COMPARATIVE EVALUATION OF QUALITY OF DIFFERENT BRANDS OF AMOXICILLIN CAPSULES AVAILABLE IN COMMUNITY PHARMACIES IN JAFFNA, SRI LANKA

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Abstract: Amoxicillin is a semisynthetic, β lactam antibiotic that is extensively prescribed among antibiotics. The effectiveness of drug therapy can be changed according to the amount of active ingredients in the dosage forms. Lack of quality may lead to toxicity or failure of therapeutic goals and may develop resistance. Therefore, this study aims to evaluate and compare the quality of different brands of Amoxicillin capsules with innovator brand purchased from private pharmacies in the Jaffna municipal area. Commonly available 7 brands of Amoxicillin 250mg capsules were collected from community pharmacies of the Jaffna municipal area and coded from A_1 to A_7. Qualities of those brands were determined by using the methods such as weight variation, dissolution, and uniformity of content tests as described in British Pharmacopoeia (BP). The dissolution profile data of seven brands were compared with the innovator brand (Amoxil) using Oneway ANOVA followed by the Dunnett T3 test.

All the tested brands complied with the official specifications for weight variation and dissolution tests. All brands of Amoxicillin Trihydrate capsules complied with the specified BP limits except brand A4 which failed to release the stated amount (89.9 % ±0.15). The statistical comparison for the drug release reported that some of the brands showed significant differences ($p < 0.05$), indicating that the *in vitro* drug release would affect their *in vivo* bioavailability. Authorities of the country should take more attention to the quality of antibiotics, especially imported drugs.

Keywords: Amoxicillin capsules, Quality, Evaluation, Sri Lanka

I. INTRODUCTION

Amoxicillin is a semisynthetic β–lactam antibiotic with a broad spectrum bactericidal activity against many gram-positive and gram-negative microorganisms. Amoxicillin interferes with the synthesis of peptidoglycan in the bacterial cell wall. They inhibit trans peptidation enzyme which crosslinks the peptide chains of the peptidoglycan soon after they attach to the binding site of bacteria [1]. There are 13 generic oral solid products of amoxicillin registered with the National Medicines Regulatory Authority (NMRA). These include locally manufactured and imported brands including the innovator product [2].

According to British Pharmacopeia (BP), Amoxicillin capsules quality is evaluated using tests such as uniformity of weight, uniformity of content, and dissolution test.

A generic drug is a medication that has the same active ingredient as the innovator and yields the same therapeutic effect. The effectiveness of drug therapy can be altered by the amount of active ingredients. When there is a lack of quality it may lead to the failure of therapeutic goals, thereby the development of resistance.

Care should be taken to avoid the change in composition among different brands due to the development of resistance. As most of the drugs are imported into Sri Lanka, the quality of antibiotics should be strictly monitored.

Therefore, this study is aimed to determine the pharmaceutical quality of amoxicillin capsules and compare them with the innovative brand.

II. MATERIALS AND METHODS

Materials and reagents

Chemicals and reagents used to experiment were 250mg Amoxicillin Trihydrate capsules, *Amoxicillin Trihydrate*, *Cefadroxil* BPCRS, Acetonitrile, *Potassium dihydrogen orthophosphate, Sodium hydroxide*, Absolute ethanol, Ether.

Equipment

The Equipment used for the experiment was an Electronic analytical balance, HPLC, United State Pharmacopeia (USP) 2 (paddle type) Dissolution test apparatus, Ultra-Violet (UV) Visible Spectrophotometer, pH meter, and Thermometer.

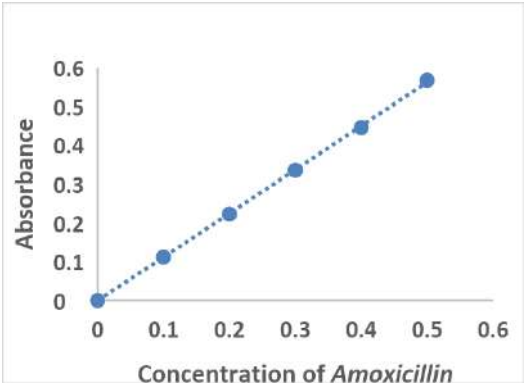

Figure 1. Calibration curve for Amoxicillin Trihydrate

Methods

This laboratory-based analytical study was carried out in State Pharmaceutical Manufacturing Corporation (SPMC), Sri Lanka. All the brands of Amoxicillin Trihydrate capsules available at community pharmacies of the Jaffna municipal area were identified by a mini survey. The pharmacies which had air-conditioning facilities for the storage of drugs were selected for the study. A sample of 50 capsules was purchased from the same batch while checking properly for their manufacturing license number, batch number, manufacturing, and expiry dates before purchasing[4]. Batches that are near to expiry date were excluded (at least a three months gap should be there). The detailed descriptions of these products are presented in table 1.

