

Research Article

Influence of Storage Conditions on Efficacy of Selected Veterinary Antimicrobials Dispensed under Different Storage Conditions in Morogoro, Tanzania

Ally MHS* and Lusekelo M

Department of Physiology, Sokoine University of Agriculture, Tanzania

Abstract

Efficacy of antimicrobials is of vital importance for patient safety and activity. The loss of potency may influence the efficacy and safety of antimicrobials. This study aimed to determine the influence of different storage conditions on the efficacy of selected antimicrobials. A significant statistical difference was observed across the efficacy data of selected antimicrobial brands. The data showed that the maximum reduction of efficacy was observed in light exposed antimicrobials compared to cool and properly store antimicrobials. These results authenticated that improper storage conditions resulted in failure to meet product characteristic and specification during shelf life. Optimum storage conditions and procedures ensure that the efficacy and integrity of medicinal products are maintained throughout their shelf life. This study emphasizes the importance of proper storage of antimicrobials from the time of their movement from manufacturing premises till reaches consumers.

Keywords: Antimicrobials; Storage; Efficacy and potency

Introduction

Veterinary Antimicrobials refers to natural or synthetic agents/ drugs used to fight against microorganisms/ pathogens which cause diseases in animals [1]. Antimicrobials may be antibiotics, antifungal or antiviral used to kill or restrain growth of the respective disease agents for the purpose of treatment, mitigation or prevention of disease or abnormal physical or mental state or symptoms in animals [2]. Antibiotics are a type of antimicrobial used to kill bacteria which cause diseases. Some examples of antibiotics include Penicillin-Streptomycin (Penistrep), oxytetracycline, sulphamexazole, and quinolones. Animal health relies heavily on qualities of antimicrobials and other veterinary drugs. In veterinary medicine, penicillin, oxytetracycline, sulphamexazole are frequently used for treatments of various infectious diseases in animals. Efficacy of antimicrobial preparation can be defined as the capability of a particular formulation (dosage form or drug product, in specific container or closure system to remain within its physical, chemical, microbiological, therapeutic and toxicological specifications throughout its shelf life [3,4]. Physical, chemical and microbiological properties of drugs are generated as a function of time and storage conditions (e.g. temperature and relative humidity). Therefore, the significance of high quality antimicrobials is important for successful therapy, enhancements of health and increased production in animals [5].

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***Corresponding author:** Ally MHS, Department of Physiology, Sokoine University of Agriculture, Tanzania, Tel: 255766661919; E-mail: ally2005mood@yahoo.com

Correct storage of antimicrobials has a substantial impact on stability and thus on shelf life of the drugs [5,6]. Shelf life claims in product labels are always based on certain assumed standard conditions, typically “store away from excessive heat (for example 104°F=40°C)” or store product at or below 77°F (25°C) or “Protect from sunlight” and relative humidity [7]. Temperature, relative humidity and sunlight are the major storage conditions influencing drugs stability and efficacy [6]. There are seasonal variation of ambient temperature, humidity and sunlight intensity in sub-Saharan Africa including Tanzania which may have a significant effect on the performance of antimicrobials if not properly handled and stored [7]. For instance, ambient temperature changes in Morogoro region ranges from 27°C during cold weather in May to 32°C in hot seasons of October to March and relative humidity ranges from 63% to 82% [8]. Improper storage of the antimicrobials products is one of the fundamental concerns in health care. The last leg of their journey at wholesale dealer’s premises and retail outlets occupies a sufficiently long period storage. Antimicrobials get exposed to varying temperature and humidity conditions during this part of movement and with prevailing conditions of the Agroveter outlet in Tanzania. Morogoro is a tropical region and several places are hot and humid at times with intense light. Antimicrobial products sometimes cannot remain stable in such conditions unless the labeled storage conditions on the products are adhered to. Accordingly, it becomes the duty of everybody in the distribution chain to value the storage conditions. The drug dealer has a specific responsibility in this regards as the retention time of the product in the establishment is fairly long. Exposures to extreme levels of relative humidity, sun sunlight or ambient temperature may accelerate drug degradation accompanied by loss of efficacy and yielding products which may be harmful [5,9]. Loss of efficacy may lead to treatment failure and development of antimicrobial resistant strains compounding even further the problem of treatment failures.

