PM Indexing
Escalating Knowledge...

Asian Journal of Bio-Medical Research

E-ISSN: 2454-6275
http://pmindexing.com/journals/index.php/AJBR

REVIEW ARTICLE

Natural Products from African Medicinal Plants for Antituberculosis Therapy

Philip Ifesinachi Anochie

Research Scientist, TB/HIV/AIDS Research Group, Philip Nelson Institute of Medical Research, Lagos, Nigeria.

Address for Correspondence:
Philip Ifesinachi Anochie,
Research Scientist,
Philip Nelson Institute of Medical Research, Lagos, Nigeria.
Telephone: +2348166582414, +2348140624643.
E-mail: philipanochie@yahoo.co.uk.

Submission: 25-07-2017
Revision : 23-09-2017
Publication : 01-10-2017

URN: 0019ajbr.v3i4.14135

How to Cite this Article:
Anochie, Philip Ifesinachi. Natural Products from African Medicinal Plants for Antituberculosis Therapy. Asian Journal of Bio-Medical Research (ISSN:2454-6275), [S.l.], v. 3, n. 4, dec. 2017. ISSN 2454-6275. Available at: <http://pmindexing.com/journals/index.php/AJBR/article/view/1413>. Date accessed: 25 Dec. 2017.

ABSTRACT

This review examines natural products from medicinal plants from Africa as a source of anti-tuberculosis agents. A good number of plant secondary metabolites are reported to have antitubercular activity comparable to the existing antitubercular drugs or sometimes even better. Information regarding the chemistry and pharmacology of plants leads to insight into their structure–activity relationship and potency. A well-defined strategy is required to exploit these phytomolecules as antitubercular drugs.

Keywords: Natural, Products, Africa, Antituberculosis

Introduction

Tuberculosis (TB), which has been and still remains a serious disease to the global human population causing millions of deaths worldwide. The recent increase in the number of multi-drug resistant clinical isolates of *Mycobacterium tuberculosis* has created an urgent need for the discovery and development of new antituberculosis drugs. Also, in Eastern Cape, South Africa has been assayed antitubercular activity of polyherbal formulations with several medicinal plants active to concentrations between 25-50 µg/mL.[1]

Emergence of New Drug Resistant Variants

There is an urgent need to discover new TB drugs. Better and safer drug regimens to shorten treatment is vital in attaining the WHO's ambitious targets of 95% reduction in TB deaths and 90% reduction in TB incidence by 2035.[2]

New Tuberculosis Drug Targets

Some selective targets essential to the survival of the microorganism considered in the development of any anti-TB drug include the cell wall which provides protection to the Mycobacteria and is impermeable to a number of drugs, while also conferring inherent resistance.[3]

Selected Natural Products with Anti-Tb Prospects

Antimycobacterial bioactive chemical molecules have been found from many natural product skeletons, mainly from plant biodiversity (Table 1), but also from other organisms, such as fungi and marine organisms.[4]

Socio-economic Need of Anti-TB Natural Products

Natural products especially plants (Table 2) have played a significant socio-economic role by fulfilling health-care needs and creating business opportunities for the less privileged population of the developing world.[5]

Also, is important to validate the ethnopharmacological uses of biodiversity, with the end to promote the proper use of plants and

Table 1: Compounds that exhibit biological activities correlating with the ethnobotanical uses of the plant species of origin

