2018 DLSU RESEARCH CONGRESS
BUILDING IMPACT ON FIRM FOUNDATIONS: From Basics to Applications

Presented at the DLSU Research Congress 2018
De La Salle University, Manila, Philippines
June 20 to 22, 2018

Generic, Branded and Veterinary Amoxicillin in the Philippine Market

Jaime Raul O. Janairo and Eron Klein C. Adan
Chemistry Department
De La Salle University
**Corresponding Author: jaime.janairo@dlsu.edu.ph*

Abstract: Amoxicillin belongs to the family of penicillin. Penicillin is a group of ß-lactam antibiotics frequently used in medications involving bacterial infections such as pneumonia, tonsillitis, bronchitis, gonorrhoea, etc. caused by exposure, to usually gram-positive organisms. In this study, capsulated amoxicillin samples available in the Philippine market were compared using high performance liquid chromatography. The results of the HPLC analysis show generic and branded formulations to be bioequivalent, although only two out of the seven samples passed the USP standards (90% minimum content) ranging from 95 to 48% of indicated content. Shelf life also appears to correlate the amoxicillin content. A parallel run on a veterinary formulation, showed an even lower value at only 10.50% amoxicillin content.

Key Words: amoxicillin; generic; HPLC; veterinary

1. INTRODUCTION

Generic medicinal drugs are "replicas" of patented brand-name products which can be retailed at a much lower cost than their branded counterparts. These drug replicas are produced following patent expiration of the brand leader preparation (Del Tacca, M. et al. 2009). Although pharmaceutical companies manufacturing generic medicinal products follow a specified guideline designed by the Food and Drug Andministration (FDA) and the World Health Organization (WHO) which certifies these products to be therapeutically equivalent to its branded counterpart (Meredith, P. 2003), the numerous medical concerns regarding the effectiveness, sensitivity and safety of these copies constantly undermine the favorability of generic products being a preferable drug to physicians and patients around the globe (Corrao G. et al. 2014). The primary purpose of developmental research in relation to generic drug production is to cut down the price of public health costs, specifically the price of marketed drugs available in local establishments, which is one of the dilemmas experienced by most third-world countries including the Philippines. The production of these brand-name counterparts for clinical use is considered as a repercussion of accumulating restrictions on the allocated economic funds by the government to public health programs (Corrao G. et al. 2014).

The difference between generic and branded medicinal products depends on various factors affecting the efficacy and quality of each drug batch manufactured by pharmaceutical companies (eMed

expert 2016). The aspect of comparison between these products may be derived from the diversity of inactive ingredients present (excipients such as magnesium stearate), the variability in terms of therapeutic efficacy along with its possible side effects which could influence the specificity of the ingested product, the amount of time involved in the approval process by the FDA, and the cost of production vis-a-vis the cost of retail merchandise. Previous studies under this topic focused on crucial characteristics of generic medicinal drugs particularly, bioequivalence and bioavailability. Bioequivalence is defined to be the chemical similarity of the generic drug to a pioneering product, which means the active ingredient and the rate of delivery to the site of action should be equivalent to the original brand drug. Bioavailability on the other hand, focused on the extent to which a drug can be absorbed for action site usage. It is the rate at which the active ingredient of the drug becomes freely available at the treatment target (Zhu, H. et al. 2009). This study focused mainly on the bioequivalence comparison of a generic drug product with its brand-name counterpart. The purchased samples of branded and generic capsulated amoxicillin formulations available in local pharmacies were compared by high precision liquid chromatography.

2. METHODOLOGY

High Performance Liquid Chromatography analyses were performed on an Agilent 1200 HPLC with a quaternary pump with an Eclipse XDB-C18 5µm 4.6x150mm column. Millipore PTFE-B membranes with pore size of 0.45µm were used. The separation was run based on related studies involving analysis of penicillins (Ashnagar, A. et. al. 2007): 24:1 v/v pH 5 KH_2PO_4 buffer:CH_3CN at a flow rate of 0.7 ml/min under room temperature conditions. Twenty µL samples were injected and detected at 230 nM. Samples were prepared at 1000 ppm concentrations with standards ranging from 300-1500 ppm. The calculated Limit of Detection and Limit of Quantitation for the method used was found to be 170 and 515 ppm respectively from a calibration curve that linearly fitted chromatogram peak areas with ppm concentrations according to the equation $Area = (20.886 \times conc.) + 2190.3$.

3. RESULTS AND DISCUSSION

The branded samples of amoxicillin illustrated a major peak eluted at about 4 minutes of running time which is indicative of the presence of the active ingredient as suggested by the chromatogram of the standards. The area percentage was used as a rough estimate of the purity of the sample as the calculation for this value involves the ratio of the major peak area and the total area which includes the other peaks detected by the instrument. Brand Y and Brand X obtained an area percent average of about 99.28% and 96.20%, respectively. These values show the purity of amoxicillin detected from the extracted capsulated samples. However, the difference between the integrated areas of the major peaks is suggestive of a difference between the two brands which may either be in terms of excipient and active ingredient ratio composition or the duration of storage.

