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Quality of Amoxycillin Preparations on the Kenyan Market

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Amoxycillin products were evaluated for quality by liquid chromatography at the Drug Analysis and Research Unit (DARU), University of Nairobi. Thirty three of these were capsule formulations and 24 were dry suspensions. Three capsule formulations failed the limits on content. The amoxycillin content in one suspension product was below the limit, while in two other products it dropped below 80% on storage at 25°C for 7 days.

Key Words: Amoxycillin, formulations, quality.

INTRODUCTION

Amoxycillin is a semisynthetic penicillin used in the management of infections caused by sensitive organisms infections especially those causing pneumonia, URTI, UTI and soft tissue infections. It is incorporated in the Ministry of Health essential drugs list [1].

Marketing of poor quality drugs is a major concern in most developing countries and has been widely reported in Africa and elsewhere [2-5]. In particular, the use of antibiotic preparations of poor quality could be a contributory factor to failure of therapy. The presence of poor quality penicillin products in the Kenyan market has been reported previously [6- 9]. This observation was recently reinforced by the findings on the quality of ampicillin preparations [10].

This paper reports on the findings on the quality of amoxycillin capsules and dry syrups found on the Kenyan market during the 10 year period 1994 – 2004 using high pressure liquid chromatography (HPLC). The preparations were from private and public sources including those submitted to the Ministry of Health drug regulatory authority, the Pharmacy and Poisons Board. The latter are intended for market in Kenya after registration, and for the purpose of this paper are treated as being on the market.

EXPERIMENTAL

Samples and standards

Amoxycillin trihydrate, working standard Batch No. M 1561193 was donated by Laboratory and Allied Ltd., Nairobi. The working standard had a content of 87.0% amoxycillin on an anhydrous basis when assayed against amoxycillin trihydrate BPCRS Batch No. 1487 CAT. 019.

The amoxycillin preparations evaluated were obtained through the office of Registrar, Pharmacy and Poisons Board, Ministry of Health, Kenya, or were commercial packs obtained from local pharmacies and manufacturers. Locally manufactured products were from Elys Chemical Industries Ltd., Dawa Pharmaceuticals Ltd., Cosmos Ltd., Mac's Pharmaceuticals Ltd. and Pharmaceutical Products Ltd., all of Nairobi. Imported products were from Mesco Laboratories Ltd., Cadila Laboratories Ltd., Ranbaxy Laboratories Ltd., Dominion Chemical Industries Ltd., Panacea Biotech Ltd., Rumax Ltd., Lennon Ltd., F. I. R. M. A. Ltd., Brown and Buck Pharmaceutical Ltd.; all of India as well as C.A.P.S. (Zimbabwe), Amoun Pharmaceutical Industries Co. Ltd. (Egypt), Servipharm Ltd., (Switzerland), and Glaxosmithkline (U.K.)

Reagents and solvents

HPLC grade acetonitrile was purchased from Rathburn chemicals (Walkerburn, Scotland, U.K.). Analytical grade, K_2HPO_4 and KH_2PO_4 salts for preparation of buffer were from Acros Organics (New Jersey, USA).

Instrumentation

The liquid chromatographic system consisted of Varian 9010 solvent delivery system, a Varian Variable wavelength UV/Visible detector (Varian Associates, Inc., Walnut Creek, USA) set at 254nm, a Valco model CV-6-UHPa-N60

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sampling valve (Valco, Houston, Texas, USA) equipped with a 25 µl loop and a Hewlett Packard HP 3396 integrating recorder (Hewlett Packard, Avondale, PA, U.S.A.). A HPLC column of dimensions 25 cm x 4.6 mm packed with RSil C_{18} 10 µm (BioRad RS, Eke, Belgium) was used and was maintained at 40 °C using a water bath.

METHOD

Mobile phase

The mobile phase consisted of 0.01 M phosphate buffer pH 7.0 – acetonitrile (97: 3 v/v) and was degassed by ultrasonication before use. The flow rate was set at 1.0 ml/min.

Amoxycillin standard solution

About 125 mg amoxycillin standard was accurately weighed into a 10.0 ml volumetric flask, dissolved in, and made to volume with distilled water. An aliquot (2.0 ml) of this solution was diluted to 25.0 ml with distilled water in a volumetric flask.