Plant Species	Phytochemical constituents	Reported pharmacological activity	References
Azadirachta indica A. Juss.	Flavonoids, tannins	Activity against *K. pneumoniae, M. smegmatis and M. aurum*	Dahiya *et al*., (2012)
Chenopodium ambrosioides L.	Phenolics, flavonoids, saponins, ecdysteroids and triterpenoids	Activity against MDR strains of *M. tuberculosis*	Kokanova-Nedialkova *et al*., (2009)
Solanum torvum Sw (fruits and leaves)	Sterols, tannins, saponins, flavonoids, glycosides	Activity against *M. tuberculosis* H37Rv	Chah *et al*., (2000)
Bidens pilosa L	Chalcone glucosides	Activity against drug sensitive *M. tuberculosis*	Nguta *et al*., (2015)
Allium sativum	Alkaloids, flavonoids, cardiac glycosides, terpenes, resin	Active against *M. tuberculosis* MDR strains and H37Rv	Gazuwa *et al*., (2013)
Allium cepa (bulb and leaves)	Alkaloids, flavonoids, cardiac glycosides, terpenes, resin	Active against *M. tuberculosis* MDR strains and H37Rv	Gazuwa *et al*., (2013)
Aloe vera var. barbadensis (aqueous and organic extracts)	Tannins, saponins, flavonoids, terpenoids	Active against *M. tuberculosis* MDR strains and H37Rv	Arunkumar and Muthuselvam (2009)
Acalypha indica, (leaves)	Kaempferol, Acalyphamide quinone, sterols, cyanogenic glycoside	Active against *M. avium*	Rai *et al*., 2010
Allium cepa (bulbs)	allicin, flavonoids; phenolic acids and sterols	Activity against *Mycobacterium tuberculosis*	Gupta *et al*., 2010
Vitex trifolia	Flavonoids-artemetin, luteolin,orientin, casticin; and iridoid glycosides	Activity against *M. smegmatis*	Tandon *et al*., 2008
Zanthoxylum capense (roots)	Benzophenanthridine, decarine, 6- acetonyldyhydronitidine, N-isobutyl-(2E,4E)-2,4-tetradecadienamide	Activity against *M. tuberculosis*	Luo *et al*. (2013)
Trichosanthes dioica (stem and leaves)	Berberine, columbin, chasmanthin, palmarin, tinosporon, tinosporic acid and tinosporol	Activity against drug sensitive *M. tuberculosis*	Arya (2011)
Ocimum sanctum (leaves and seeds)	Ursolic acid, apigenin, orientin, luteolin	Activity against *M. tuberculosis* H37Rv	Birdi *et al*. (2012)
Garcinia nobilis (Stem bark	Smeathxanthone, 8-hydroxycudraxanthone, morisignin, 4-prenyl-2-(3,7-dimethyl-2,-octadienyl) -1,3,5,8-tetrahydroxyvanthone	Activity against *M. tuberculosis* H37Rv	Fouotsa *et al*. (2013)
Ficus chlamydocarpa (stem bark)	Alpinumisoflavone, genistein, laburnetin and luteolin	Activity against drug resistant *M. tuberculosis*	Kuete *et al*. (2010)
Cirtullus colosnthis (deseeded fruits)	Ursolic acid, cucurbitacine E and cucurbitacin I	Activity against *M. tuberculosis* H37Rv	Mehta *et al*. (2013)
Morinda citrifolia, (leaves, roots and fruits)	Anthraquinonesalizarin, nordamnacanthol, Ursolic acid; β-Sitosterol, asperuloside and caproic acid	Activity against drug sensitive *M. tuberculosis*	Birdi *et al*. (2012)
Terminalia avicennioides (Root bark)	Arjunolic acid, friedelin and friedelin-3β-ol	Activity against drug sensitive *M. tuberculosis*	Mann *et al*. (2011)
Oricia suaveolens (stem bark)	Evoxanthine and 1-hydroxy-2,3-dimethoxy-10-methylacridone	Activity against drug sensitive *M. tuberculosis*	Fouotsa *et al*. (2013)
Andrographis paniculata (Leaves)	Andrographolide	Activity against drug sensitive *M. tuberculosis*	Shrivastava and Garg (2014)

Table 2: Biological activity of some derived natural products versus ethnobotanical uses of plant species derived from African flora.