Calibration curve

The calibration curve of Amoxicillin trihydrate was constructed as shown in Figure 1 using the following procedure. Stock solution for amoxicillin trihydrate was prepared by dissolving 100 mg of amoxicillin in 100 ml of distilled water in the volumetric

flask with shaking till the drug is completely dissolved. The stock solution of 1 ml was diluted into 100 ml of distilled water. The further Stock solution was diluted with distilled water to prepare different concentrations of drug solutions by serial dilutions. Then the drug solutions were analyzed spectrophotometrically at 254 nm using distilled water as blank.

Methods

A. Uniformity of Weight

Twenty (20) capsules from each brand were selected randomly and weighed individually. The average weight of each capsule and the percentage deviation for each brand was determined [5].

B. Uniformity of Content

The uniformity of content of each brand is carried out according to BP (2017) by HPLC [6]. This test was replicated four times for each brand and the average area for the chromatogram was taken to calculate the mean assay percentage.

The reverse-phase chromatography was used. Mobile phase A and Mobile phase B consisted of *Acetonitrile* and 25% v/v solution of 0.2 M *potassium dihydrogen orthophosphate* at 1:99 and 20:80 volume ratios respectively with pH adjusted to 5.0 with 2 M *sodium hydroxide*. A flow rate of 1ml/min was employed with an injection volume of 50µl of each solution at < 60 °C temperature.

Mobile phase A with a volume of 80 ml was added to a quantity of the mixed contents of 20 capsules containing an equivalent of 60mg of Amoxicillin and shaken for 15 minutes. The content was mixed with the aid of Ultrasound for 1 minute. Sufficient mobile phase A was added to produce 100ml. The content was mixed and filtered by using Whatman GF/C filter paper. Then it was analysed by HPLC.

Table 1. Different brands of Amoxicillin capsules

Code	Batch number	Country
A_1	PTG15	Sri Lanka
A_2	18AX15	Sri Lanka
A_3	AA10381	India
A_4	MXCC1904	India
A_5	PXABV0036	Bangalore
A_6	S364190101	India
A_7(Amoxil)	LOTWP2P	Sri Lanka

Dissolution test

The dissolution test was performed by using USP 2(paddle type) operated at 75rpm for 60 minutes using 900ml of water maintained at a temperature of 37 ±0.5 °C. The test was performed 12 times for each brand. Six (6) capsules were placed in each reciprocating glass cylinder and the sample solution was collected at intervals of 15, 30, 45 & 60 minutes. A volume of 10ml of the sample solution was collected at every time interval and immediately replaced 10ml of fresh distilled water. Each collected sample solution was filtered by using a filter with a porosity of 0.45µm. The filtrated solution with a volume of 10ml was diluted to 100ml with water. Then 10ml from the resulting diluted solution was diluted again to 100ml with water. The amount of dissolved Amoxicillin was determined by measuring the absorbance value at a wavelength of

maximum absorbance at 254 nm using UV-Visible Spectrometer[1].

Statistical analysis

Results obtained were presented as means with standard deviations. The data were computed and analyzed using SPSS (Statistical Package of Social Science) 25. One-way ANOVA with Dunnett T3 post hoc test was conducted to compare the quality of different brands of Amoxicillin capsules with the innovator brand at a 95% confidence interval. 30 minutes time interval of dissolution time was used for comparison between the brands. A *p*-value less than 0.05 was considered a statistically significant difference.

III. RESULTS AND DISCUSSION

A. Uniformity of Weight

The weight variation standard shows that the recommended procedures were followed to ensure uniformity of distribution of the drug in capsules.

The results on the uniformity of weight as represented in table 2 revealed that all the capsule weights complied with BP, as not more than two of their weights deviated from the average weight by more than the percentage deviation of 7.5 and none deviated by more than twice that percentage.

A similar study conducted in Kenya reported that all the Amoxicillin capsules except three brands passed the weight variation test [7]. While a study done in Brazil [8] also showed that three out of thirteen brands were found to be disapproved on average weight assay. It might be due to the less amount of content in the capsules resulting in a poor manufacturing process.

This test ensures that the drug is distributed in a narrow range around the active ingredient to produce a consistent and correct dosage. [9].

B. Uniformity of Content

The uniformity of content of 7 brands was evaluated by the HPLC method. The assay test was done three times for each brand and the average area for the chromatogram was used to determine the mean assay percentage.

Table 2. Mean Assay % of all seven brands of Amoxicillin capsules

Code	Mean assay%
A1	103.38 ±0.05
A2	100.41 ±0.52
A3	105.59 ±0.18
A4	89.9 ±0.15
A5	103.54 ±0.11
A6	98.54 ±0.41
A7	98.67 ±0.02

Table 2 represents that all the Amoxicillin capsules except A4 met the specified BP limits where the amount of active ingredient released should be in the range of 92.5- 110%.

