Substandard Amoxicillin in Sierra Leone

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INTRODUCTION

Bacterial resistance to antibiotics is posing a global health threat as many antibiotics no longer work against urinary and skin infections.

Prevalence of substandard medicine in developing countries can lead to further development of new strains with antibiotic resistance [1].

Sierra Leone is one of such countries where the multidrug resistant *Shigella dysenteries* serotype 1[2] and *tet(X)*-containing clinical isolates [3] are already detected.

A mystery shopper has visited a local market in Sierra Leone and purchased 6 different brands of amoxicillin capsules, which has been analysed using spectroscopic methods.

MATERIALS AND METHODS

The samples of the amoxicillin capsules have been purchased using a convenience sampling approach at an undisclosed location in Sierra Leone.

The 100 mg of sample was dissolved in D_2O and 100 mg of sample was dissolved in CD_3OD. The dissolved samples were vortexed for 30 seconds, followed by centrifugation.

The supernatants were filtered when transferred into NMR tubes. The 1D ^1H and ^1H 2D COSY NMR spectra were acquired using JEOL ECA 600 MHz at 298 K and were processed JEOL Delta software.

RESULTS AND DISCUSSION

The weighing of the content of the capsules has provided initial indication that some of the purchase medicine is substandard (Table 1). Furthermore, preliminary NIR measurements have suggested that there is a significant variation in the sample composition between manufactures

Table 1. The list of the amoxicillin samples with declared antibiotic doses and actual weights of the capsule contents for each sample (the values in red indicate samples that certainly do not provide adequate dose).

Sample ID	*Declared Amx content (mg)*	*Total weight of the capsule content (mg)*
Amx-1a	*250*	*290.0*
Amx-2a	*500*	*570.7*
Amx-3a	*250*	***230.2***
Ams-4a	*500*	***490.0***
Amx-5a	*500*	*530.5*
Amx-6a	*250*	***210.5***

NMR spectra have shown that all samples had amoxicillin present in capsules, with varying relative ratio of API to excipient content (Fig. 1). Furthermore, additional peaks around 1.15 ppm were observed which could be attributed to declared excipients.

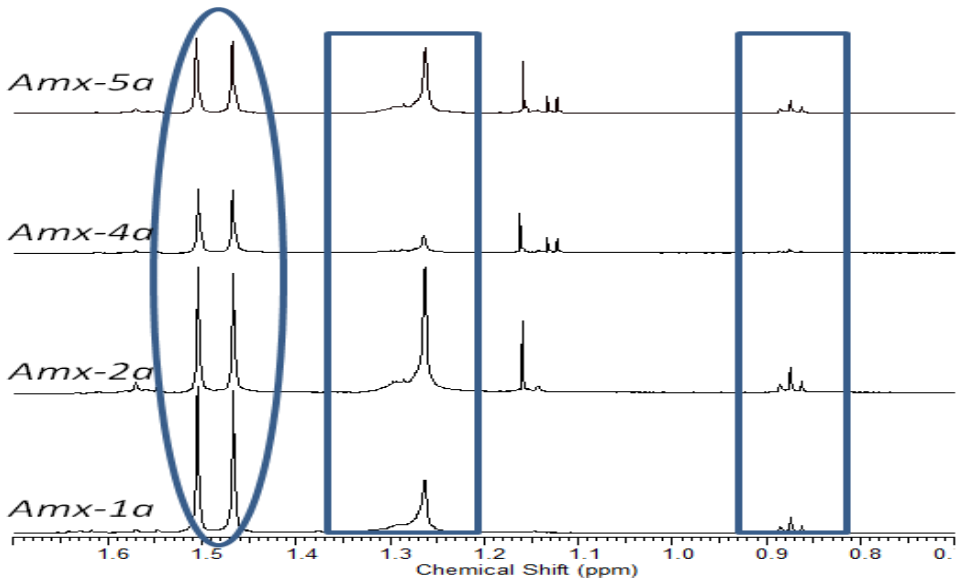


Fig. 1. Overlay of expansion of 1D ^1H NMR spectra of selected amoxicillin samples. Amoxicillin peaks are encircled with oval shape, magnesium stearate are encircled with rectangular shapes.

The ^1H NMR spectra of Amoxicillin have shown singlet at Position 1.46 and 1.55 (ppm) for CH_3 group at peak 1 and 2, While duplet peak have represented at 6.77 and 7.30 (ppm) at 1H peak at aromatic group, figure 2 illustrate ^1H NMR data for Amoxicillin compound in CD_3OD as following :

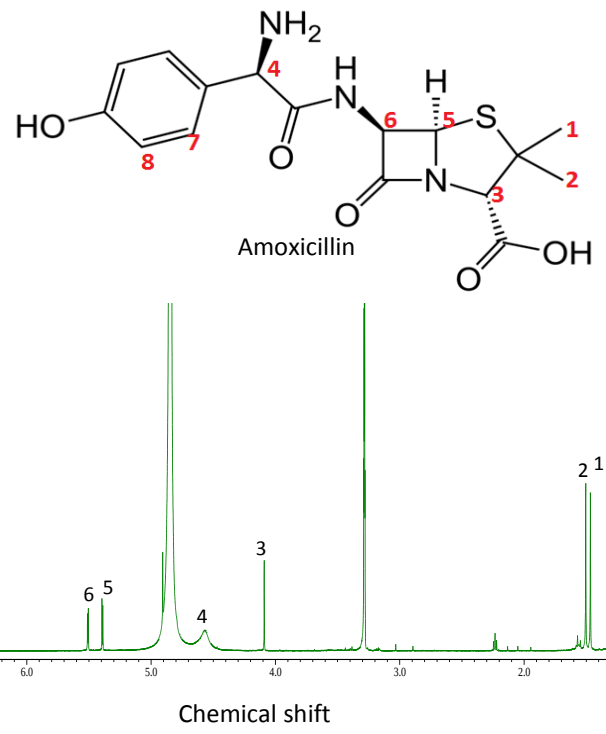


Figure 2: ^1H NMR Amoxicillin spectra represent peaks positions for functional group of Amoxicillin compound dissolved in CD_3OD.

The area under the NMR signal is directly proportional to the number of protons giving rise to the signal. The following table show area under the curve for ^{1}HNMR spectra of Amoxicillin (table 2):

Table 2: Area under the curve of Amoxicillin samples

	Amoxicillin	Mgstearate	Un known	Amox/MgSt	Amox/unkn
Chemical shift	1.465	0.88	1.15		
Sample 1	3.48	0.73	0	4.77	0
Sample 2	3.5	0.9	0.7	3.9	5
Sample 3	3.55	0.75	0.21	4.73	16.9

CONCLUSIONS

The pilot study of the quality of medicine in developing countries has indicated that substandard medicine is freely available on the markets despite efforts by governments to improve their healthcare systems. The poor quality medicine can harm patients directly via lack of effect or toxicity of additional components, but it can also contribute to the spread of bacterial resistance to antibiotics.

REFERENCES

1. Johnston, A. and D.W. Holt, *Substandard drugs: a potential crisis for public health.* British Journal of Clinical Pharmacology, 2013: p. n/a-n/a. DOI: 10.1111/bcp.12298
2. Guerin, P.J., et al., *Shigella dysenteriae serotype 1 in west Africa: intervention strategy for an outbreak in Sierra Leone.* The Lancet, 2003. **362**(9385): p. 705-706.
3. Leski, T.A., et al., *Multidrug-resistant tet(X)-containing hospital isolates in Sierra Leone.* International Journal of Antimicrobial Agents, 2013. **42**(1): p. 83-86.