Plant species	Family	Isolated metabolite	Ethnobotanical use	Measured activity	Reference
Tabernaemontana elegans	*Apocynaceae*	Voacangine and dregamine	Applied as a wash to wounds, and drunk for pulmonary diseases and chest pains	Antimicrobial activity	[48]
Artemisia afra	Asteraceae	α-Myrin and betulinic acid	used to treat coughs, colds, diabetes, malaria, sore throat, asthma, headache, dental care, gout and intestinal worms	Antimicrobial activity	[50]
Euclea natalensis	Ebenaceae	Shinanolone, 7- methyljuglone and diospyrin	Used to relief toothache, headache and chest complaints.	Antimycobacterial activity	[51]
Lippia javanica	Verbenaceae	Euscaphic acid, (E)-2 (3)-Tagetenone epoxide, myrcenone, piperitenone or 3- methyl-6-(1-methylethylidene)-cyclohex-2-en-1-one	Infusion is commonly used in Africa as a tea against various ailments like influenza, measles, rashes, malaria, stomach problems, fever, colds, cough, headaches	Antimycobacterial and antimicrobial activity	[52; 53]
Knowltonia vesicatoria	Ranunculaceae	5-(hydroxymethyl) furan-2 (5H)-one and 5- (hydroxymethyl) dihydrofuran-2 (3H)- one	Used traditionally to treat tuberculosis	Antimycobacterial	[55]
Bolusanthus speciosus	Fabaceae	4,7,2'-trihydroxy-4'-methoxyisoflavanol and 5,7,3',4'- tetrahydroxy-5'-(2-epoxy-3-methylbutyl) isoflavanone	dried inner bark of the tree is Used traditionally to relieveabdominal pains, emetism and tuberculosis	Antimicrobial activity	[56; 57]
Helichrysum melanacme	*Asteraceae*	2,4′,6′-trihydroxy-3′-prenylchalcone and 4′,6′,5″-trihydroxy- 6″,6″-dimethyldihydropyrano [2″,3″-2′,3′] chalcone	Used to treat cough, fever, headache, colds and chest pain		[58]
Leonotis leonurus	Lamiaceae	9,13-Epoxy-6-hydroxy-16,15-labdanolide and 9,13:15,16-diepoxy-6,16- labdanediol	Treating colds, bronchitis, tuberculosis, coughs, asthma, feverish headaches, dysentery and chest infections	Antimycobacteria	[53; 54]
Bridelia micrantha	Euphorbiaceae	Friedelin, epifriedelin, gallic acid, ellagic acids, anthocyanidin, taraxerol, taraxerone and caffeic acid.	For treatment of stomach aches, tapeworms, diarrhoea, headaches, sore joints, sore eyes, venereal diseases, and fevers		[59, 60, 61]
Piper capense	Piperaceae		Used for cough, bronchial problems, leprosy and infertility		[62, 63, 64]
Ziziphus mucronata	Rhamnaceae		Bark, leaves and roots are used to treat boils, sores, glandular swellings, diarrhoea, dysentery, expectorant, emetic for coughs, chest problems, boils, sores, glandular swellings	Antimycobacteria	[65, 66, 67]

(Contd...)

Table 3: Biological activity of some derived natural products versus ethnobotanical uses of plant species derived from African flora.

Plant species	Family	Isolated metabolite	Ethnobotanical use	Measured activity	Reference
Berchemia discolor	Rhamnaceae (	(3 S)-discoloranone	Infertility and Menorrhagia	Antimycobacteria	[68; 69]
Peltophorum africanum	Fabaceae	Catechin (flavonoid), bergenin, betulinic acid	Used to treat tuberculosis, stomach complains and intestinal parasites	Antimycobacteria	[70, 71, 72, 73,74,]

find new sources of medicines. This approach is necessary especially in the countries with tuberculosis high burden.[6]

Evaluation of The Bioactive Natural Products

In many countries especially in sub Saharan Africa, ethnobotanical and ethnomedical knowledge have been greatly exploited to evaluate the antimycobacterial properties of plants (Table 3) in vitro using crude extracts.[7] Some crude extracts have shown remarkable antimycobacterial activities against Mycobacterium tuberculosis and other mycobacteria.[8]

The most used methods in antitubercular *in vitro* drug discovery have been described as agar dilution, broth dilution, MGIT 960 fluorescence assay, microplate alamar blue assay (MABA), resazaurin microtiter assay (REMA) and tetrazolium microplate assay. Also, MBEC™ assay system (MBEC™ Biofilm Technologies Ltd. Calgary, AB, Canada) has been employed for to evaluate antibiofilm activity of new drugs so it can be very useful to complement antimicrobial assays of natural products from medicinal plants.[9,10]

Outcome of Evaluated Bioactive Compounds

Interesting results for classes of compounds which exhibit antituberculosis biological activities correlating with the ethno botanical uses of the plant species of origin have been widely obtained. [26] It has been previously reported that extracts of this plant has demonstrated antibacterial activity against *S. aureus* and antimycobacterial activity against *M. smegmatis*.[11]

In vitro studies of A. afra extracts have revealed that the plant is a potential antidepressant, cardiovascular, spasmolytic effects, antioxidant, and antimycobacterial.[12,14]

The three naphthoquinones; shinanolone, 7-methyljuglone and diospyrin demonstrated significant activity against drug sensitive and drug-resistant strains of *Mycobacterium tuberculosis* and lends credence to the ethnomedicinal use of the plant.[15,16]

Green et al. carried out a study in which some selected medicinal plants were collected and their inhibitory properties against *Mycobacterium tuberculosis* was evaluated.[17] The acetone extracts of *Bridelia micrantha*, *Terminalia sericea*, and *Warbugia salutaris* showed a MIC of 25µg/mL against the two tested MTBs trains. The acetone extracts of Berchemia discolor demonstrated the highest antimycobacterial activity with MIC of 12.5µg/mL.[18] According to Ngemenya et al.,some drugs do show potent activity in vivo due to metabolic transformation of their components into highly active intermediates, so can some of these plants with weak activity.[19]

Challenges of Developing Anti-TB Drug from Plants

The classic pathway towards anti-TB drug discovery from natural products and other infectious diseases must overcome a number of challenges. The first is to reliably detect efficacious and safe hits and be able to identify already known compounds at the early stages of the drug discovery program.