Amoxycillin sample solution

Capsules: Powder equivalent to 125 mg amoxycillin accurately weighed was dissolved in distilled water as completely as possible, to make 100.0 ml in a volumetric flask. This solution was filtered though a 0.45 mm membrane filter and 4.0 ml of the filtrate made to volume with distilled water in a 25.0 ml volumetric flask.

Dry suspensions: Powder for amoxycillin suspensions was reconstituted with distilled water according to the manufacturer's label instructions. The reconstituted volume of the suspension was determined after sonication to remove air bubbles. A volume of suspension equivalent to 125 mg amoxycillin was pipetted into a 100.0 ml volumetric flask, rinsing the pipette with water. The volume was made to the mark with water and filtered through a 0.45 mm membrane filter. An aliquot (4.0 ml) of the filtrate was used to prepare the sample solution as described for the standard solution.

RESULTS AND DISCUSSION

The content of active ingredient of some 33 amoxycillin capsule formulations were evaluated and are shown in Table 1. The pharmacopoeal limits [11] of amoxycillin content expressed as a percentage of label claim are 92.5 - 110.0. Products Ia, III and VI failed in this test. All the failed products were manufactured locally. The failed product Ia was by a manufacturer whose other product batch Ib passes in the test.

Table 1: Amoxycillin Content of Some Amoxycillin Capsule Products

Product	Amoxycillin content (% label claim)
I a	90.4
I b	10[illegible]
II	108.0
III	75.6
Va	100.7
IVb	93.3
Va	94.4
Vb	93.0
Vc	94.7
Vd	96.0
Ve	95.5
VI	79.2
VII	96.7
VIIIa	96.0
VIIIb	100.6
IX	108.4
X	104.6
XIa	103.0
XIb	101.6
XIIa	95.6
XIIb	93.8
XIIIa	108.3
XIIIb	108.3
XIVa	106.8
XIVb	101.8
Xva	99.6
XVb	96.9
XVI	101.6
XVIIa	96.9
XVIIb	96.9
XVIIc	95.2
XVIII	98.3
XIX	100.3

I - XVII denote manufacturers; a, b, c, d and e: indicate batches from the same manufacturer.

Table 2 shows the amoxycillin content as determined on day 0 and day 7 for the 24 different amoxycillin suspensions examined. One product, SVII was far below the lower limit of 80% specified by the pharmacopoeia. On storage for 7 days at 25°C the amoxycillin content of SXb and SXIa fell below the acceptable limit of 80%. The content of SX1a fell drastically from 107.8% to 44.1% of the label claim. The content of amoxycillin in all the products examined changed within the 7 days. Amoxycillin suspensions are normally buffered to maintain stability once reconstituted. The products that failed to comply with the 7-day limit were probably not appropriately buffered.

Table 2: Amoxycillin Content of Some Amoxycillin Oral Suspensions

Product	Amoxycillin content (% of label claim)	
	Day 0	Day 7
SIa	108.0	n d
SIb	94.1	n d
SIc	107.6	96.6
SId	109.2	96.7
SIia	107.3	114.2
SIib	114.1	126.7
SIII	114.1	112.6
SIVa	99.3	91.6
SIVb	94.1	107.0
SIVc	99.1	103.3
SIVd	99.5	104.9
SIVe	99.5	101.4
SV	95.0	n d
SVI	98.5	102.2
SVII	42.9	32.1
SVIII	83.6	80.5
SIX	97.3	86.2
SXa	96.9	85.7
SXb	84.4	67.5
SXia	107.8	44.1
SXib	99.5	96.6
SXII	98.4	102.8
SXIII	98.1	n d
SXIV	95.3	n d

I – XIII denote manufacturers; a, b, c, d and e: refer to batches from the same manufacturer; n d: not determined.

The content of amoxycillin in oral suspensions is specified not to exceed 120% label claim on reconstitution. However, on storage for 7 days, any drop in content should not be lower than 80% of the label claim (11).

In this regard products SVII, SXb and SXIa failed the requirements. The manufacturers of products SXb and SXIa are also the manufacturers of products SXa and SXIb respectively, which passed the requirements. One was a local and the other a foreign manufacturer.

There is therefore need for manufacturers to pay attention to such batch to batch variations that may arise and identify causes for them, for example a less than optimum buffering system.

The use of poor quality products, especially antibiotics, such as amoxycillin, can have serious consequences including development of drug resistance and therapeutic failure.

The results of this study support the continuing need for quality certification before and marketing surveillance after products are released into the market by reputable laboratories.

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