

Microbiological Evaluation of Ten Commercial Cough Syrups during Storage

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ABSTRACT

Fifty samples of 10 different brands of cough syrups were analyzed for microbial quality during storage at ambient temperature ($28 \pm 2^\circ\text{C}$) and refrigeration temperature ($4 \pm 2^\circ\text{C}$). Physicochemical studies were also conducted to ascertain the stability of their active ingredients. Alcoff[®] cough syrup recorded the highest average bacterial count of 2.0×10^5 cfu/ml at ambient temperature, and 1.5×10^5 cfu/ml at refrigeration temperature, while Benylin[®] with 9.0×10^4 cfu/ml at ambient temperature and Tutolin[®] with 6.4×10^4 cfu/ml at refrigeration temperature were the least. Parkalin[®] had the highest average fungal count of 5.6×10^4 cfu/ml at ambient temperature while Emzolyln[®] with 2.2×10^4 cfu/ml was least. The fungal counts at refrigeration temperature showed that Tutolin[®] and Piriton[®] with 2.4×10^4 cfu/ml each was the highest, while Coflin[®] with 4.0×10^3 cfu/ml was the least. The percentage occurrence of isolates were *Staphylococcus aureus* (100%), *Micrococcus* spp. (80%), *Bacillus subtilis* (90%), *Azotobacter* spp. (10%), *Proteus* spp. (20%), *Lactobacillus* spp. (40%), *Pseudomonas aeruginosa* (20%), *Aspergillus fumigatus* (100%), *Aspergillus niger* (100%), *Aspergillus flavus* (100%), *Fusarium solani* (50%) and *Penicillium* spp. (40%). The antibiotic susceptibility of isolates showed that *S. aureus* was sensitive to gentamycin (100%) and resistant to cloxacillin (100%), ampicillin (100%), and penicillin (100%). *Proteus* spp. was sensitive to gentamycin (100%) but resistant to colistin (100%), nitrofurantoin (100%), cotrimoxazole (100%), tetracycline (100%), and ampicillin (100%). *P. aeruginosa* was resistant to all antibiotics tested. The level of antibiotic resistance of bacterial isolates in cough syrup is a problem to public health. The cough syrups evaluated did not generally meet the standards for microbial limit as specified in official monographs. These products can adversely affect health status of consumers, hence, the need for regular quality control and assurance.

Keywords: antibiotic susceptibility, bacteria, fungi, quality, temperature

Abbreviations: AF, Alcoff[®]; BN, Benylin[®]; CN, Coflin[®]; DK, D-koff[®]; EN, Emzolyln[®]; NB, Nichben[®]; PA, Parkalin[®]; PN, Piriton[®]; TD, Tuxil-D[®]; TN, Tutolin[®]

INTRODUCTION

The warm and humid climatic conditions that are characteristic of tropical countries like Nigeria tend to support the survival and growth of many microorganisms (Hugbo *et al.* 2003). The climatic condition is responsible for a number of infectious diseases and the spoilage of food, cosmetic and pharmaceutical products (Bos *et al.* 1989; LeChevallier *et al.* 1996; Ballereau *et al.* 1997). In a situation whereby a nutritionally-rich pharmaceutical or cosmetic product is contaminated, rapid growth and multiplication of microorganisms would be expected. According to Bos *et al.* (1989), it could lead to biodegradation and the risk of infection to consumers of the product. Several cases of infection caused by the administration of non sterile medicaments contaminated by microorganisms have been reported (Ringertz and Ringertz 1982; Spooner 1988; de la Rosa *et al.* 1993). In addition, many of these microorganisms become resistant to one or more antimicrobial agents used in therapy after exposure to these non sterile pharmaceuticals (de la Rosa *et al.* 1993). Therefore, consumption of products contaminated by these microorganisms may lead to the spread of drug resistance. Product contamination may be from raw materials or water used in formulation or accidentally during use (Hugbo *et al.* 2003). The unhygienic conditions that prevail usually make these contaminations possible.