Different antimicrobials have a choice of storage requirements [6,7]. For examples; Kombitrim 240 (Sulfamethoxazole/Trimethoprim 200/40) need a storage temperature below 15°C under protection from sunlight. Penistrep 400 (Procaine penicillin G-200, dihydrostreptomycin sulphate-200) need to be stored in dark at a temperature of 8°C to 15°C and oxytetracycline 10% injection (Oxytetracycline hydrochloride 100 mg), need a storage temperature of below 25°C and protection from sunlight. Changes in government policies have always been accompanied with merits and demerits. Privatization of veterinary services in Tanzania seems to have contributed to changes including an increased number of veterinary shops, movements of veterinary drugs in open markets by vendors. Despite the presence of regulatory authorities and guiding laws and regulations, controls of handling, storage and uses of veterinary drugs is a challenge. This is partly because, enforcements of the existing controls measures on veterinary drug's quality and availability in many areas especially in rural areas are simply not efficiently done.

The quality and efficacy of the veterinary drugs sold in open livestock markets, exposed to ambient temperature, humidity and sunlight is questionable. Although, there shortages of studies reporting on the efficacy of various veterinary drugs sold by vendors in open markets in Tanzania. Whether prolonged exposure to ambient temperatures and sunlight as it is done by vendors in open livestock markets have any significant effects on the efficacy of the commonly used Veterinary antimicrobials needs to be known. Therefore the current study was carried out to assess the effects on efficacy of selected antimicrobials of veterinary importance dispensed under different handling and storage conditions as practiced in Morogoro region, Tanzania.

Materials and Methods

The study was cross-sectional and experimental in design carried out in Morogoro region in Tanzania.

Collection of drug samples

Similar batches of drug samples were collected from livestock markets and veterinary shops in Morogoro region, Tanzania. A total of 9 drug samples were collected, 3 drug samples consisting of Penicillin-Streptomycine (penistrep) 20%, Oxytetracycline 10% and sulphamexazole 20% from each sampling area of Melela, Parakuyo and Nanenane livestock markets in Morogoro urban and peri-urban in Tanzania. Nine other samples were collected from three different veterinary shops in Morogoro municipality where drugs are kept under the prescribed storage conditions. Each shop provided three types of antibiotics.

Sample preparation and efficacy determination

Efficacy determination was done in the bacteriology laboratory in the College of Veterinary Medicine and Biomedical Sciences at Sokoine University of Agriculture. The efficacy of each drug was determined by using Agar-well diffusion method. Broth cultures of *Escherichia coli* and *Bacillus subtilis* diluted to match a 0.5 McFarland turbidity standard were used in efficacy determination.

The experiment started with testing each of the three drugs collected from livestock markets and Agrovet shops. Each of the 9 drugs from livestock market and Agrovet shops was tested in three petri dishes. Then 9 drugs from Agrovet shops were experimentally exposed to sunlight at an ambient temperature ranges of 27°C to 29°C, 5 hours per day for 7 days in January and each antibiotic was tested for drug sensitivity.

Petri dishes containing 20 ml Mueller Hinton medium were

seeded with either *E. coli* or *B. subtilis* strains. Wells were cut and 20 µl of specific drugs were added into the wells in the petri dishes. Then the Petri dishes were incubated at 37°C for 24 hours and efficacy was determined by measuring the diameters of inhibition zones formed around the wells.

Data analysis

Data analysis for means, standard deviation was carried out by using SPSS version 20. T-test was used to compare for mean inhibition zones between the groups at a significant level of $p < 0.05$.

