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Medicinal plants used to treat TB in Ghana

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ABSTRACT

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), *Zingiber officinale* Roscoe, rhizomes (Zingiberaceae), *Allium cepa* L. bulbs (Amaryllidaceae), *Allium cepa* L. leaves (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 antimycobacterial activity. The current paper documents for 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 by the staff of CSRPM 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].

Fig. 1 – Map of Ghana. *Source:* www.mapsofworld.com.

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

Table 1 – Plant species collected from Ghana based on literature reports on their use as anti-tb plants.

Plant species	Voucher specimen Number	Family	Plant part
Azadirachta indica A. Juss.	MND14/7	Meliaceae	Stem bark
Hygrophila auriculata Heine.	MNS14/7	Acanthaceae	Whole plant
Chenopodium ambrosioides L.	MNA14/7	Amaranthaceae	Leaves
Coix lacryma-jobi L.	MNO-K24/7	Poaceae	Glumes
Solanum torvum Sw.	MNB-N(A)24/7	Solanaceae	Unripe fruits
Solanum torvum Sw.	MNBL-N(A)24/7	Solanaceae	Leaves
Bidens pilosa L.	MNM24/7	Asteraceae	Whole plant
Phyllanthus fraternus G.L. Webster	MNM20/7	Phyllanthaceae	Leaves
Dissotis rotundifolia (Sm.) Triana	MNM22/7	Melastomataceae	Leaves
Cymbopogon giganteus Chiov.	MNM21/7	Poaceae	Leaves
Cyperus articulatus L.	MNB31/7	Cyperaceae	Roots
Allium sativum L.	MNK31/7	Amaryllidaceae	Bulbs
Zingiber officinale Roscoe	MNK24/7	Zingiberaceae	Rhizomes
Allium cepa L.	MNKB14/7	Amaryllidaceae	Bulbs
Allium cepa L.	MNKL14/7	Amaryllidaceae	Leaves
Aloe vera var. barbadensis	MNMA26/11	Xanthorrhoeaceae	Leaves (aqueous extract)
Aloe vera var. barbadensis	MNM026/11	Xanthorrhoeaceae	Leaves (Organic extract)
Cocos nucifera Linn.	MNKW14/12	Arecaceae	Coconut water
Cocos nucifera Linn.	MNKH14/12	Arecaceae	Husk

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); *S. 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); *Zingiber officinale* Roscoe rhizomes (Zingiberaceae); *Allium cepa* L. bulbs (Amaryllidaceae); *A. cepa* L. leaves (Amaryllidaceae); *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

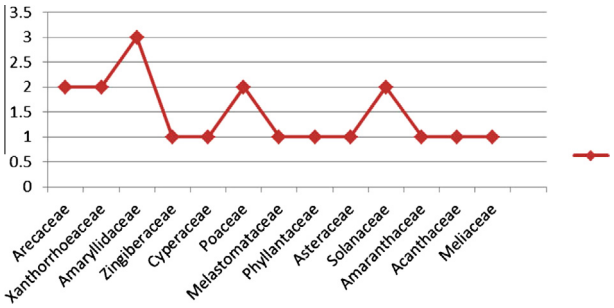

Fig. 2 – Families with plant species used against tuberculosis.

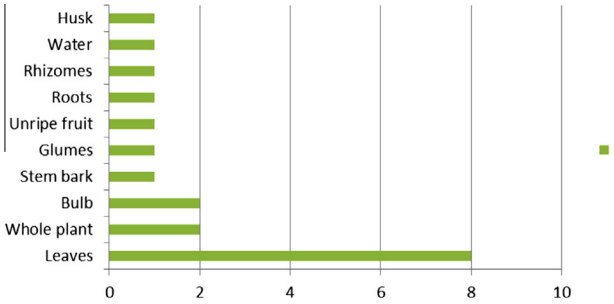

Fig. 3 – Plant part used to treat tuberculosis.

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.