In recent years, manufacturers of pharmaceuticals have improved the quality of syrups such that the majority contains a minimal microbial population. Nevertheless, a few rogue products with unacceptable levels and type of contamination do occasionally escape the quality control net and

when used contribute to the spread of diseases (Eze and Asogwa 2006). According to Akarele and Ukoh (2003), this is more of concern in tropical countries where pharmaceutical preparations are frequently stored under uncontrolled conditions). Eze and Asogwa (2006) reported that dispensing of most of these medicaments in patent medicine stores take an average of 3-4 weeks under uncontrolled and therefore unhygienic conditions.

There is the possibility that microorganisms present in syrups during the shelf life may contribute to physical deterioration of the product as well as inactivate the therapeutic activity of the product which could affect the health of the patients (European Pharmacopoeia 2007). The risk of this happening is higher in cough syrups which contain additives like plant extracts, sucrose, that could serve as substrate for microorganisms.

Eka *et al.* (1987) reported the development of diarrhea in children in Western Nigeria after the use of contaminated syrup. Their studies of microbial contamination of oral liquids, tablets, and raw materials in some Nigerian hospitals recorded organisms such as *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, *Micrococcus* spp., *Bacillus* spp., yeasts and moulds. The study suggested raw materials, storage environment, water, containers, air and personnel as possible sources of contamination. Mendie *et al.* (1993) examined 104 samples of syrups, elixirs, solutions, mixtures, tonics and suspensions and reported that fungi accounted for 72.2% of isolates, and, the rest were mainly *Staphylococcus aureus* (5.9%), *Micrococcus* spp. (4.9%), *Klebsiella* spp. (4.0%), *Escherichia coli* (8.0%) and *Pseudomonas* spp. (5.0%). In a similar study by Oyeleke *et*

al. (2005), 20 brands of cough syrup were analyzed for microbial contamination, and result revealed the microbial count of 1.6×10^6 to 7.2×10^6 cfu/ml bacteria for 13 samples and 1.4×10^3 to 8.6×10^3 cfu/ml fungi for nine samples. This study therefore, is aimed at assessing the microbial quality of cough syrup during storage at ambient temperature ($28 \pm 2^\circ\text{C}$) and refrigeration temperature ($4 \pm 2^\circ\text{C}$), as well as to determine the antibiotic susceptibility of bacterial isolates in the cough syrup samples.

MATERIALS AND METHODS

Sample collection

A total of 50 samples (5 each of 10 commercial cough syrups) purchased from registered pharmaceutical stores in Umuahia metropolis were used in this study. They were all non-expired cough syrups and manufactured in different states in Nigeria. The cough syrups were: Tuxil-D[®] (TD), Emzoklyn[®] (EN), D-Koff[®] (DK), Piriton[®] (PN), Benylin[®] (BN), Tutolin[®] (TN), Parkalin[®] (PA), Alcoff[®] (AF), Nichben[®] (NB) and Coflin[®] (CN). The container labels were examined for the date of manufacture and expiry, active ingredients and other compositions were noted. The samples purchased aged between two and six months. All the products were approved by the National Agency for Food and Drug Administration and Control (NAFDAC), as they all had the NAFDAC registration number.

Sample processing

The sample containers were topically disinfected with 1% hydrochloric acid in 95% ethanol as described by Collins and Lyne (1984). The sample cover was flamed briskly by passing it through a Bunsen burner flame for about 3 times before the sample was opened. The samples both in ambient ($28 \pm 2^\circ\text{C}$) and refrigeration temperatures ($4 \pm 2^\circ\text{C}$) were investigated for microbial and physicochemical characteristics during storage.

