Research Paper

Some Nigerian anti-tuberculosis ethnomedicines: A preliminary efficacy assessment

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ARTICLE INFO

ABSTRACT

Ethnopharmacological significance: Nigerian herbalists possess indigenous ethnomedicinal recipes for the management of tuberculosis and related ailments. A collaborative preliminary modern scientific evaluation of the efficacy of some Nigerian ethnomedicines used by traditional medicine practitioners (TMPs) in the management of tuberculosis and related ailments has been carried out.

Materials and methods: Ethnomedicinal recipes (ETMs) were collected from TMPs from locations in various ecological zones of Nigeria under a collaborative understanding. The aqueous methanolic extracts of the ETMs were screened against Mycobacterium bovis, BCG and Mycobacterium tuberculosis strain $H_{37}Rv$ using the broth microdilution method.

Results: Extracts of ETMs screened against BCG showed 69% activity against the organism. The activities varied from weak, $\leq 2500\ \mu g/mL$ to highly active, $33\ \mu g/mL$ 64% of the extracts were active against Mycobacterium tuberculosis The activities of the extracts against Mycobacterium tuberculosis varied from weak,

$\leq 2500\ \mu g/mL$ to highly active, $128\ \mu g/mL$. There was 77% agreement in results obtained using BCG or Mycobacterium tuberculosis as test organisms.

Conclusion: The results show clear evidence for the efficacy of the majority of indigenous Nigerian herbal recipes in the ethnomedicinal management of tuberculosis and related ailments. BCG may be effectively used, to a great extent, as the organism for screening for potential anti-Mycobacterium tuberculosis agents. A set of prioritization criteria for the selection of plants for initial further studies for the purpose of antituberculosis drug discovery research is proposed.

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1. Introduction

1.1. Tuberculosis as a global health problem

Tuberculosis (TB) is a chronic bacterial infection caused by the bacillus, Mycobacterium tuberculosis and easily transmitted from person to person through the air by droplet nuclei (Moulding, 1988). Tuberculosis remains a leading cause of death in the world from a single infectious agent. It is estimated that one-third of the world's population is infected with the tubercle bacillus and about 80% of individuals diagnosed with the disease every year live in the 22 most populous countries (Dye et al., 1999; Dye, 2006).

Effective treatment of TB has been hampered by the emergence of drug resistant strains of *Mycobacterium tuberculosis*. Particularly, ominous is the emergence of multi-drug resistant TB (MDR-TB) and extensively-drug resistant TB (XDR-TB), which has been accelerated by the rise of Human Immune Virus/Acquire Immune Deficiency Syndrome, HIV/AIDS (Smith and Moss, 1994; CDC, 2006). Despite the introduction of Directly-Observed Therapy Short course (DOTS) by WHO in 1995 (The Economist, 1995), a control strategy to detect and cure TB, millions of TB patients continue to perish (Whalen, 2006).

1.2. Antituberculosis drug discovery efforts and the need for more vigorous drug discovery efforts

Though there are many efforts being made to discover new drugs to treat TB, these efforts are not a major focus of many pharmaceutical companies. There are some notable successes from pharmaceutical companies as exemplified by the recently FDA-approved Bedaquiline. The reasons for the lack of more vigorous investments by the industry are mainly economic as the countries, most in need of new anti-TB drugs, are primarily developing countries whose populations are not able to buy expensive drugs that would arise from the costs of investing huge sums to develop. Current antituberculosis chemotherapy demands the taking of up to four drugs simultaneously over a period of six months which leads to poor adherence by patients and demands close supervision of patients to mitigate the development of drug-resistance. MDR-TB and XDR-TB, which require therapy for up to two full years with multiple poorly-active second-line drugs, have compounded the problem of achieving success and have a high percentage of treatment failure (Mitnick et al., 2003;Gandhi et al., 2010). Many of the drugs used in the treatment of MDR-TB and XDR-TB also have serious toxic effects (Carroll et al., 2012). New drug scaffolds and drugs need to be found and developed which will reduce the current long duration of therapy, reduce the pill burden, successfully treat MDR-TB and XDR-TB, be co-administrable with anti-HIV and anti-diabetes drugs and exhibit less toxic side effects (Barry, 2003).

