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Full Length Research Paper

Antibacterial activity of some of the commonly sold cough mixtures in South Western Nigeria

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Cough is a common upper respiratory tract condition usually complicated by microbial infections. It is a common public health problem worldwide. Cough mixtures, for which antibacterial activities are rarely indicated are commonly used in cough management. This study investigated the antibacterial activities of some commonly used cough mixtures in South Western Nigeria against different bacterial isolates of clinical importance. The isolates exhibited varied degree of susceptibility to different cough mixtures commonly used in the region. Of all the bacterial isolates, 94.3% were susceptible to both CPS and CCL. 68.8, 45.7 and 31.4% of all the bacterial isolates were correspondingly inhibited by MCL, CNDCS and TCS cough mixtures. The clinical strains were more susceptible than the typed strains and CPS was considered more active than other cough mixtures. Though cough mixtures mainly contain antihistaminic agents, the study shows that most of them have antibacterial activities against *Streptococcus species, Escherichia coli, Salmonella typhi, Staphylococcus aureus and Klebsiella pneumoniae.* Their ability to inhibit the growth of wild and typed bacterial isolates indicates that they can be effective antibacterial agents in upper respiratory tract infections.

Key words: Antihistaminic agents, antibacterial activity, cough mixtures, inhibition zones.

INTRODUCTION

Cough is a sudden and often repetitively occurring reflex that helps the body to clear the respiratory tract from secretions, irritants, foreign bodies and microbes. It can be acute, subacute or chronic and may be dry or non-productive or productive cough. It is the most common complaint for which patients seek medical attention and the second most common reason for a general medical examination (Schappert, 1993). It is an important defensive reflex of the upper airway and a common symptom of respiratory disease (Chung and Chang, 2002) occurring in conjunction with upper respiratory tract infection involving bacteria and viruses (URI) (Middleton and Hing, 2006). Cough is also an important factor in the spread of microbial infections to other host. Chronic cough of unknown etiology have been shown to account for 10 to 38% of a pulmonologist's outpatient practice (Irwin et al., 1981, 1990). In healthy individuals, it is an important natural reflex and defense mechanism that helps to clear excessive secretions and prevent foreign matter from entering the airways (Morice et al., 2007). Cough is commonly triggered when sensory cough-inducing receptors in the respiratory tract are stimulated by mechanical and/or chemical irritation and for which various agents are used in the cough mixtures for its management (Irwin et al., 1998). Although, coughing is a symptom and not a disease, both viral and bacterial agents have been implicated with an underlying cause being required to be treated. Accordingly, expectorant cough mixture containing guaifenesin, ipecachuana or ammonium citrate and opiates have long been advocated for the suppression of cough (Chung, 2003; 2005). Some

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of the expectorants may contain antibacterial agents or activity but these are not commonly indicated in the remedy. Hence, this study investigated the antibacterial activity of some cough mixtures used in the cough management in the South Western region of Nigeria.

MATERIALS AND METHODS

This study was conducted in the Department of Biosciences and Biotechnology, Babcock University, Ilishan Remo, Nigeria. The clinical isolates were obtained from three University teaching hospitals in the South Western region in Nigeria. The cough mixtures were randomly selected on the basis of their consumers' demands indicating their possible, rate of use and effectiveness in cough management.

Selection of bacterial isolates

The selected clinical strains of bacteria used in this study included *Streptococcus species* (21 strains), *Escherichia coli* (3 strain), *Salmonella typhi* (6 strains) and *Klebsiella pneumoniae* (3 strains). *Staphylococcus aureus* (ATCC 25923), *Escherichia coli* (ATCC 25922), *Klebsiella pneumoniae* (ATCC 13883) and *Shigella sonnei* (ATCC 25913) were included as control organisms.

Isolation and identification of bacterial isolates

The clinical strains were identified and confirmed using morphological, microscopy and biochemical tests following standard procedures described by Cowan and Steel (1974) and Cheesborough (2006). The bacteria were grown in nutrient broth (Lab M Limited, UK) at 37°C and maintained on nutrient agar (Lab M Limited, UK) slants at 4°C.