Microbiological analysis

The pour plate method of isolation of microbes from pharmaceutical products as described by United States Pharmacopoeia (1980) was adopted for the analysis. This involved serial dilution of samples. An aliquot of 1ml of each sample was measured and introduced into test tubes containing 9 ml sterile water. Exactly 1 ml of the appropriate dilution was placed into each of two sterile Petri dishes. Thereafter, approximately 20 ml of each of the sterile Nutrient agar, Sabouraud Dextrose agar and MacConkey agar previously cooled to 45°C was added into the Petri dishes for the enumeration or isolation of bacteria, fungi and coliform counts respectively. The Petri dishes were covered immediately and the sample mixed with the agar by tilting or rotating the dishes. The agar was allowed to solidify at room temperature. Afterwards, the Petri dishes were inverted and incubated for 24-48 hrs at $35-37^\circ\text{C}$ for Nutrient agar and MacConkey agar while Sabouraud Dextrose agar Petri dishes were incubated for 3-5 days at $26-30^\circ\text{C}$. Each procedure was repeated independently in 3 replicates. After incubation, acceptable colonies, (within 30-300) were counted. Actual microbial population was obtained by multiplying the plate count by the dilution factor and recorded as the colony forming unit per ml (cfu/ml).

Antibiotic susceptibility testing

Antibiotic susceptibility was determined by the agar diffusion technique as described by Baker and Breach (1980). A sterile cotton swab dipped into the broth culture of isolate was streaked evenly all over the surface of Mueller Hinton's agar (Oxoid), and, antibiotic disk was placed aseptically on the inoculated plates using sterile forceps. The plates were then incubated for 24 hrs at $35-37^\circ\text{C}$. Isolates were considered as sensitive or resistant to an antibiotic according to the diameter of inhibition zone size interpretative chart (Clinical Laboratory Standards Institute 2006).

The antibiotics (Oxoid) tested and their standard concentrations were as follows: ampicillin (10 μg), chloramphenicol (10 μg),

cloxacillin (5 μg), erythromycin (5 μg), gentamycin (10 μg), penicillin (1 μg), streptomycin (10 μg) and tetracycline (10 μg) for Gram positive organisms, while that of Gram negatives are ampicillin (25 μg), gentamycin (25 μg), tetracycline (25 μg), colistin (25 μg), streptomycin (25 μg), nalidixic acid (25 μg), nitrofurantoin (200 μg) and cotrimoxazole (25 μg).

Identification of fungal isolates

Moulds were identified according to Barnett and Hunter (1972). The morphological characteristics of colony both surface and reverse, rate of growth, colour and pigmentation in the medium were considered. The wet mount technique explained by Cheesbrough (1984) was employed. Two drops of lactophenol was placed on a clean grease free slide. Then, a sterile inoculating needle was used to transfer a small portion of mycelia growth to the lactophenol. The fungal growth was then teased, covered with a cover slip and observed using $\times 40$ objective lens.

Statistical analysis

The student's *t*-test was used to compare the values of the samples at ambient and refrigeration temperature.

RESULTS

Microbiological analyses showed that the cough syrups were generally contaminated to a varying degree. **Figs. 1** and **2** showed the total count of bacteria and fungi at ambient temperature (At) and refrigeration temperature (Rt) for the different brands of cough syrup samples for thirty five days of storage. From the result, Product AF had the highest average bacterial count of 2.0×10^5 cfu/ml at ambient temperature while product BN with 9.6×10^4 cfu/ml had the least. At refrigeration temperature, product AF had the highest with 1.5×10^5 cfu/ml, while product TN with 6.4×10^4 cfu/ml was the least. For fungi, product PA with 5.6×10^4 cfu/ml had the highest average fungi count at ambient temperature, while product EN with 2.2×10^4 cfu/ml had the least, but at refrigeration temperature, product TN and PN with 2.4×10^4 cfu/ml each had the highest count, while product CN with 4.0×10^3 cfu/ml had the least average fungi count. Generally there were a significant differences observed between microbial counts in samples stored at ambient and refrigeration temperatures.

Based on their cultural morphology, microscopic, biochemical and physiological characteristic the isolates include: *Staphylococcus aureus*, *Bacillus subtilis*, *Micrococcus* spp., *Lactobacillus* spp., *Pseudomonas aeruginosa*, *Azotobacter* spp. and *Proteus* spp. for bacteria. Moulds were *Aspergillus flavus*, *Aspergillus niger*, *Aspergillus fumigatus*, *Fusarium solani* and *Penicillium* spp. The percentage occurrences of these microorganisms were presented in **Figs. 3** and **4** for bacteria and fungi respectively.

