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Research Article

EVALUATION OF CONTENT AND DISSOLUTION PROFILE OF GENERIC AMOXICILLIN TABLETS MARKETED IN INDONESIA

Nyi Mekar Saptarini* and Rusniyanti

Faculty of Pharmacy, Padjadjaran University, Indonesia

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*Email: n_mekars @yahoo.com

ABSTRACT

Amoxicillin is the penicillin derivatives and used to treat bacterial infection that caused by Gram-positive and Gram negative bacteria. Generic amoxicillin tablets in Indonesia produced by government and private. The aims this study were to compare the content and dissolution profiles of generic amoxicillin tablets marketed in Indonesia which produced by government and private was determined using a method from the United Stated Pharmacopoeia. The result showed that there was no significant difference between public and private generic amoxicillin tablets which contain 95.36-114.11% of amoxicillin with 80.58- 99.56% of amoxicillin dissolved in 30 minutes.

Keywords: Amoxicillin, Tablet, Generic, Content, Dissolution profile

INTRODUCTION

Amoxicillin is a penicillin derivate with broad spectrum bacterisid properties. Its mechanism of action based on inhibition of bacterial cell wall mucopeptide synthesis. Amoxicillin used in treatment of ear, nose, throat, urinary, skin and skin structure, lower respiratory tract, and acute uncomplicated gonorrhea infections caused by susceptible strains of specific organisms.[1] Amoxicillin is the most widely usage of antibiotic in Indonesia, either in the generic or non generic form. Due to economical reasons, the use of generic medicines has been given much incentive by health authorities throughout the world.[2] Generic amoxicillin tablet produced by government and private industries. Generic amoxicillin tablets both government and private products on the market is expected to guarantee quality.[3]

In the pharmaceutical field, drug quality inspection is important so the drugs can interacted with their target at the right dose to provide therapeutic effects, especially antibiotics. Improper dose of antibiotics causing bacterial resistance.[3] The drugs absorption from solid pharmaceutical forms after oral administration depends on the drug liberation from the pharmaceutical form, its dissolution or solubility in physiological conditions, and its permeability through the gastrointestinal tract. The *in vitro* dissolution tests can be predicted the *in vivo* drug performance, so dissolution tests used to assure the quality of the pharmaceutical product.[4] Different bioavailability of the drug with the same active substances occur due to differences in the formulas and methods used, quality control procedures in the production process, and handling methods, equipment, packaging, and storage.[5] The aims this study were to compare the content and dissolution profiles of generic amoxicillin tablets marketed in Indonesia which produced by government and private.

MATERIALS AND METHODS

Samples

Three different brands of tablet containing 500 mg of amoxicillin produced by government industries (A, B, and C) and three different brands of tablet containing 500 mg of amoxicillin produced by private industries (D, E, and F) were tested.

Determine of Amoxicilin Content in Tablet[6]

pH 5.0 Buffer Solution: Dissolve 27.2 g of monobasic potassium phosphate in 3 L of water, adjust with a 45% (w/w) solution of potassium hydroxide to a pH of 5.0 $\pm$ 0.1, dilute with water to obtain 4 L of solution and mix.

Standard Solution: Pipetted 3 mL solution of 1000 ppm to a 20 mL volumetric flask and filled with pH 5.0 buffer solution (150 ppm). The absorbance measured at 271 nm using a spectrophotometer Shimadzu model 1401 and pH 5.0 buffer solution as a blank.

Sample Solution: Five tablets were weighted, then powdered. Weighted the powder equivalent to 100 mg anhydrous amoxicillin and diluted with pH 5.0 buffer solution in a 100 mL volumetric flask. Sample absorbance measured at 271 nm using a spectrophotometer Shimadzu model 1401 and pH 5.0 buffer solution as a blank.

Statistical analysis using analysis variance (ANOVA) in order to detect the existence of significant differences between the samples.

