100 ppm was diluted using a phosphate buffer solution at pH 6.8 to a final volume of 10 mL, and the absorbance was measured at a wavelength of 276 nm. The study yielded values showing an intercept (a) of 0.0056, slope (b) of 0.0062, and correlation coefficient (r) approaching perfection with a value of 0.999. The equation of the calibration curve is y = 0.0056x + 0.0062y = 0.0056x + 0.0062 y = 0.0056x + 0.0062, where yyy represents the absorbance and xxx represents the concentration. The relationship between the various concentrations and their absorbance was linear, as indicated by the straight line, demonstrating linearity. The calibration curve equation was used to determine the concentration of the released drug. The results demonstrated a linear relationship between the concentration of the salbutamol solution and its absorbance, with the correlation coefficient approaching 1, indicating a near-perfect linear relationship between concentration and absorbance.

c. Determination of Salbutamol Content in Generic and Branded Tablets

To ensure that the drug content in the tablets met the requirements specified in Indonesian Pharmacopoeia Edition VI, content determination was performed. The results of content determination for both generic and branded salbutamol tablets are presented in Table IX.

Table IX. Determination of Salbutamol Content

Products	Salbutamol Content (%)	Remarks
Generic	103,38% ± 0,10	Meets Requirements
Brand A	109,74% ± 0,15	Meets Requirements
Brand B	106,93% ± 0,11	Meets Requirements
Brand C	104,38% ± 0,08	Meets Requirements
Brand D	98,89% ± 0,05	Meets Requirements
Brand E	95,03% ± 0,07	Meets Requirements

Table IX shows a comparison between the salbutamol content in generic and branded tablets against the requirements specified in the Indonesian Pharmacopeia Edition VI. The results of salbutamol content determination revealed that all tablet products met the standards set by the Indonesian Pharmacopeia Edition VI, which states that salbutamol tablets must contain salbutamol sulfate equivalent to albuterol, with a content of no less than 90.0% and no more than 110.0% of the amount stated on the label. According to the data, the salbutamol content in the tablets ranges from 95.03% ± 0.07 to 109.74% ± 0.15. The lowest content was found in salbutamol Brand E at 95.03% ± 0.07, while the highest content was found in salbutamol Brand A at 109.74% ± 0.15. This result indicates that all tested salbutamol products fall within the range that meets Indonesian Pharmacopeia standards.

3. Dissolution Testing of Generic and Branded Salbutamol Tablets

a. Dissolution Profile

Dissolution testing is closely related to the effectiveness of medication. For a drug to be effective quickly, its concentration in the bloodstream must be high. The absorption process is a crucial stage in dissolution testing as it provides insight into the rate at which the drug is released from the dosage form. The release rate determines how quickly the drug can be absorbed by the body and begins to exert its therapeutic effects. The results of the salbutamol content determination are presented in

Table X.

Table X. Comparison of Dissolved Salbutamol Content (%)

Products	Time (minutes)					
	5	10	15	20	25	30
Generic	60,40% ± 0	64,77% ± 0	66,47% ± 0	69,87% ± 0	84,78% ± 0	94,45% ± 0
Brand A	59,39% ± 0	64,76% ± 0	69,49% ± 0	74,92% ± 0	84,79% ± 0	95,49% ± 0
Brand B	58,38% ± 0	60,72% ± 0	71,47% ± 0	73,85% ± 0	89,73% ± 0	96,62% ± 0
Brand C	50,29% ± 0	55,62% ± 0	65,30% ± 0	85,71% ± 0	90,27% ± 0	105,46% ± 0
Brand D	50,29% ± 0	56,61% ± 0	66,31% ± 0	86,73% ± 0	90,31%± 0	106,55% ± 0
Brand E	50,29% ± 0	56,61% ± 0	67,32% ± 0	86,74% ± 0	90,32% ± 0	107,58% ± 0

As shown in

Table X, the dissolution profiles of both generic and branded salbutamol tablets varied. Over the 30-minute period, all products showed an increasing percentage of dissolved salbutamol. Generic salbutamol showed a dissolution of 94.45%, while Brand A reached 95.49%. Brand B reported 96.62%, and Brand C climbed to 105.46%. Brand D achieved 106.55%, and Brand E ended at 107.58%.

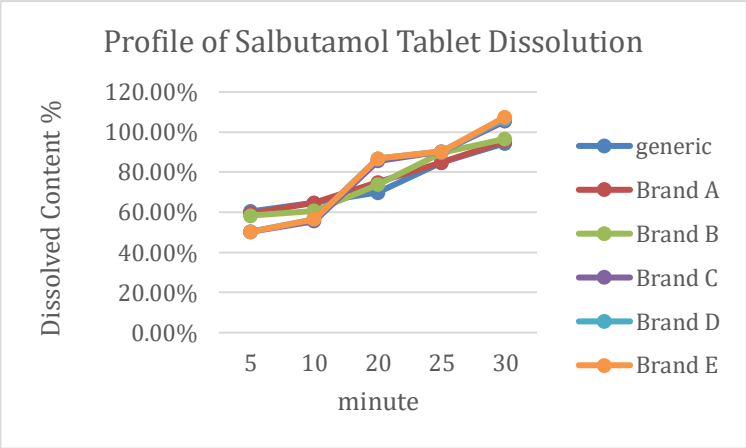

Figure 1. Dissolution profile of generic and branded salbutamol tablets

Figure 1 illustrates the relationship between dissolution rate and sampling time over a specified time range. The dissolution characteristics of each salbutamol product showed a peak tendency at the 30-minute mark. Variations in dissolution characteristics can be attributed to several factors, including the unique formulation of each tablet produced by different manufacturers as well as the choice of solvent used as the medium in the dissolution process. Additionally, the environmental temperature and agitation speed play crucial roles in influencing the rate of dissolution.