The antibiotic sensitivity patterns of the isolates are shown in **Tables 1** and **2**. All the *Staphylococcus aureus* isolates were resistant to ampicillin, cloxacillin and penicillin, while they were all sensitive to gentamycin. All the *Pseudomonas aeruginosa* isolates were resistant to all the antibiotics tested. Also, *Proteus* spp. was resistant to colistin, nitrofurantoin, cotrimoxazole, tetracycline and ampicillin, while it showed sensitivity to gentamycin.

DISCUSSION

Microbiological properties of cough syrup samples during storage were investigated at both ambient and refrigeration temperature. However, higher bacteria count was recorded at ambient temperature whereas lower fungi count was recorded at both temperatures compared to that of bacteria.

The level of microbial contamination and the isolation of *Staphylococcus aureus* and *Pseudomonas aeruginosa* showed that the products did not comply with standard (United States Pharmacopoeia 1980; European Pharmacopoeia 2007), indicating a defect in production. This finding

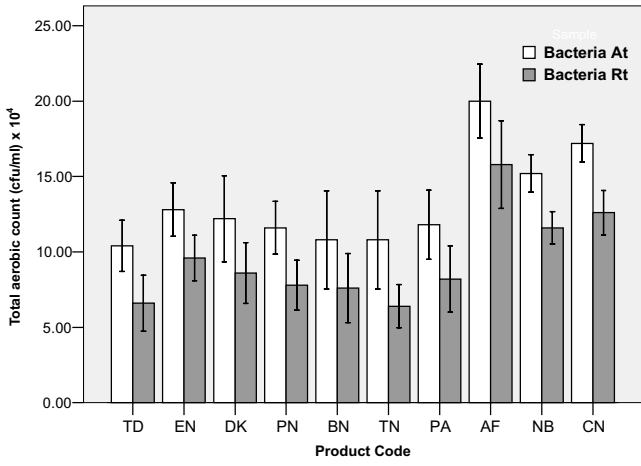


Fig. 1 Total viable count of bacteria at ambient temperature (At) and refrigeration temperature (Rt) in different brands of cough syrup samples for 35 days of storage. TD = Tuxil-D[®]; EN = Emzolyn[®]; DK = D-Koff[®]; PN = Piriton[®]; BN = Benylin[®]; TN = Tutolin[®]; PA = Parkalin[®]; AF = Alcoff[®]; NB = Nichben[®]; CN = Coflin[®].

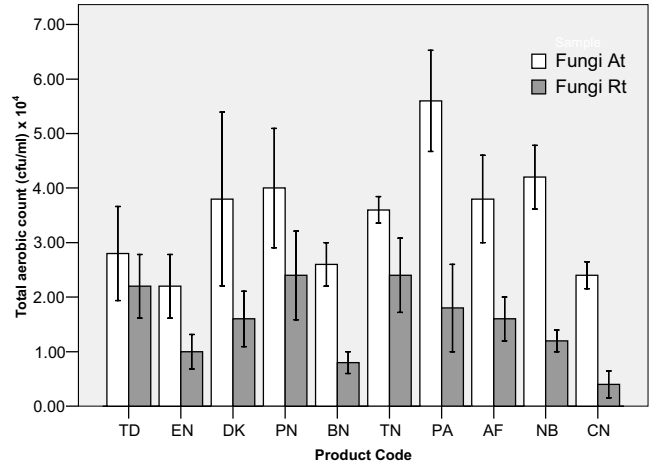


Fig. 2 Total viable count of fungi at ambient temperature (At) and refrigeration temperature (Rt) in different brands of cough syrup samples for 35 days of storage. TD = Tuxil-D[®]; EN = Emzolyn[®]; DK = D-Koff[®]; PN = Piriton[®]; BN = Benylin[®]; TN = Tutolin[®]; PA = Parkalin[®]; AF = Alcoff[®]; NB = Nichben[®]; CN = Coflin[®].