Dissolution Test[6]

Studies were performed using Hanson Research Corp. model SR-6 equipment. Samples were submitted to the dissolution test as is described by the American Pharmacopoeia in Table 1 for amoxicillin tablet. Dissolution profiles were obtained under the same conditions. Aliquots (10 mL) were removed in 1, 5, 10, 20, and 30 minutes, and analyzed spectrophotometrically in 271 nm using a spectrophotometer Shimadzu model 1401. Aliquots from the dissolution medium without the drug (the same volume and temperature) were immediately added to the dissolution medium in order to maintain a constant volume during the test. Dissolution profiles were determinated by the USP 31 methods to six tablets. Dissoluted percentage calculated by equation (1). Statistical analysis using analysis variance (ANOVA) in order to detect the existence of significant differences between the samples.

$$Cu = \frac{Au}{As} \times \frac{Cs}{Cr} \times \frac{Vl}{Vp} \times 900 \quad (1)$$

Where Cu = amoxicillin content were calculated to the amoxicillin standard (%), Au and As = absorbance of the sample and standard solution, Cs = concentration of standard,

Cr = average dose, Vl and Vp = volume of volumetric flask and pipetted.

Table 1 Condition Used for Dissolution Test for Amoxicillin Tablets

Agitation system	Apparatus 2 (paddle apparatus)
Stirring rate	75 rpm
Dissolution medium	Water
Medium volume	900 mL
Detection method	Spectrophotometer UV (271 nm)
Sampling time	30 minutes

RESULTS AND DISCUSSION

Content uniformity testing is one of the tablet evaluation which being made to determine the percentage of the active substance in the solid pharmaceutical form. Table 2 showed that the amoxicillin content in generic amoxicillin tablets is 95.36- 114.11%. Content uniformity values of all samples meet the USP 31, i.e. each tablet contain 90-120% of amoxicillin which indicated on the packaging.[6] The result showed there was no significant difference in amoxicillin content in generic amoxicillin tablets between government and private products.

Table 2 Amoxicillin Content in Generic Amoxicillin Tablet

Sample Code	Content (%)	Sampel Code	Content (%)
A1	110,71 ± 1,82	D1	98,11 ± 2,80
A2	111,63 ± 0,14	D2	95,36 ± 1,40
A3	100, 93 ± 11,01	D3	98,26 ± 0,33
B1	112,23 ± 2,32	E1	103,84 ± 1,97
B2	114,11 ± 1,33	E2	103,95 ± 0,82
B3	115,40 ± 1,16	E3	103,95 ± 1,48
C1	99,54 ± 0,47	F1	103,84 ± 0,00
C2	99,73 ± 0,74	F2	103,95 ± 0,82
C3	98,00 ± 2,02	F3	103,14 ± 2,63

Table 3 Dissolution Efficiency of Generic Amoxicillin Tablet

Sampel	Amoxicillin content (%) at minutes to-					
	0	1	5	10	20	30
A1	0	19.17 ± 1.11	52.12 ± 2.04	92,07 ± 2,55	98,65 ± 2,32	99,56 ± 2,45
A2	0	18.98 ± 1.21	52.13 ± 1.89	82,08 ± 3,93	92,16 ± 2,21	96,67 ± 1,78
A3	0	19.18 ± 2.03	52.20 ± 1.56	82,08 ± 3.93	87,68 ± 4,47	94,92 ± 4,05
B1	0	15.67 ± 1.34	47.25 ± 2.32	43,80 ± 6,55	66,27 ± 6,46	81,36 ± 1,57
B2	0	15.58 ± 1.72	47.35 ± 2.12	83,61 ± 4,42	92,47 ± 4,09	95,97 ± 3,59
B3	0	16.09 ± 1.65	47.75 ± 1.97	85,06 ± 5,36	92,49 ± 4,01	94,35 ± 2,60
C1	0	21.06 ± 2.56	49.67 ± 2.81	93,35 ± 5,50	102,33 ± 3,98	103,57 ± 3,15
C2	0	20.99 ± 2.31	49.82 ± 1.59	94,64 ± 3,22	103,45 ± 5,91	103,12 ± 2,02
C3	0	21.76 ± 1.56	49.79 ± 1.46	51,84 ± 3,01	70,02 ± 4,30	82,71 ± 2,40
D1	0	18.73 ± 3.21	42.80 ± 1.90	60,22 ± 4,82	79,70 ± 4,45	89,77 ± 3,48
D2	0	18.87 ± 2.78	42.56 ± 2.05	56,26 ± 5,52	74,03 ± 5,58	84,03 ± 2,74
D3	0	19.22 ± 2.67	43.10 ± 2.64	57.47 ± 1,77	74,25 ± 3,69	84,48 ± 3,27
E1	0	17.67 ± 1.67	38.58 ± 1.99	56,29 ± 3,31	73,69 ± 4,59	85,47 ± 3,32
E2	0	17.52 ± 1.93	38.69 ± 2.07	52,44 ± 6,53	72,91 ± 8,89	80.58 ± 5,46
E3	0	17.58 ± 1.82	38.59 ± 2.11	47,65 ± 6,50	68,51 ± 7,82	83,42 ± 4,49
F1	0	22.37 ± 2.334	49.56 ± 1.44	73,29 ± 7,51	88,45 ± 7,45	96,10 ± 7,12
F2	0	22.24 ± 1.75	49.32 ± 2.06	74,88 ± 6,42	91,30 ± 3,14	97,22 ± 1,76
F3	0	22.44 ± 3.14	49.44 ± 1.94	76,32 ± 5,62	89,92 ± 4,93	95,23 ± 4,00