Antibiotic susceptibility testing – disc diffusion method

Each of the isolates was standardized using colony suspension method. Each strain's suspension was matched with 0.5 McFarland standards to give a resultant concentration of 1.5×10^8 cfu/ml. The antibiotic susceptibility testing was determined using the modified Kirby-Bauer diffusion technique (Cheesbrough, 2002) by swabbing on the Mueller-Hinton agar (MHA) (Oxoids UK) plates with the resultant saline suspension of each strain. Wells were then bored into the agar medium with heat sterilized 6 mm cork borer. The wells were filled with 100 µl of each of the cough mixtures taking care not to allow spillage of the solutions onto the surface of the agar. The plates were allowed to stand for at least 30 min before being incubated at 37°C for 24 h (BSAC, 2002). The determinations were done in duplicates. After 24 h of incubation, the plates were examined if there is any zone of inhibition (Bauer et al., 1966). The diameters of the zones of inhibition produced by each of the cough mixtures were measured in millimeters (CLSI, 2007) and interpreted using the CLSI zone diameter interpretative standards (CLSI, 2008).

Data analysis

All the data were subjected to one way analysis of variance (ANOVA) and the mean values were separated at ($p<0.05$) using Duncan's Multiple Range Test. The one way ANOVA test was used to determine if there was any statistically significant difference in the diameter of the zones of inhibition obtained from the respective cough mixtures. All statistical analyses were done using SAS software (1999) model.

RESULTS

In this study, the different cough mixtures were identified and coded with their active ingredients as presented in Figure 1. Seventy five percent (75%) of the cough mixtures had antihistamine and expectorant respectively, 50% had suppressant while 12.5% only had sympathomimetic and preservative respectively. While three different cough mixtures had two different expectorants, others had one type of expectorant in their compositions. The tested bacteria exhibited varied degree of susceptibility to the different cough mixtures investigated for antibacterial activities. Their bacterial susceptibility profile indicated that 94.28% of the bacteria were equally susceptible to both CPS and CCL, followed by 68.57% (MCL), 45.71% (CNDS), 25.71% (TCS), 14.29% (BDCS), 17.14% (OCS) and 11.43% (OCM). For *Streptococcus species*, 57.14% were inhibited by CPS and had zone of inhibition equal to or greater than 18 ± 1.00 mm and 71.43% were inhibited by CCL and had zone of inhibition equal to or greater than 18 ± 1.00 mm. In the same manner, BDCS inhibited 14.29% of the isolates and 4.76% of the isolates was independently inhibited by OCM and OCS. While CNDS inhibited 9.52% of the isolates, none of the bacteria inhibited by MCL and TCS had inhibition zones greater than 18 ± 1.00 mm. CPS inhibited the *E. coli* with the zone of inhibition of 18 ± 1.00 mm in two strains. Other cough mixtures had little activity against all the *E. coli* strains. With the exception of *S. aureus* (ATCC 25923), SAT_2 and SAT_4 being inhibited by CPL and had a zone of inhibition greater 18 ± 1.00 mm, all other bacteria were either resistant or slightly susceptible to all other cough mixtures (Table 1). Despite possible morphological differences between the wild or clinical strains and the typed bacterial strains, the ability of the effective cough mixtures to inhibit the clinical strains more than the typed strains was obvious and CPS was considered more active than other cough mixtures.

DISCUSSION

In the determination of the antibacterial activities of many drugs, studies are usually performed with their pure forms while the pharmaceutical forms are hardly considered as they usually consist of additive substrates used as filling or protective agents. However, to bridge the gap between the results obtained with their laboratory and commercial forms which are not the same, it becomes imperative to investigate drugs for their antibacterial effects in routine practice in pharmaceutical forms and not for their pure active substrates alone. In this study, cough mixtures, containing mixtures of antihistamines, decongestants, suppressant and expectorants (Martindale, 2002) had a varied degree of antibacterial activity against clinical