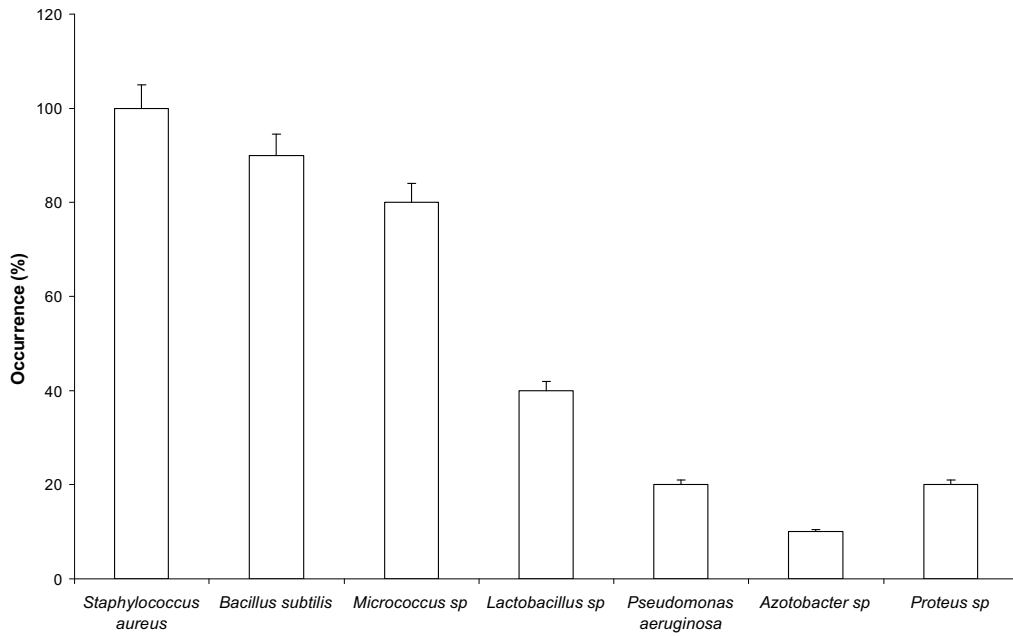


Fig. 3 Percentage occurrence of bacteria in cough syrup samples.

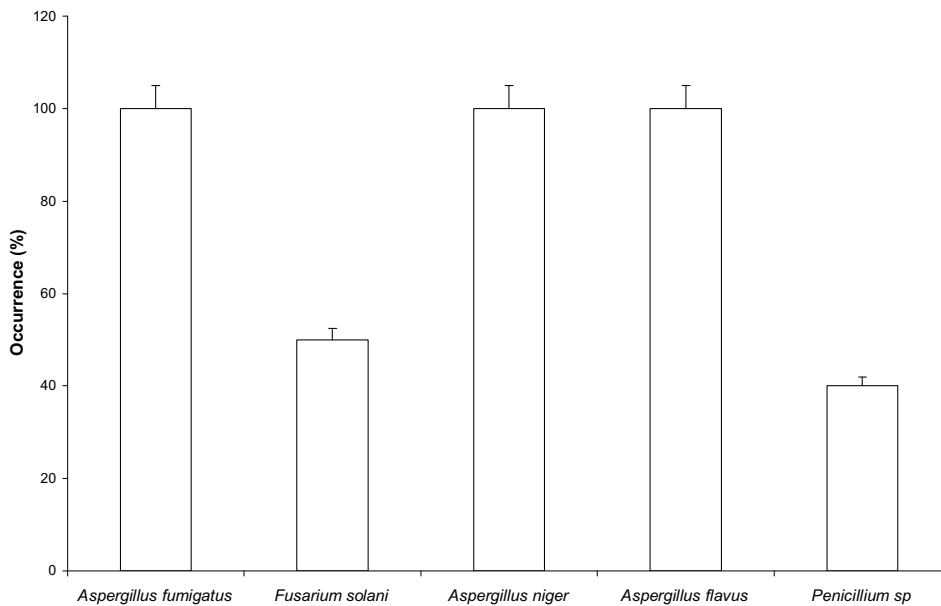


Fig. 4 Percentage occurrence of fungi in cough syrup samples.