Table 1. Measured Amoxicillin

Sample	Average Peak Area	Measured Conc'n (ppm)	Indicated Weight (mg)	Expt'l Weight (mg)
Brand A	10772	483.2	500	236.6
Brand B	18785	936.0	500	468.0
Generic W	18735	950.6	500	475.30
Generic X	17525	819.3	500	409.6
Generic Y	14921	748.6	500	374.3
Generic Z	15808	718.5	500	359.2
Veterinary	2676	42.0	1200	126.0

The four samples of generic amoxicillin formulations illustrated major peaks eluted at about 4 minutes of running time similar to the branded formulations and is also indicative of the evident presence of amoxicillin in the sample. The area percent averages of Generic W, Generic X, Generic Y, and Generic Z were 96.98%, 99.15%, 98.95%, and 97.37%, respectively. The differences in the integrated areas of the major peaks was indicative of the relativity of Generic W and Generic X to branded amoxicillin samples and the inferiority of the other two generic formulation in terms of analytical response.

The veterinary amoxicillin samples were purchased at a relatively equal cost of generic amoxicillin formulations. It is expected to be inferior to both generic and branded in terms of quality and quantity of the active ingredient, amoxicillin due to the necessary addition of supplementary excipients to coup with the metabolic process of the animal involved. There were no available capsulated veterinary drug within the vicinity due to the inconvenience in the process of drug ingestion for domesticated farm animals. Therefore analysis was done on a water-soluble veterinary product which was initially stored in a sachet prior to the extraction process.

Notable results showed that Generic W the contained the highest amoxicillin content at 475.3 mg out of the 500 mg weight label. The deviation of the results from the indicated weight on the label of amoxicillin samples is indicative of the presence of matrices in the analyte such as the binders and other excipients which has contributions to the bioavailability of the drug product upon ingestion, hence, a 500 mg label on the product should not be assumed 500 mg of amoxicillin, but rather, excipients should be taken into consideration. Roughly similar to Generic W, is a branded formulation Brand B which contained 468.0 mg of amoxicillin. Other generic formulations ranged from 350 to 410 mg. The variation of the results were compatible with the statements from several researchers of related studies regarding the differences in the excipients used by pharmaceutical companies which affects the bioavailability of the product. However, the other branded sample, Brand A, showed an amoxicillin content of only 236.6 mg which is not expected from a premier product. A plausible cause for the large deviation is the expiration date of the sample. The analysis was done on samples expiring in 2017, months away from the time of sample analysis. Possible changes during storage may be responsible.

4. CONCLUSIONS

The results of the HPLC analysis provided insights regarding the quality of capsulated amoxicillin formulations available in the Philippine market. Branded, generic, and veterinary formulations of amoxicillin, though initially hypothesized to differentiate from each other, were found to be significantly similar. Generic W can be considered to be bioequivalent to Brand B, a brand-name counterpart, at 475.3 and 468.0 mg per 500 mg capsule, respectively. The comparison between the amoxicillin concentrations confirms the variability of the excipients used by different pharmaceutical companies in formulating its amoxicillin product. Veterinary X showed amoxicillin at similar retention times as those for human consumption. The deviation of the values for Brand A could be caused by the duration of storage. Further analysis of Brand A samples with varying expiration dates is recommended in order to confirm the effect of storage duration on the amoxicillin content of the drug. LC-MS may also identify potential impurities and excipients as well as degradation products of amoxicillin.

6. REFERENCES

Ashnagar, A., & Gharib Naseri, N. (2007). Analysis of three penicillin antibiotics (Ampicillin, Amoxicillin, and Cloxacillin) of several Iranian Pharmaceutical Companies by HPLC. E-Journal of Chemistry. 4(4), 536-545.

Corrao G, Soranna D, Merlino L, Mancia G. (2014) Similarity between generic and brand-name antihypertensive drugs for primary prevention of cardiovascular disease: evidence from a large population-based study. Eur J Clin Invest. 44(10):933-9.

Del Tacca, M., Pasqualetti, G., & Di Paolo, A. (2009). Lack of pharmacokinetic bioequivalence between generic and branded amoxicillin formulations. A post-marketing clinical study on healthy volunteers. Br J Clin Pharmacol. 68(1), 34-42.

Meredith, P. (2003). Bioequivalence and other unresolved issues in generic drug substitution. Elsevier Inc. 25(11), 2875-2890.

Zhu, H., Zhou, H., & Seitz, K. (2009). Chapter 15 – Bioavailability and Bioequivalence. Developing Solid Oral Dosage Forms. Academic Press. 341-364.