b. Dissolution Efficiency (DE)

The parameter established for the next step in dissolution testing is the Dissolution Efficiency (DE). This evaluation provides insights into the dissolution results of all products from different manufacturers through the lens of the Dissolution Efficiency. The DE measures how effectively a drug releases its active ingredient within a specific time range. DE was assessed at three significant time points: the beginning, middle, and end of the dissolution process, specifically at 5, 15, and 30 minutes. The DE calculations at these points were then illustrated in a histogram, offering a visual representation of the dissolution performance for each salbutamol test product, whether branded or generic. The data are shown in Figure 2.

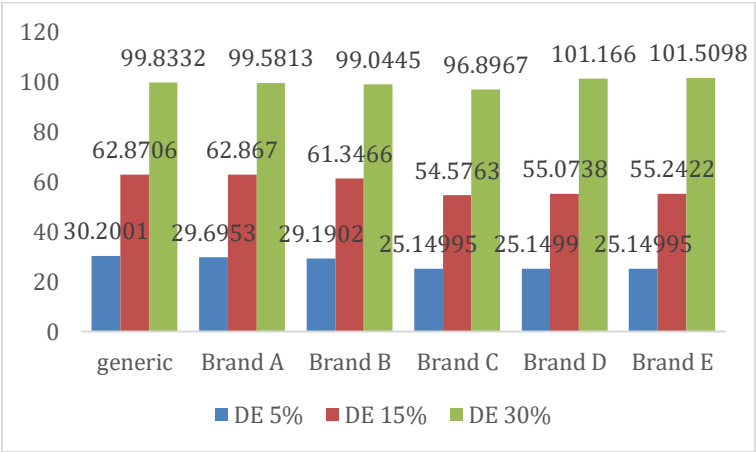

Figure 2. Histogram $DE_{5\%}$, $DE_{15\%}$, and $DE_{30\%}$

From Figure 2, it can be concluded that all six pharmaceutical products demonstrated satisfactory dissolution efficiencies. At the initial point (DE5%), approximately 25–30% of the active ingredient was dissolved from the total tablet, increasing to 54–62% at the midpoint (DE15%), and approaching or exceeding 100% by the end of the dissolution process (DE30%). This dissolution efficiency is reflected in the percentage of the active ingredient in the tablet that dissolves at each DE measurement stage. The data indicated that as the dissolution time progressed, the DE value increased. Conceptually, in an in vivo context, this could represent a rising concentration of salbutamol in the blood over time, with concentrations potentially approaching or even surpassing 100% by the 30-minute mark.

c. Similarity Factor (*f2*)

To measure the similarity between the two dissolution profiles, the similarity factor (*f2*) is used. This factor was calculated to compare the dissolution profiles of generic and branded salbutamol products. An *f2* value is considered equivalent when it is equal to or greater than 50 (ranging from 50 to 100), indicating that the two dissolution curves are similar and that their dissolution profiles are comparable. Information regarding the similarity factor between generic salbutamol tablets and branded salbutamol tablets can be found in Table XI.

Table XI. Similarity Factor (*f2*) Between Generic and Branded Salbutamol Tablets

Product	*f2*	Requirement	Category
Generic – Brand A	99.99319	>50	Identical
Generic – Brand B	99.9836	>50	Identical
Generic – Brand C	99.89392	>50	Identical
Generic – Brand D	99.846409	>50	Identical
Generic – Brand E	98.632731	>50	Identical
Brand A – Brand B	99.99131	>50	Identical
Brand A – Brand C	99.9225	>50	Identical
Brand A – Brand D	99.9186	>50	Identical
Brand A – Brand E	99.91523	>50	Identical
Brand B – Brand C	99.4249	>50	Identical
Brand B – Brand D	99.3439	>50	Identical
Brand B – Brand E	99.3219	>50	Identical
Brand C – Brand D	98.3849	>50	Identical
Brand C – Brand E	98.3839	>50	Identical
Brand D – Brand E	99.9994	>50	Identical

Table XI illustrates that all six tested products achieved *f2* values exceeding the threshold of 50, indicating a significant similarity in the dissolution profiles among the products. This similar dissolution relationship is closely related to drug absorption in the body. It can be concluded that generic salbutamol tablets have a drug absorption profile comparable to that of branded salbutamol tablets, affirming the potential equivalence between the two types of tablets.

CONCLUSION

The results of the study indicate that generic salbutamol tablets and brands A, B, C, D, and E met the established requirements. This demonstrates that all six products possessed equivalent qualities. Based on the research conducted, it can be concluded that the generic and branded salbutamol products show significant similarities, indicating significant bioequivalence among the six products.

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