Table 1 Antibiotic sensitivity pattern of *Staphylococcus aureus* isolates (n = 10).

Antibiotic (conc.)	Number (%) of sensitive isolates
Ampicillin (10 µg)	0 (0)
Chloramphenicol (10 µg)	5 (50)
Cloxacillin (5 µg)	0 (0)
Erythromycin (5 µg)	4 (40)
Gentamycin (10 µg)	10 (100)
Penicillin (1 iu)	0 (0)
Streptomycin (10 µg)	3 (30)
Tetracycline (10 µg)	2 (20)

n = Number of organisms tested.

Conc. = Concentration of antibiotic disk in microgram.

Table 2 Antibiotic sensitivity pattern of *Pseudomonas aeruginosa* and *Proteus* sp isolates (n = 2).

Antibiotic (conc.)	Number (%) of sensitive isolates	
	<i>P. aeruginosa</i>	<i>Proteus</i> sp.
Colistin (25 µg)	0 (0)	0 (0)
Gentamycin (10 µg)	0 (0)	2 (100)
Nalidixic acid (30 µg)	0 (0)	1 (50)
Nitrofurantoin (200 µg)	0 (0)	0 (0)
Cotrimoxazole (25 µg)	0 (0)	0 (0)
Streptomycin (25 µg)	0 (0)	1 (50)
Tetracycline (25 µg)	0 (0)	0 (0)
Ampicillin (25 µg)	0 (0)	0 (0)

n = Number of organisms tested.

Conc. = Concentration of antibiotic disk in microgram.

is in agreement with the studies conducted by other workers (Mendie *et al.* 1993) who reported high microbial counts and organisms such as *Micrococcus* spp., *Bacillus* spp., *Azotobacter* spp., *Pseudomonas* spp., *Klebsiella* spp., and *Escherichia coli*. The yeast isolates were *Saccharomyces* spp., and *Candida* spp., while the mould isolated include *Rhizopus* spp., *Penicillium* spp., and *Aspergillus* spp. Charnock (2004) reported the presence of Gram positive endospore forming rods and Gram negative organisms. Similarly, Oyeleke *et al.* (2005) identified organisms such as *Escherichia coli*, *Bacillus subtilis*, *Salmonella typhi* and *Staphylococcus aureus* for bacteria; *Aspergillus flavus*, *Aspergillus fumigatus*, *Aspergillus niger*, *Penicillium notatum* and *Fusarium solani* for fungi. They identified *Staphylococcus aureus* as having the highest prevalence (65%) and *Bacillus subtilis* the least (5%) for bacteria; *Aspergillus fumigatus* (33%) was the most prevalent among the fungi isolates while *Penicillium notatum* (11%) had the least. The microflora of the cough syrup was found to consist mainly of Gram positive bacteria and mould.

However, the microbial quality of the cough syrups examined in this study was relatively lower than the products described in the report of Oyeleke *et al.* (2005), where microbial counts above 10^5 and *Salmonella typhi* and *Escherichia coli* was not recorded. The isolation of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Proteus* spp. and *Aspergillus* spp. is of public health concern because of the pathogenic potential of these organisms.

The likely source of contamination of these products are raw materials or water used in formulation, personnel as well as the condition prevalent in the environment in which the products are manufactured and packed (Mendie *et al.* 1993; Okeke and Lamikanra 2001). In addition, most products were observed to be loosely coked and not firmly closed, and it could serve as a source of contamination. The European Agency for the Evaluation of Medicinal Products (2003) stated that orally administered aqueous solutions, suspensions and emulsion are among the preparations at greatest risk of contamination. Since most of these liquid preparations are administered to children or infants who are highly prone to infection, it may pose a real danger even when the level of contamination is low. According to Oyeleke *et al.* (2005), it could lead to gastrointestinal disorders and possible complication for the initial ailment.

