Medicinal plants used to treat TB in Ghana

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Aims: The current study was designed to document medicinal plant species that are traditionally used to treat tuberculosis (TB) by Ghanaian communities.

Methods: The medicinal plants used against TB or its signs and symptoms were selected using library and online published data searches. A guided questionnaire interview was also conducted with a botanist involved in plant collection at the Centre for Scientific Research into Plant Medicine (CSRPM) at Mampong. Data obtained were entered in Excel and summarized into means and frequencies using SPSS 12.0.1 for windows, and expressed as tables and bar graphs.

Results: A total of 15 medicinal plant species distributed between 13 genera and 13 families were documented. The following medicinal plant species were found to be used against TB in Greater Accra and Eastern parts of Ghana: Azadirachta indica A. Juss. Stem bark (Meliaceae), Hygrophila auriculata Heine, whole plant (Acanthaceae), Chenopodium ambrosioides L. leaves (Amaranthaceae), Coix lacryma-jobi L. glumes (Poaceae), Solanum torvum Sw. unripe fruits (Solanaceae), Solanum torvum Sw. leaves (Solanaceae), Bidens pilosa L. whole plant (Asteraceae), Phyllanthus fraternus G.L. Webster leaves (Phyllanthaceae), Dissotis rotundifolia (Sm.) Triana, leaves (Melastomataceae), Cymbopogon giganteus Chiov. Leaves (Poaceae), Cyperus articulatus L. roots (Cyperaceae), Allium sativum L. bulb (Amaryllidaceae), Aloe vera var. barbadensis aqueous extract from leaves (Xanthorrhoeaceae), Aloe vera var. barbadensis organic extract from leaves (Xanthorrhoeaceae), Cocos nucifera Linn, water (Arecaceae) and Cocos nucifera Linn. Husk (Arecaceae).

Conclusions: The collected plant species could be a source of a new class of drugs against TB. Bioactivity guided fractionation is recommended to identify lead compounds for antitubercular activity. The current paper documents the first time medicinal plant species used by Ghanaian communities to treat TB. These results are a basis for selection of plants for further pharmacological, toxicological and phytochemical studies in developing new plant-based antimycobacterial drugs.

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Introduction

Tuberculosis (TB) is a major public health concern with over 2 billion people currently infected, 8.6 million new cases per year, and more than 1.3 million deaths annually [1]. The current drug regimen combination for TB consists of isoniazid, rifampicin, ethambutol and pyrazinamide, administered over six months [2,3]. Although this treatment has a high success rate, the utility of this regimen is limited by compliance issues, which has resulted in the rise of strains that are resistant to some or all of the first- and second-line antibiotics [4]. These strains, called multidrug resistant (MDR), extensively drug resistant (XDR) and totally drug resistant (TDR) strains of Mycobacterium tuberculosis (M. tb), have worse disease outcomes [5]. Widespread introduction of antibiotics in the 1940s, beginning with penicillin [6–8] and streptomycin [9] transformed medicine, providing effective cures for the most prevalent diseases of the time. Resistance development limits the useful lifespan of antibiotics and results in the requirement of a constant introduction of new compounds [10]. However, antimicrobial drug discovery is uniquely difficult [11], primarily due to poor penetration of compounds into bacterial cells. Recent efforts in TB drug development have resulted in the discovery of new therapeutics, including delamanid (previously known as OPC 67683) and bedaquiline (previously known as TMC 207), which retain activity against MDR and XDR M. tb strains. However, additional drugs are urgently needed. Natural products and their plant-derived analogs are often a source of drugs or drug templates with limited toxicity, which has the potential to mitigate compliance issues during protracted administration. Plant-based drugs have been used worldwide in traditional medicines for the treatment of various diseases and Ghana is no exception. Approximately 60% of the world’s population still relies on medicinal plants for their primary healthcare. According to a survey by the National Cancer Institute (NCI), United States of America (USA), 61% of the 877 small-molecule new chemical entities introduced as drugs worldwide during the period 1981–2002 were inspired by natural product research [12]. Plant species still serve as a rich source of many novel biologically active compounds, yet very few plant species have been thoroughly investigated for their medicinal properties [13], and thus, there is renewed interest in phytomedicine research.