A study on amoxicillin formulations conducted in Ghana, Nigeria and the United Kingdom[3] declared that 19 out of 20 amoxicillin capsules tested complied with USP tolerance limits. A relative study done in Mexico declared that eight of the studied ten brands have passed the content uniformity test with the HPLC method[6].

This failure could be due to low active ingredients or poor formulation and processing. Although all the brands have desired quality at the time of manufacturing

poor storage conditions and transport conditions may affect the quality of drugs.

C. Dissolution test

Table 3 represents the results of the dissolution test that was done on 12 capsules for each brand at four-time points (15, 30, 45, and 60 minutes).

Table 3. Drug release % of different brands of Amoxicillin Capsules

Code	Percentage drug release			
	15min	**30min**	**45min**	**60min**
A1	63.81 ±3.99	82.49 ±3.51	95.37 ±2.33	99.87 ±1.23
A2	80.72 ±4.2	97.00 ±0.92	103.25 ±0.98	104.04 ±1.24
A3	78.46 ±2.81	85.26 ±5.26	93.24 ±4.41	94.79 ±4.67
A4	67.53 ±3.84	84.29 ±3.48	92.56 ±2.82	94.18 ±2.57
A5	94.93 ±3.25	100.00 ±4.06	101.53 ±3.57	100.71 ±3.57
A6	92.87 ±3.12	100.05 ±4.15	101.8 ±3.08	103.52 ±2.3
A7	62.28 ±2.99	82.83 ±5.00	90.25 ±6.12	95.37 ±5.49

Data represented as mean ± SE (n=12)

Drug dissolution is a vital condition required for drug absorption into the body where it directly relates to bioavailability[10]. This acts as a key factor that ensures the release of a batch which thereby determines the batch quality and the constant quality of the product throughout its shelf life[11].

According to the British pharmacopoeia specifications, the drug should be released by more than 80% within 60 minutes. All the brands complied with the BP limit for the dissolution test as shown in figure 2. A study conducted in Brazil[8] with 13 different brands and also similar studies conducted in Ghana, Nigeria and the United Kingdom explored that all brands passed the dissolution test[3].

A study done in Bangladesh to study 20 national and 4 multinational brands of Amoxicillin Trihydrate capsules reported that except for two national brands, the rest of the 24 brands comply with the pharmacopoeia specifications for the in vitro drug release[1].

Figure 2 represents the pattern of in vitro drug release of amoxicillin brands at different time points.

Statistical analysis

There was a significant difference ($p < 0.05$) in drug release at 30 minutes time point was observed between the innovator brand and other different brands of Amoxicillin Trihydrate capsules except A1, A3 and A4 using One-Way ANOVA with Dunnett T3 post hoc test as shown in table 4. This could be because of the varied GMP processes followed by different manufacturers for their brands[12].

Table 4. *p* values of Amoxicillin brands with innovator brand

Code	Significance value
A1	1.000
A2	0.000*

A3	0.996
A4	1.000
A5	0.000*
A6	0.000*

**significant difference at p-value < 0.05*

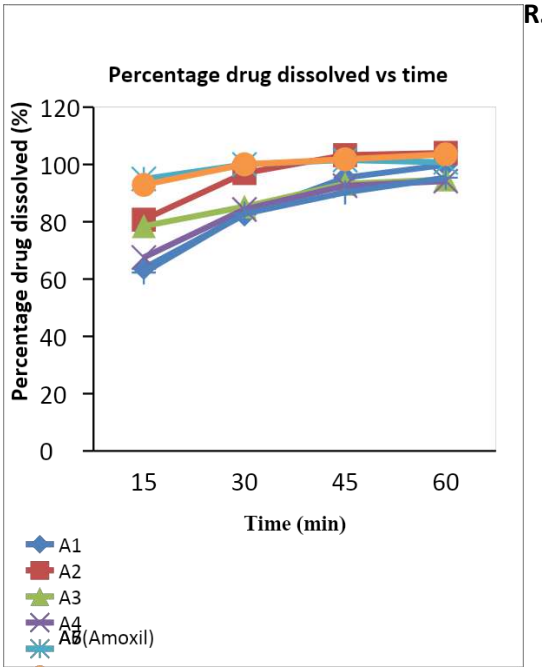

Figure 2. Drug Release % for different brands of Amoxicillin capsules

IV. Conclusion and Recommendation

This study revealed that all the brands of Amoxicillin Trihydrate capsules except A4 complied with the official specification of BP. Statistical comparison for the *in vitro* drug release showed that some of them have significant differences indicating that it might affect the *in vivo* bioavailability and the bioequivalence of the products.

Authorities of the country should take more attention to the quality of antibiotics especially imported drugs.

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