The sensitivity tests (Tables 1, 2) indicated that the isolates were resistant to one or more antibiotics, although generally, a low percentage of the isolates were sensitive to the antibiotics tested. The result of the sensitivity test indicates that *S. aureus* and *Proteus* spp. were very sensitive to gentamycin. The Gram positive and Gram negative isolates showed high resistance to commonly available antibiotic such as ampicillin, penicillin, cloxacillin, cotrimoxazole, tetracycline, colistin and nitrofurantoin. This implies that, treatment of possible infection due to these organisms may not be feasible and would require a new antibiotic which are not commonly available. Of particular concern is the sensitivity pattern of *P. aeruginosa* isolates to the antibiotics, although the organism is known to be resistant to many chemical antimicrobial agents or antibiotics. The level of antibiotic resistance recorded in this study is similar to the report of Charnock (2004), who reported an unusual antibiotic resistance among isolates from pharmaceuticals and allied products.

The possible explanation of the antibiotic resistance pattern among the isolates may be due to pre-existing factors in the microorganisms or synthesis of excess enzymes over the amount that can be inactivated by the antibiotic, or, inability of the drug to penetrate the cell due to some alteration of the cell membrane (Pelczar *et al.* 1993). Possibly, some biochemical changes in the product may contribute to antibiotic resistance. de la Rosa *et al.* (1993) reported that organisms become resistant to one or more antimicrobial agents after exposure to non sterile pharmaceuticals. The level of antibiotic resistance observed in this study is surprising and it is a very serious public health problem, and brings to light the need for good manufacturing protocol and use of effective preservative system to prevent possible contamination by these microbes.

According to Lamikanra (1999), Booth (2000) and European Pharmacopoeia (2007), the presence of certain microorganisms in non sterile preparations may have the potential to reduce or even inactivate the therapeutic activity of the product and has the potential to adversely affect the health of the patient. The microbial quality of pharmaceutical products is influenced by the environment and quality of the raw materials used during formulation (Mendie *et al.* 1993; Hugbo *et al.* 2003). Hence, manufacturers should prevent the contamination of raw materials, finished products and the packaging components so as to maintain appropriate quality, safety and efficacy of the product. Sufficient quantity of a suitable preservative should be included to prevent or reduce contamination of the product (Lamikanra 1999).

This study revealed that cough syrups are susceptible to microbial contamination. Organisms like *Staphylococcus aureus* and *Pseudomonas aeruginosa* known as opportunistic pathogens and are considered as objectionable by competent authorities were recovered in the products. Colony forming units per ml (cfu/ml) recovered was higher than that stipulated by same authority; and a worrisome level of antibiotic resistance of the isolates. Therefore, consumption of these cough syrup by children or infants and the critically ill who are highly prone to infection may present a potential hazard.

This study also indicated the possible proliferation of microorganisms even in the presence of a preservative. Higher microbial counts were observed at ambient temperature than refrigeration temperature; hence, cough syrups may be stored in refrigerator or preferably at temperature below ambient temperature. More research should be focused on cough syrups as potential source of infection.

REFERENCES

- Akarele JO, Ukoh GC (2002) Aspects of microbial contamination of tablets dispensed in hospitals and community pharmacies in Benin City, Nigeria. *Tropical Journal of Pharmaceutical Research* 1 (1), 23-28
- Baker FJ, Breach MR (1980) *Medical Microbiological Techniques* (1st Edn), Butterworth and Co. Ltd., London, 547 pp