TB is a huge public health problem in Ghana [14]. It is estimated that approximately 20,000 people contracted TB in Ghana in 2011, of which around 22% were not detected and/or reported [13,14]. According to 2011 data from the World Health Organization (WHO), 14,962 cases of TB were reported, comprising an incidence of 79 cases per 100,000. Of these, 18 cases per 100,000 corresponded to co-infection with Human Immunodeficiency Virus-Tuberculosis (HIV-TB) co-infection [15]. The Ghanaian population still suffers the problems typical of an underdeveloped, tropical country, with clear and markedly high death rates resulting from malnutrition, tropical infectious diseases, and low vaccine coverage. In Ghana, it is estimated that around 70% of healthcare is provided by traditional healers using medicinal plants. There is an estimated one traditional healer for every 400 inhabitants, and one physician with conventional medical training for every 6200 (in Accra, the capital city) to 42,200 inhabitants in the rural areas [16]. To achieve global control of this epidemic, there is an urgent need for new TB drugs which can: (1) shorten treatment duration; (2) target MDR or XDR strains; (3) simplify treatment by reducing the daily pill burden; (4) lower dosing frequency (for example, a once-weekly regimen); and (5) be co-administered with HIV medications [17]. The current study was thus designed to document medicinal plant species traditionally used by the Greater Accra and Eastern communities of Ghana to treat TB.

Materials and methods

Library and online published data searches

A library search was carried out on medicinal plant species used in traditional medicine to treat TB. In particular, plants cited in the book “African traditional medicine: a dictionary of plant use and applications” [18] and growing in Ghana were selected, verified if they already had been identified at the Herbarium of the Centre for Scientific Research into Plant Medicine (CSRPM), Mampong, and assigned a voucher number as a specimen collection of the CSRPM, with the help of the CSRPM botanist team, led by Mr. Ofori Lartey. Plant species were collected from the Greater Accra and Eastern regions of Ghana as shown in Fig. 1.

Guided questionnaire interview

A guided questionnaire interview was also administered to the botanist at CSRPM. The interview elicited information on plant species used in the traditional treatment of TB. All species obtained from literature and those mentioned during the interview were collected during July and December 2014 and are indexed as MN (Mwanzia Nguta). The specimens were identified at the Herbarium of the Centre for Scientific Research into Plant Medicine (CSRPM), Mampong, and named according to the Flora of West Tropical Africa in accordance with the international code for botanical nomenclature. The specimens were deposited at the CSRPM. Data obtained were entered in Excel and summarized into means and frequencies using SPSS 12.0.1 for windows, and expressed as tables and bar graphs. Ethical approval for this study was granted by the Scientific and Technical Committee of Noguchi Memorial Institute for Medical Research (STC-NMIMR), project identification number EC/060/08. Before interviewing the botanist at CSRPM, the objectives of the study, method and planned use of the information were explained, and permission to conduct the interview was sought. Verbal consent was obtained in all cases before the interview was carried out. Selected plants used against TB were also checked if they were published elsewhere in Africa, apart from the work of Neuwinger [18].
Information on plant extraction procedures utilized by the Greater Accra and Eastern communities of Ghana was also sought after from the online and library search. The interview conducted with the botanist at CSRPM also generated information in regard to the methods used traditionally to extract the active constituents from the anti-TB medicinal plant species.

Results

Medicinal plant species used by the Greater Accra and Eastern communities to treat TB