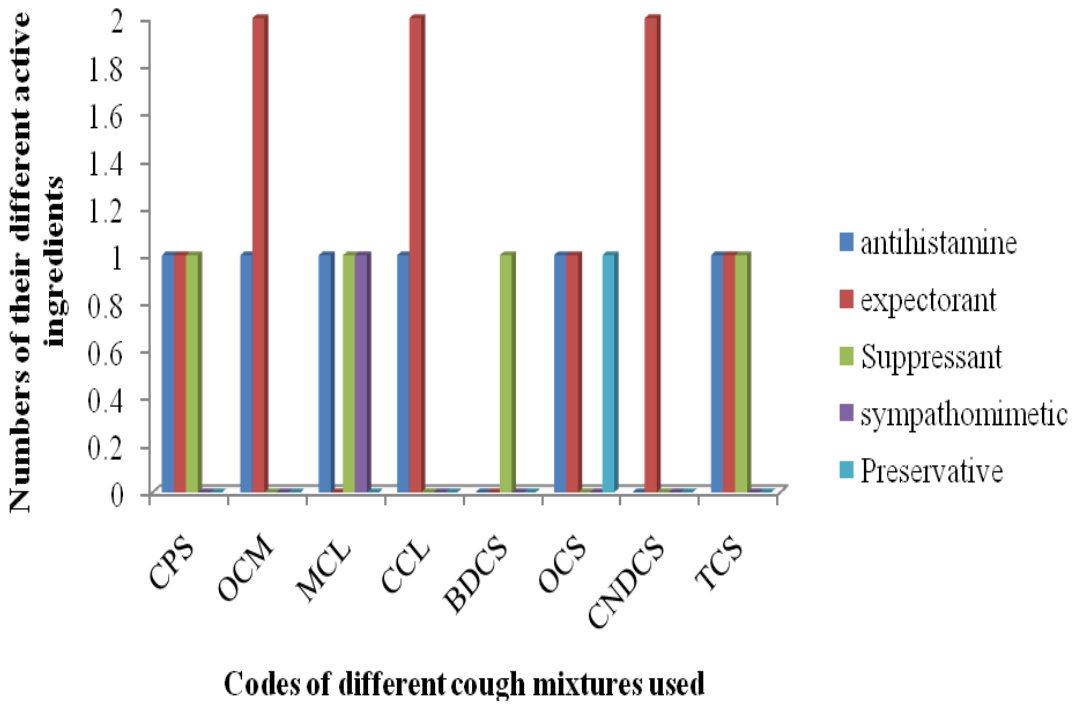

Figure 1. Codes and active ingredients in each cough syrup mixture.

isolates of bacteria. Being non-antibacterial agents, the exhibited antibacterial activity of these mixtures agreed with previous reports on several pharmacological agents often termed non-antibiotics (Dastidar et al., 1997; Mazumder et al., 2002; Sarkar et al., 2003) which have been found to have antibacterial activity (Yao and Moellering, 1999). Although, in cough management, protussive therapy is indicated when cough performs a useful function by producing phlegm and needed to be encouraged (Puchelle et al., 1980), specific antitussive therapy is directed at the etiology or presumed operant pathophysiologic mechanism responsible for cough or coughing (Irwin et al., 1981). The active ingredients in cough formulations are not meant to have antibacterial effects, but both protussive and antitussive effects. However, the antibacterial activity of some antihistamines, which are non-antibiotic agents, including chlorpromazine (Kristiansen and Blom, 1981; Molnar et al., 1976), bromodiphenhydramine (Dastidar et al., 1976; Karak et al., 2003) promethazine, methdilazine and trimeprazine (Chakrabarty et al., 1989, Chattopadhyay et al., 1988; Kristiansen and Amaral, 1997; Kristiansen et al., 2007) has been reported. While the antimicrobial activity of quaternary ammonium salts with long hydrocarbon chains has been indicated by Goldsmith et al. (1954), Lashen (1971) and Seshadri and Bhat (2005), those of silver-containing materials used in medicine to reduce infections and prevent bacteria colonization on prostheses (Roldán et al., 2005), catheters (Yin et al., 2004; Zhu et al., 2006), dental materials (Maillard et al., 2002), human skin (Maillard et al., 2002; Duran et al., 2005) and water treatment (Chou et al., 2005) have also been reported. The cations have been implicated in electrostatic interaction and physical disruption of the membrane to enhance the release of electrolytes and nucleic materials, leading to cell death in bacteria (Abel et al., 2002; Ramachandran et al., 2004). Thus, the recorded antibacterial activity with cough mixtures containing cations could have resulted from either the antibacterial action of each of these components or their combinatory synergistic effects. This could be the reason for the prominent antibacterial activity exhibited by CPS and CCL in comparison with other cough mixtures. Hence, inclusion of polyvalent metallic ions in cough formulations will enhance the antibacterial potentials of the antihistaminic agents of these cough mixtures, even though, the suppressant and decongestant agents have not be implicated in any antibacterial activity.