- Ballereau F, Prazuck T, Schrive I** (1997) Stability of essential drugs in the field: Results of a study conducted over a two-year period in Burkina Faso. *American Journal of Tropical Medicine and Hygiene* **57**, 31-36
- Barnett HL, Hunter BB** (1972) *Illustrated Genera of Imperfect Fungi* (3rd Edn), Burgess Publication Co., USA, 241 pp
- Booth C** (2000) Microbiology of pharmaceutical products – spoilage and preservation. Research and Development Glaxo-Wellcome, Waire, pp 18-29
- Bos CE, Van DH, Olerk CF** (1989) Microbiological stability of tablets stored under tropical conditions. *International Journal of Pharmacology* **55**, 175-183
- Charnock C** (2004) Microbial content of non-sterile pharmaceuticals distributed in Norway. *Journal of Hospital Infection* **57** (3), 233-240
- Cheesbrough M** (1984) *Medical Laboratory Manual for Tropical Countries*, Butterworth Heinemann Ltd., London, pp 58-69
- Clinical and Laboratory Standards Institute** (2006) *Performance Standards for Antimicrobial Disk Susceptibility Test*, Wayne, PA, vol. 26, No 1, pp 11-23
- Collins CH, Lyne PM** (1984) *Microbiological Methods* (5th Edn), Butterworth and Co. Publishers Ltd., London, 486 pp
- De La Rosa MC, Mosso MA, Garcia ML, Plaza C** (1993) Resistance to antimicrobial agents of bacteria isolated from non sterile pharmaceuticals. *Journal of Applied Bacteriology* **74**, 570-577
- Eka OU, Eka H, Richard RME** (1987) Microbial contamination of non sterile pharmaceutical preparation in some Nigerian hospitals. *Nigerian Journal of Microbiology* **7** (1-2), 90-97
- European Agency for the Evaluation of Medicinal Products** (2003) Note for guidance on excipients, antioxidants and antimicrobial preservatives in the dossier for application for marking authorization of a medicinal product, CPMP/QWP/419/03. Available online: <http://www.emea.europa.eu/htms/human/epar/a.htm> from http://www.who.int/medicines/services/expertcommittees/pharmprep/PharmDevelGener_QAS08_251_11012008.pdf
- European Pharmacopoeia** (2007) *Directorate for the Quality of Medicine of the Council of Europe* (5th Edn), Strasburg, France, pp 4451-4452
- Eze EN, Asogwa AN** (2006) Microbiological profile of non sterile pharmaceuticals sold in patent medicine stores in Nsukka, Nigeria. *Global Journal of Pure and Applied Sciences* **12**, 487-490
- Hugbo PG, Onyekweli AO, Igwe I** (2003) Microbial contamination and preservative capacity of some brands of cosmetic creams. *Tropical Journal of Pharmaceutical Research* **2** (2), 229-234
- Lamikanra A** (1999) *Essential Microbiology* (2nd Edn), Miobic Publishers Ltd., Nigeria, pp 55-68
- LeChevallier M, Welch N, Smith D** (1996) Full-scale studies of factors related to coliform re-growth in drinking water. *Applied and Environmental Microbiology* **62**, 2201-2211
- Mendie UE, Ifudu ND, Brown SA** (1993) How safe are non sterile liquid preparations? *Journal of West African Pharmacy* **7**, 8-10
- Okeke IN, Lamikanra A** (2001) Bacteriological quality of skin moisturizing creams and lotions distributed in tropical developing country. *Journal of Applied Microbiology* **91**, 922-928
- Oyeleke SB, Faruk AK, Oyewole OA, Ejemai O** (2005) Microbial assessment of some retailed cough syrups in Minna, Niger State. *Ife Journal of Science* **7** (1), 53-57
- Pelczar MJ, Chan ECS, Krieg NR** (1993) *Microbiology: Concepts and Application* (1st Edn), McGraw-Hill Publication Co. Ltd., New York, 630 pp
- Ringertz O, Ringertz SH** (1982) The clinical significance of microbial contamination in pharmaceutical products. *Advances in Pharmaceutical Sciences* **5**, 201-225
- Spooner DF** (1988) Hazards associated with microbiological contamination of non sterile pharmaceuticals, cosmetics and toiletries. In: Bloomfield SF, Leak RE, Leech R (Eds) *Microbial Quality Assurance in Pharmaceuticals, Cosmetics and Toiletries*, Ellis Horwood, Chichester, pp 15-34
- United States Pharmacopoeia** (1980) *Microbial Limit Test* (15th Edn), United States Pharmacopoeia Convention Inc., pp 9-1035