1.3. TB in Nigeria and the need to investigate the efficacy of ethnomedicines and medicinal plants in Nigeria for the purpose of discovering new TB drugs

Tuberculosis was declared a national emergency in Nigeria in June 2006. The country was ranked one of the most highly TB burdened countries in the world with an estimated incidence of all forms of TB at 311 per 100,000 population (WHO, 2008).

In Nigeria, a large percentage of the population, particularly in the rural areas, depend on traditional medicines for their primary health care. Traditional medicine is a broad term used to describe non-western medicine. Ethnomedicine is a form of traditional medicine that includes the use of plants for healing by humans (Iwu, 2002). Ethnomedicine is a preferred choice for many people as it is readily available and more affordable. Plants have contributed significantly as starting points for the development of modern drugs (Newman et al., 2005; Newman and Cragg, 2007; Khazir et al., 2013) as evidenced by taxol in cancer and artemisinin in malaria. This may be attributed to their chemical diversity, biochemical specificity, possession of a greater number of chiral centers than in synthetic or combinatorial libraries, and evolutionary pressures to create biologically active compounds by interactions with different proteins and biological targets (Queiroz et al., 2009; Wolfender, 2009). Plants therefore, represent potential sources of new drugs acting through novel mechanisms in the search for new and more potent and safe antituberculosis agents. There are a number of natural plant metabolites that have

been reported to have inhibitory or bactericidal activities *in vitro* against *Mycobacterium tuberculosis* at micromolar concentrations (Copp, 2003; Okunade et al., 2004; Copp and Pearce, 2007). Such reports carry hope of success in fully planned isolation and synthetic strategies to discover new antituberculosis drugs in plants. It is estimated that there are about 250,000–500,000 plant species and only about 10 percent of these has been phytochemically investigated for the purpose of determining biological activity of their components (Hostettmann et al., 1996). A very high percentage of these unstudied plants are endemic to Africa and Asia. Nigeria's bio-resource is massive and diverse and is divided into various climatic zones that include marine mangrove, rainforest, Sudan savannah, derived savannah and the Mediterranean. Nigeria possesses over 5000 plant species and also has a culture and history that is very rich in ethnomedicine.

1.4. The aim of the study

The aim of the work reported here was to initiate a collaborative and preliminary sample study of Nigerian ethnomedicines used by the traditional medicine practitioners (TMPs), living across various ecological zones in the Country, for the management of coughs including bloody cough (tuberculosis), and to evaluate the scientific basis for the use of these traditional remedies.

2. Materials and methods

2.1. Study sites

Eight states of the Federation located in various climatic zones (Fig. 1) were visited between August 2005 and February 2006 for the purpose of interviewing individual traditional medicine practitioners (TMPs) about their experience of treating TB and collection of herbal anti-TB recipes and medicines. Ethnobotanical studies were carried out in four geographical regions of Nigeria comprising the South West, South South, South East and North Central. This survey included Lagos, Ogun, Oyo, Edo, Enugu, Niger, Plateau, Kaduna states and the Federal Capital territory, Abuja.

2.1.1. Interviews

The TMPs were interviewed using copies of the same questionnaire for all the TMPs. The questionnaire was titled "The effectiveness of Nigerian Traditional Medicines for the Treatment of Tuberculosis" and included in it were the following sections: (a) Personal details of the healer, (b) Questions about the healer and his/her practice, (c) Questions about tuberculosis and (d) Herbal remedy. Information was also collected on (i) the nomenclature; botanical, common and native names of the plants used, (ii) part of the plant used (stem, leaves or roots), (iii) special time of collection, (iv) the habitat and mode of growth of plant (wild, cultivated), and (v) mode of collection and drying of plant. The questionnaire requested the TMPs, Table 1 to provide their bio-data, knowledge about TB, their anti-TB recipes, dosage and duration of treatment, plant collection guidelines and procedure for preparing the medicines. In most of the interviews, the TMPs could only communicate in their local language, and a person was at hand to translate and complete the questionnaire in English.

(c) Many of the TMPs could not be reached for recollection and collection of their respective ETM formulation plant details. Nevertheless, such ETMs have been included and the names and location of the TMPs concerned are in Table 1 to guide further investigation.