Results

There was a significant difference ($P < 0.05$) on sensitivity of *B. subtilis* to oxytetracycline from different storage conditions as follows; oxytetracycline from livestock market and the sunlight exposed displayed markedly reduced inhibition zone against *B. subtilis* when compared to similar antibiotics from Agrovet (Figure 1). On the other hand, no inhibition zones of Oxytetracycline against *E. coli* were observable for all the Oxytetracycline regardless of the sources (Figure 2). Similarly, Penistrep from Agrovet shops displayed a significantly larger inhibition zone ($P < 0.05$) against *B. subtilis* when compared to similar drug from livestock market and the sunlight exposed. As for *E. coli*, mean inhibition zone were marginally smaller ($P > 0.05$) for the antibiotics from open livestock market and the sunlight exposed when compared to penistrep from Agrovet shops. As for sulphamexazole, mean inhibition zone on *B. subtilis* of the drug from Agrovet shops was marginally wider than that of similar antibiotics from open livestock markets and the sunlight exposed (Figure 3). For *E. coli*, mean inhibition zone displayed by sulphamexazole was marginally larger for antibiotics obtained from Agrovet shops when compared to similar drugs from open livestock market and the sunlight exposed (Figures 4 and 5).

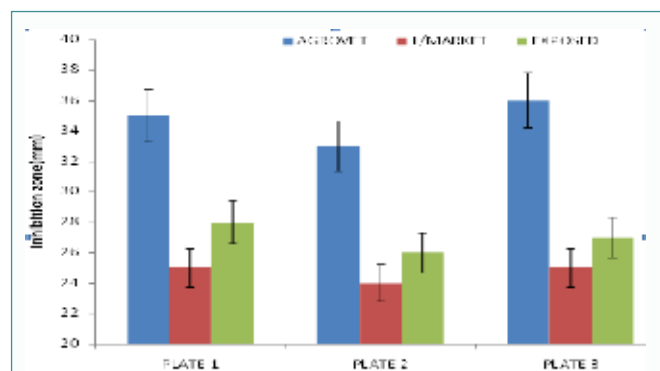


Figure 1: Mean inhibition zones (mm) per plate oxytetracycline on *Bacillus subtilis*.

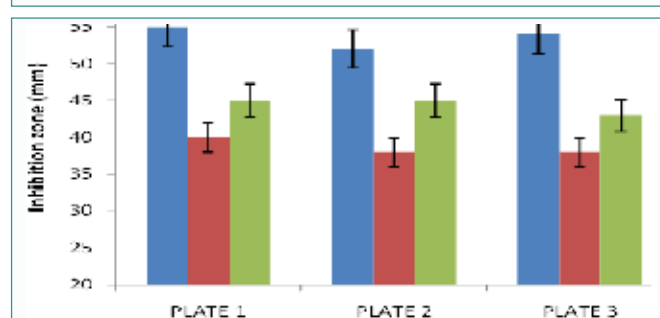


Figure 2: Mean inhibition zones (mm) per plate of penistrep on *Bacillus subtilis*.

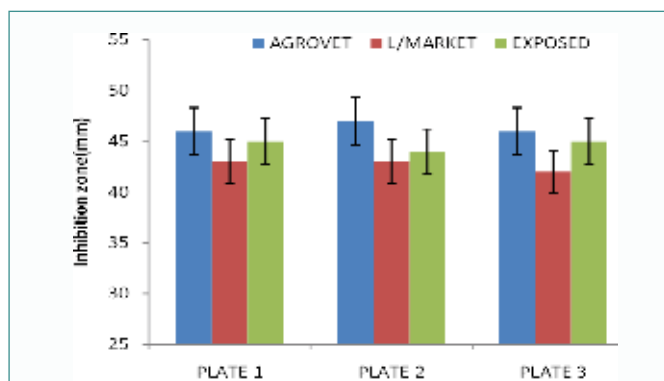


Figure 3: Mean inhibition zones (mm) per late of sulfamethoxazole on *Bacillus subtilis*.