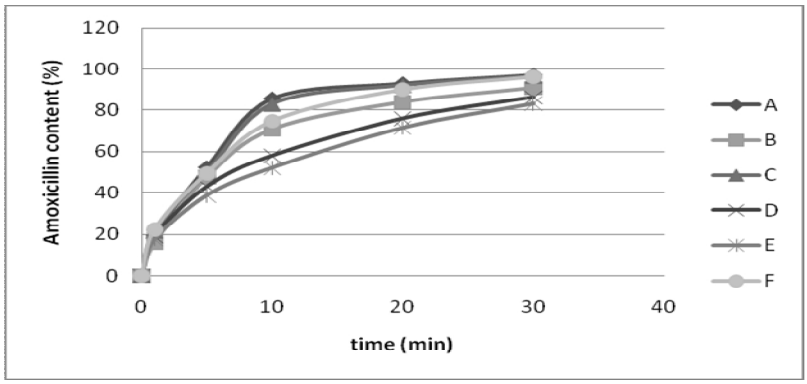

Figure 1: Dissolution profile of generic amoxicillin tablet

To achieve the therapeutic effects, the solid pharmaceutical form had to disintegrated into granules. The granules had to deagregated into particles, then the active substances dissolved and absorbed to systemic circulation and provided therapeutic response. Fast dissolution resulted in better absorption. Dissolution profiles used to determine the active substance solubility in the dissolution medium, because tablet with fast disintegration, not necessarily high solubility.

Figure 1 showed that amoxicillin solubility in generic amoxicillin tablets meet USP 31, i.e. no less than 80% (Q ± 5%) should be dissolved in 30 minutes.[6] Table 3 showed that amoxicillin solubility in 30 minutes was 80.58-99.56%. The result showed there was no significant difference in dissolution profiles of generic amoxicillin tablets between government and private products.

The study of dissolution used to assure the quality of solid pharmaceutical forms for oral use, guarantee the quality from lot to lot, orientate the development of new formulations, and secure the uniformity quality and performance of the drug. This study allows formulation optimization in the development phase and it allows stability studies, manufacturing process monitoring, and the establishment of *in vivo/in vitro* correlations.[7,8] The evaluation of the dissolution profile could be auxiliary to the identification of formulations that presented potential risk in relation to the drug bioavailability.[9] Dissolution is the stage that limiting or controling the absorption rate of active substances which

have low solubility, because this stage is the slowest stage in the active substance liberation from the pharmaceuutical dosage form and distribution into the systemic circulation.[10] If dissolution rate of the active substance is fast or if the active substance is administered as a solution, so the absorption rate of active substance depends on the ability of the active substance to penetrate the membrane cell. But, if the dissolution rate of the active substance is slow, because of the characteristics of active substance or the dosage form, so the dissolution is a determining stage in the absorption process. The oral dosage form which difficult to dissolve, probably not absorbed perfectly, because its absorption depends on the retained time of the active substance in the stomach or intestines.[11, 12]

CONCLUSION

There was no significant difference between public and private generic amoxicillin tablets which contain 95.36-114.11% of amoxicillin with 80.58- 99.56% of amoxicillin dissolved in 30 minutes.

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