The global problem presented by the rise in multidrug-resistant strains of TB has necessitated research for new sources
of lead antimycobacterial compounds. The current study was designed to document antimycobacterial plants traditionally used by Ghanaian communities to treat TB. A total of 15 plant species distributed between 13 genera and 13 families were documented as illustrated in Table 1. The documented medicinal plants were: Azadirachta indica A. Juss. Stem bark (Meliaceae); Hygrophila auriculata Heine. whole plant (Acanthaceae); Chenopodium ambrosioides L. leaves (Amaranthaceae); Coix lacryma-jobi L. glumes (Poaceae); Solanum torvum Sw. unripe fruits (Solanaceae); Solanum torvum Sw. leaves (Solanaceae); Bidens pilosa L. (Asteraceae); Phyllanthus fraternus G.L. Webster leaves (Phyllanthaceae); Dissotis rotundifolia (Sm.) Triana leaves (Melastomataceae); Cymbopogon giganteus Chiov. Leaves (Poaceae); Cyperus articulatus L. roots (Cyperaceae); Allium sativum L. bulb (Amaryllidaceae); Zingiber officinale Roscoe rhizomes (Zingiberaceae); Allium cepa L. bulbs (Amaryllidaceae); A. cepa L. leaves (Amaryllidaceae); Aloe vera var. barbadensis leaves (Aloe vera var. barbadensis leaves (Xanthorrhoeaceae); Cocos nucifera Linn. Water (Arecaceae) and C. nucifera Linn. husk (Arecaceae).

Different families produced varying numbers of anti-TB plant species, with the highest number of medicinal plants documented belonging to the Amaryllidaceae family as demonstrated in Fig. 2.

Leaves were reported to be the most commonly used plant to treat TB as shown in Fig. 3 below.

The local Ghanaian communities use water mainly to prepare anti-TB treatments from the listed plant parts as decoctions or infusions. These extraction methods have been utilized since time immemorial, and to the best of their knowledge, they yield active principles required to treat TB. The studied plant species have been shown to possess activity against the slow growing pathogenic strain of M. tb as shown in Table 2 below. This observation further validates the ethnomedical use of the studied ethnobotanicals in traditional medicine to treat conditions with signs and symptoms that closely resemble TB. These reports clearly indicate that Ghanaian communities can be trusted with their knowledge, and the documented medicinal plants are a potential source of a new class of drugs against TB.

Discussion

TB remains a major global health problem [19]. It causes ill-health among millions of people each year and ranks as the second leading cause of death from an infectious disease.
Table 2 – Literature reports on pharmacological and phytochemical properties of documented anti-tb plants.