Plant species	Family	Pharmacological activity reported	Reported phytochemical constituents
Azadirachta indica A. Juss.	Meliaceae	Activity against *S. aureus*; *E. coli* and *K. pneumoniae* [22], *M. smegmatis* and *M. aurum* [23]	Flavonoids, tannins [22]
Hygrophila auriculata Heine.	Acanthaceae	No reports	Saponins, alkaloids, steroids, tannins, flavonoids and triterpenoids [23,31]
Chenopodium ambrosioides L.	Amaranthaceae	Activity against MDR strains of *M. tb* [32]	Phenolics, flavonoids, saponins, ecdysteroids and triterpenoids [32]
Coix lacryma-jobi L.	Poaceae	Antimutagenic activity [34]	p-Hydroxybenzaldehyde, vanillin, syringaldehyde, trans-coniferylaldehyde, sinapaldehyde, and coixol [34]
Solanum torvum Sw. (unripe fruits)	Solanaceae	Activity against *M. tb* $H_{37}Rv$ [26]	Sterols, tannins, saponins, flavonoids, glycosides [33]
Solanum torvum Sw. (leaves)	Solanaceae	Activity against *M. tb* $H_{37}Rv$ [26]	Sterols, tannins, saponins, flavonoids, glycosides [33]
Bidens pilosa L.	Asteraceae	Activity against drug sensitive *M. tb* [27]	Chalcone glucosides [35]
Phyllanthus fraternus G.L. Webster	Phyllanthaceae	No reported activity	Alkaloids, tannins, saponins, terpenoids and steroids [36]
Dissotis rotundifolia (Sm.) Triana	Melastomataceae	No reported activity	C-glycosyl-flavones, orientin, vitexin, isovitexin [37]
Cymbopogon giganteus Chiov.	Poaceae	No reported activity	Acyclic alcohol (1-hentriacontanol), three triterpenes (sistosterol, stigmasterol and methoxyparkeol) and a dipeptide (N-benzoylphenylalanine-Nbenzoylphenylalanilate) [38]
Cyperus articulatus L.	Cyperaceae	Anti-Onchocerca activity [39]	Terpenoids, hydrocarbons and fatty acids [39]
Allium sativum L.	Amaryllidaceae	Active against *M. tb* MDR strains and $H_{37}Rv$ [21]	Alkaloids, flavonoids, cardiac glycosides, terpenes, resin [40]
Zingiber officinale Roscoe	Zingiberaceae	Antimicrobial activity [29]	Monoterpenoids, sesquiterpenoids, phenols [29]
Allium cepa L. (bulb)	Amaryllidaceae	Active against *M. tb* MDR strains and $H_{37}Rv$ [21]	Alkaloids, flavonoids, cardiac glycosides, terpenes, resin [40]
Allium cepa L. (leaves)	Amaryllidaceae	Active against *M. tb* MDR strains and $H_{37}Rv$ [21]	Alkaloids, flavonoids, cardiac glycosides, terpenes, resin [40].
Aloe vera var. barbadensis (organic extract)	Xanthorrhoeaceae	Active against *M. tb* MDR strains and $H_{37}Rv$ [21]; Active against *S. pyogenes* and *P. aeroginosa*[42]	Tannins, saponins, flavonoids, terpenoids [42]
Aloe vera var. barbadensis (aqueous extract)	Xanthorrhoeaceae	Active against *M. tb* MDR strains and $H_{37}Rv$ [21]; *S. pyogenes* and *P. aeroginosa* [42]	Tannins, saponins, flavonoids, terpenoids [42]
Cocos nucifera Linn. (water)	Arecaceae	Anticancer activity [41]	Phytohormones (cytokinins, auxin, gibberellins, abscisic acid, salicylic acid) [41]
Cocos nucifera Linn. (husk)	Arecaceae	Selective activity against *S. aureus* [30]	Catechin, epicatechin, tannins [30]

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 (2), 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 Middlebroook 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. aurum* has been reported [23]. The observed biological activities, especially those against mycobacterial species, adds more weight to the ethnobotanical 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 acetonic 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

bracket and very often the medicinal plant use is the only affordable treatment option. Medicinal plant use will therefore remain an integral part of the health care system to the community for a long time to come. Consequently, ethnobotanical exploration should not only be a cost-effective means of locating new and useful tropical plant compounds against TB, but also be linked to the urgent need for sustainable conservation strategies for medicinal plants, since human expansionist demands can be expected to cause environmental deterioration and biotic destruction well into the next century.

Conclusions

The documented medicinal plant species used by the Ghanaian communities are a potential source of a new class of antituberculous drugs. The current study recommends bioactivity guided isolation and purification of lead compounds for antimycobacterial activity from the selected plant species. Many plant species reported in this study have been investigated for their phytoconstituents and pharmacological activities, the latter being in agreement with ethnomedical uses associated with the documented species in Ghana. Nine plant species documented in the current study have not been investigated for their antimycobacterial activity. In Ghana, traditional methods of treatments based on medicinal plants are still an important part of social life and culture, and the acceptability of these plants as claimed effective remedies is quite high among the population of this area. The claimed therapeutic value of the reported species call for modern scientific studies to establish their safety and efficacy and to preserve and document this flora which may otherwise be lost due to erosion of age-old traditional methods of biodiversity conservation and medicinal knowledge [43]. There is a general consensus that traditional knowledge on the use of medicinal plants must be conserved because of its vital role for human well-being. It is often argued that if traditional knowledge which has been generated over a long period of time is lost, exploitation of plants among other things will become difficult, if not impossible. Among the reasons traditional knowledge is considered reliable for the exploitation of herbal remedies is that indigenous communities through a period of long experimentation with herbal medicines are likely to have retained those that are effective and tolerably safe while discarding preparations with low efficacy or acute toxicity [44].

Conflict of interest

We have no conflict of interest to declare.

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