Conclusion

The study shows that cough mixtures containing antihistamines and polyvalent cations could exhibit antibacterial activity to a varied extent and possibly provide protection in infections of upper respiratory tract as a result of the susceptibility pattern exhibited by the *Streptococcus species*. However, their degree of antibacterial activity, effectiveness in controlling any disease causing cough as well as desensitizing cough

Table 1. Susceptibility profile of different bacterial isolates to different cough mixtures.

S/n	Zones of inhibition (± 1.0 mm) produced by different cough mixtures							
Tested Isolates	**CPS**	**OCM**	**MCL**	**CCL**	**BDCS**	**OCS**	**CNDCS**	**TCS**
ST_3	16	0	13	18	0	0	14	0
ST_4	26	0	12	23	0	0	0	0
ST_7	16	0	12	18	0	0	10	0
ST_{9R}	16	0	12	17	0	0	11	10
ST_{12}	21	0	12	21	0	0	13	0
ST_{13}	20	23	17	18	18	16	15	14
ST_{15}	18	0	17	20	0	10	12	11
ST_{16}	16	0	0	24	22	21	20	0
ST_{17}	18	0	12	20	0	0	10	10
ST_{19R}	17	0	15	22	0	0	11	14
ST_{21}	14	0	11	15	0	0	0	10
ST_{35}	15	0	11	16	0	0	12	11
ST_{36r}	22	0	0	21	23	11	15	0
ST_{43}	12	0	10	10	0	0	0	0
ST_{45}	18	0	12	18	0	0	0	0
ST_{47}	30	0	0	28	0	0	0	0
ST_{49}	23	0	12	23	0	0	0	0
ST_{51R}	18	0	14	20	0	10	12	11
ST_{53R}	30	13	13	15	0	0	17	11
ST_{59}	27	0	13	32	0	0	18	15
ST_{60}	13	0	0	10	0	0	0	0
EC_7	20	13	14	17	11	0	0	0
EC_{10}	18	0	10	16	0	0	0	0
KLP_5	14	0	0	13	0	0	0	0
KLP_6	11	18	16	10	17	0	0	0
SAT_1	0	0	0	0	0	0	0	0
SAT_2	19	0	10	13	0	0	12	0
SAT_4	22	0	0	21	0	0	0	0
SAT_6	13	0	0	13	0	0	0	0
SAT_7	13	0	0	12	0	0	0	0
SAT_8	13	0	0	12	0	0	0	0
EC (ATCC 25922)	13	0	14	14	0	0	0	0
KLP (ATCC 13883)	0	0	0	0	0	0	0	0
SA (ATCC 25923)	18	0	17	16	0	0	13	0
SS (ATCC 25913)	13	0	10	12	0	13	0	0

ST series: *Streptococcus species*, EC series: *Escherichia coli*, KLP Series: *Klebsiella pneumoniae*; SAT series: *Salmonella typhi*, SA: *Staphylococcus aureus,* SS: *Shigella sonne.*

pathways will depend on the quantity per milliliter volume of each of the active ingredients included in their compositions.

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