<table>
<thead>
<tr>
<th>Plant species</th>
<th>Family</th>
<th>Pharmacological activity reported</th>
<th>Reported phytochemical constituents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azadirachta indica A. Juss.</td>
<td>Meliaceae</td>
<td>Activity against S. aureus; E. coli and K. pneumoniae [22], M. smegmatis and M. aurum [23]</td>
<td>Flavonoids, tannins [22]</td>
</tr>
<tr>
<td>Hygrophila auriculata Heine.</td>
<td>Acanthaceae</td>
<td>No reports</td>
<td>Saponins, alkaloids, steroids, tannins, flavonoids and</td>
</tr>
<tr>
<td>Chenopodium ambrosioides L.</td>
<td>Amaranthaceae</td>
<td>Activity against MDR strains of M. tb [32]</td>
<td>triterpenoids [23,31]</td>
</tr>
<tr>
<td>Coix lacryma-jobi L.</td>
<td>Poaceae</td>
<td>Antimutagenic activity [34]</td>
<td>p-Hydroxybenzaldehyde, vanillin, syringaldehyde,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>trans-coniferylaldehyde, sinapaldehyde, and coixol [34]</td>
</tr>
<tr>
<td>Solanum torvum Sw. (unripe fruits)</td>
<td>Solanaceae</td>
<td>Activity against M. tb H37Rv [26]</td>
<td>Sterols, tannins, saponins, flavonoids, glycosides [33]</td>
</tr>
<tr>
<td>Bidens pilosa L.</td>
<td>Asteraceae</td>
<td>Activity against M. tb H37Rv [26]</td>
<td>Sterols, tannins, saponins, flavonoids, glycosides [33]</td>
</tr>
<tr>
<td>Dissotis rotundifolia (Sm.) Triana</td>
<td>Melastomataceae</td>
<td>No reported activity</td>
<td>Chalcone glucosides [35]</td>
</tr>
<tr>
<td>Cymbopogon giganteus Chiov.</td>
<td>Poaceae</td>
<td>No reported activity</td>
<td>Alkaloids, tannins, saponins, terpenoids and steroids</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>C-glycosyl-flavones, orientin, vitexin, isovitexin [37]</td>
</tr>
<tr>
<td>Cyperus articulatus L.</td>
<td>Cyperaceae</td>
<td>Anti-Onchocerca activity [39]</td>
<td>Acyclic alcohol (1-hentriacontanol), three triterpenes</td>
</tr>
<tr>
<td>Allium sativum L.</td>
<td>Amaryllidaceae</td>
<td>Active against M. tb MDR strains and H37Rv [21]</td>
<td>(sistoloster, stigmasterol and methoxyparkeol) and a</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>dipeptide (N-benzoylphenylalanine-Nbenzoylphenylalaninate) [38]</td>
</tr>
<tr>
<td>Zingiber officinale Roscoe</td>
<td>Zingiberaceae</td>
<td>Antimicrobial activity [29]</td>
<td>Monoterpenoids, sesquiterpenoids, phenols [29]</td>
</tr>
<tr>
<td>Allium cepa L. (bulb)</td>
<td>Amaryllidaceae</td>
<td>Active against M. tb MDR strains and H37Rv [21]</td>
<td>Alkaloids, flavonoids, cardiac glycosides, terpenes,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>resin [40]</td>
</tr>
<tr>
<td>Allium cepa L. (leaves)</td>
<td>Amaryllidaceae</td>
<td>Active against M. tb MDR strains and H37Rv [21]</td>
<td>Alkaloids, flavonoids, cardiac glycosides, terpenes,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>resin [40]</td>
</tr>
<tr>
<td>Aloe vera var. barbadensis</td>
<td>Xanthorrhoeaceae</td>
<td>Active against M. tb MDR strains and H37Rv [21]; Active against S. pyogenes and P. aeruginosa [42]</td>
<td>Tannins, saponins, flavonoids, terpenoids [42]</td>
</tr>
<tr>
<td>(organic extract)</td>
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</tr>
<tr>
<td>(aqueous extract)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Cocos nucifera Linn. (water)</td>
<td>Arecaeeae</td>
<td>Anticancer activity [41]</td>
<td>Phytohormones (cytokinins, auxin, gibberellins,</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>abscisic acid, salicylic acid [41]</td>
</tr>
</tbody>
</table>
worldwide, after HIV [20]. Today, many of the drugs currently used are derived from natural products or have depended upon a natural product for their development, and the recent discoveries of the antimalarial artemisinin and the anticancer agent taxol indicate the continuing importance of plant species in drug discovery. However, only a small proportion of plant species have been thoroughly investigated for their medicinal properties [19] and undoubtedly there are many novel biologically active compounds yet to be discovered. The current study was designed to document antimycobacterial plant species used by the Greater Accra and Eastern communities of Ghana. A database of medicinal plants used to treat TB by Ghanaian communities was generated. To the best of the present research’s knowledge, the current paper reports for the first time medicinal plant species used in Ghana to treat TB. This repository of selected anti-TB plants can be used in future studies aimed at high throughput screening for antimycobacterial activity using fast-growing laboratory strains of Mycobacterium smegmatis. Such studies may lead to the isolation of active ligands against sensitive, latent and drug-resistant strains of M. tb. A total of 15 plant species belonging to 13 genera and distributed in 13 families as summarized in Table 1 were documented. The majority of these species belonged to the families Amaryllidaceae (3), Xanthorrhoeaceae (3), Arecaceae (2), Poaceae (2) and Solanaceae (2) as indicated in Table 1. A diverse group of phytochemical compounds and pharmacological activities have been associated with the documented plant species as reported in Table 2, supporting their ethnopharmacological use against TB by the Ghanaian communities.