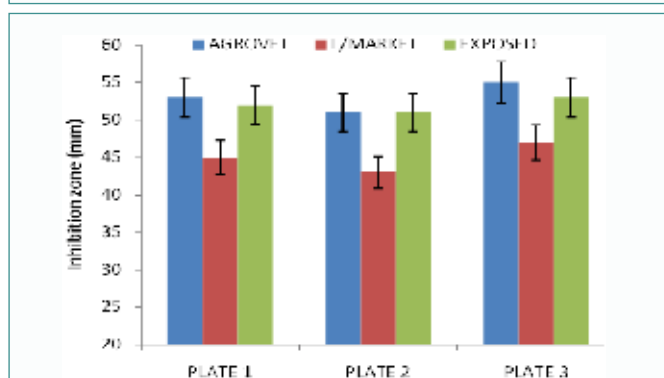


Figure 4: Mean inhibition zones (mm) per plate of sulfamethoxazole on *Escherichia coli*.

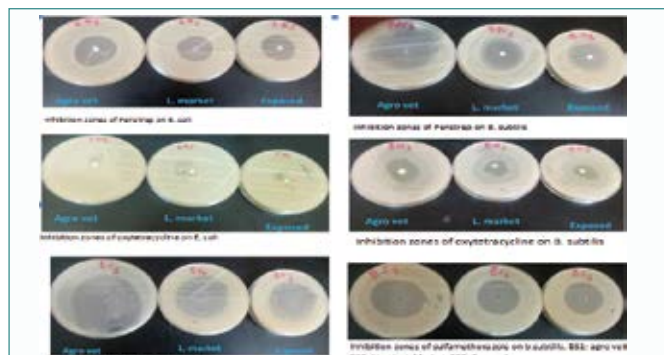


Figure 5: Representative plates showing inhibition zone as displayed by antibiotics from agrovet shops, open livestock market and that experimentally exposed to light and ambient temperature of 27°C to 29°C.

Discussion

The study indicates that, different handling and storage conditions of antibiotics may have a varying degree of affect on the efficacy of antimicrobials as tested by Agar- well diffusion method. For instance, *B. subtilis* was relatively less sensitive to oxytetracycline from open livestock market and the sunlight exposed when compared to similar antibiotics from agrovet shops indicating some loss of efficacies. Similar results have been reported by Wu and Fassihi [10], and Wei et al. [11]. It is reported that, prolonged exposure of oxytetracycline to sunlight may accelerate drug degradation yielding products which are ineffective and toxic. On the other hand, *E. coli* offered highest level of resistance against all the tested oxytetracycline regardless of the storage condition. This is mostly because oxytetracycline is no longer effective against *E. coli* [12,13]. A marked and slight reduction

in sensitivity of *B. subtilis* to Penistrep from open livestock market and that exposed to sun sunlight in comparison to similar drugs from Agrovet shops was an indication of efficacy reduction. As for, although was statistically insignificant, a slightly reduced level of sensitivity of *E. coli* against penistrep from open livestock market and the sunlight exposed when compared to Agrovet, could still be clinically significant as it can contribute to treatment failure and antibiotic resistance. In the same way, a slightly reduced sensitivity of sulphamexazole from open livestock market and the sunlight exposed as compared to sulphamexazole from Agrovet shops could still be clinically significant as it can contribute to treatment failure and antibiotic resistance [14].

Conclusion

The study conclude that prolonged exposure to sunlight of oxytetracycline, penicillin-streptomycin and sulphamexazole as it is done in open livestock markets may contribute to loss of drugs potency against bacteria agents. Loss of drugs potency may lead to increased risk of treatment failure and development of antibiotic resistance. This suggests for increases efforts on enforcements of the laws and regulations involved in the control of Veterinary drugs sales and distribution in order to preserve qualities and shelf life of the drugs. Knowledge from this study enables understanding of the long term effects of the environment on drugs.

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