The use of some of the documented antituberculous plants is supported by earlier observations of antimycobacterial activity [21] against MDR strains and laboratory reference strain H37Rv while screening aqueous extracts of A. sativum, A. cepa and Aloe vera using Lowenstein–Jensen medium and Middlebrook 7H9 broth. The observed antimycobacterial activity validates the ethnopharmacological utilization of the medicinal species to treat TB, and calls upon further investigation to isolate the phytochemical compounds responsible for the reported activity. Methanolic and ethanolic crude extracts obtained from A. indica have been reported to possess potent activity against Escherichia coli, K. pneumonia and methicillin resistant S. aureus [22], while moderate activity from methanolic leaf extracts against M. smegmatis and M. aeurum has been reported [23]. The observed biological activities, especially those against mycobacterial species, adds more weight to the ethnomedical reports in regard to the use of A. indica crude extracts against TB, justifying why more studies are required to isolate and purify the active constituents responsible for the reported activity. This observation further validates the ethnobotanical usage of the documented plants against TB by Ghanaian communities. The utilization of leaves from H. auriculata as antituberculous agents has been reported in Uganda, East Africa [24]. This cross-cultural acceptance and use of the same plant species in different geographical zones is an indication of the potential of the plant species as a future source of a new class of drugs against TB. The documentation of the plant species in Uganda supports the Ghanaian traditional claims in regard to the antituberculous activity of H. auriculata, calling for more studies aimed at isolating and characterizing the phytochemicals responsible for the reported anecdotal efficacy of the said plant. Antimicrobial activity from the acetonolic leaf extracts obtained from Chenopodium ambrosoides against MDR strains of M. tb has been reported [25], validating the ethnopharmacological use of the plant among Ghanaian communities and the inclusion of the plant in Ghanaian pharmacopoeia as a potential source of anti-TB drugs. This observation adds more weight to the documentation of the said plant in regard to its traditional use against TB. Moderate inhibition of the pathogenic laboratory reference strain H37Rv by hydromethanolic fruit extracts from S. torvum has been observed [26] in Malaysia, validating the ethnopharmacological use of the unripe fruits against TB by the Ghanaian communities. This observation is in agreement with this documented report and supports further studies in search for anti-TB drugs from Ghanaian pharmacopoeia.

The use of the plant in different continents throws more weight into the antimycobacterial potential of the documented plant, calling for more resources to disclose the active ligands behind the reported observation. The leaves of B. pilosa from Rwanda have been reported to possess activity against M. tb [27] further validating the use of this plant in Ghanaian ethnotherapy and this subsequent documentation of the said plant for further investigations in search of an agent against TB. Scientists from Kwazulu Natal have reported C. articulatus to be used traditionally against cough and related upper respiratory tract conditions [28], supporting the traditional use of the plant against TB in Ghana. The use of the plant for related illnesses in different countries further validates its ethnopharmacological utilization and positions it as a possible source of future agents against TB. Ginger (Z. officinale) extract (10 mg/kg) administered intraperitoneally has been shown to possess a dose-dependent antimicrobial activity against Pseudomonas aeruginosa, Salmonella typhimurium, E. coli and Candida albicans. In addition, out of 29 plant extracts screened, ginger extract was found to have the broadest range of anti-fungal activity measured either by the fungi inhibited or as the average diameter of the zones of inhibition and was the only crude extract that was active against Rhizopus sp., an organism that was not inhibited by any of the other plant extracts tested or by the anti-fungal agent ketoconazole or berberine [29]. Based on these findings, it is plausible to argue out that the crude extract could be efficacious against M. tb, underpinning its traditional use by the Ghanaian communities to treat TB. This calls for evaluation of the antimycobacterial activity of Z. officinale crude extracts using M. tb specific assays. Selective antimicrobial activity against S. aureus has been observed while evaluating C. nucifera for antimicrobial activity [30]. Since this plant enjoys diverse medicinal uses [30], other activities, including antimycobacterial activity, may be identified using different biological assays. C. nucifera may be important in the identification of some novel agents against drug-resistant strains of M. tb. The majority of the plants documented in this study were collected from community land, which is facing great pressure due to overutilization of indigenous trees and hence medicinal plants may disappear before their uses are documented. Most of the inhabitants of Greater Accra and Eastern regions of Ghana are in the low social-economic
We have no conflict of interest to declare.

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REFERENCES