The second major challenge is the de novo structure elucidation of new molecular entities. Though current advances in spectroscopic techniques, specifically the high resolution neutron magnetic resonance (NMR) technologies have been contributed to the resolution of this challenge. Many approaches have been developed to solve the major hurdle, but it still remains a major challenge in anti-TB drug discovery from natural products.

Concluding Remarks

It will be difficult to resolve the aforementioned challenges without increased funding for anti-TB drug discovery and construction of a more robust drug development pipeline through well-coordinated international efforts. Plants are sole treatment of leprosy and tuberculosis in some African countries. Though anti-mycobacterial MIC of plant materials is higher but they have resistance modifying properties. Therefore, plant derived drugs can help in fighting the drug resistance.

Acknowledgement

We acknowledge the staff and members of Fundación centro de investigación de bioprospección y biotecnología de la biodiversidad BIOLABB, Colombia for their kind assistance.

References

1. Arun Kumar S and Muthuselvam M. Analysis of phytochemical constituents and antimicrobial activities of aloe vera L. against clinical pathogens. World J Agric Sc 2009; 5(5): 572–576.
2. Bhunu B, Mautsa R and Mukanganyama S. Inhibition of biofilm formation in Mycobacterium smegmatis by Parinari curatellifolia leaf extracts. BMC complementary and alternative medicine 2017; 17(1): 285.
3. Chandrasekhar B, Veeramuthu D, Naif AA, Balakrishna K, Nitin PK, Vikrant SR, et al. Antimicrobial and antimycobacterial activities of methyl caffeate isolated from Solanum torvum Swartz fruit. Indian Journal of Microbiology 2012; 52(4): 676–681.
4. Famewo EB, Clarke AM, Wiid I, Ngwane, A, van Helden P, Afolayan A J , et al. Anti-mycobacterium tuberculosis activity of polyherbal medicines used for the treatment of tuberculosis in Eastern Cape, South Africa. African Health Sciences 2017; 17(3): 780-789.
5. Fomogne-Fodjo MCY, van Vuuren S, Ndinteh DT, Krause RWM and Olivier DK. Antibacterial activities of plants from central Africa used

traditionally by the Bakola pygmies for the treatment of respiratory and tuberculosis related symptoms. J Ethnopharmacol 2014; 155: 123–131.
6. Garcı´a A, Bocanegra-Garcı´a V, Palma-Nicolas JP and Rivera G. Recent advances in antitubercular natural products, Eur J Med Chem 2012; 49: 1–23.
7. GóMez-CANsiNo R, GUZMÁN-GUTIÉRREZ SL, CAMPOS-LARA, MG, ESPITIA-PINZÓN CI and Reyes-Chilpa R. Natural compounds from mexican medicinal plants as potential drug leads for anti-tuberculosis drugs. Anais da Academia Brasileira de Ciências (AHEAD) 2017.
8. Gupta R, Thakur B, Singh P, Singh HB, Sharma VD and Katoch VM. Anti- tuberculosis activity of selected medicinal plants against multi-drug resistant Mycobacterium tuberculosis isolates. Indian J Med Res 2010; 131: 809–813.
9. Gupta VK, Kumar MM, Bisht D and Kaushik A. Plants in our combating strategies against Mycobacterium tuberculosis: progress made and obstacles met. Pharmaceutical Biology 2017; 55(1): 1536-1544.
10. Guzman JD, Gupta A and Bucar F. Antimycobacterials from natural sources: ancient times, antibiotic era and novel scaffolds. Front Biosci (Landmark Ed.)2012; 17: 1861–1881.
11. Sánchez JGB and Kouznetsov VV. Antimycobacterial susceptibility testing methods for natural products research. Brazilian Journal of Microbiology 2010; 41(2): 270-277.
12. Sieniawska E, Swatko-Ossor M, Sawicki R, Skalicka-Wo–niak K and Ginalska G. Natural Terpenes Influence the Activity of Antibiotics against Isolated Mycobacterium tuberculosis. Medical Principles and Practice 2017; 26(2): 108-112.
13. Global Tuberculosis Report; WHO press; Geneva, Switzerland, 2012.
14. World Health Organization WHO. Tuberculosis (TB) Fact sheet Reviewed March 2017.
15. Zofou D, Ntie-Kang F,Sippl W and Efange SM. Bioactive natural products derived from the Central African flora against neglected tropical diseases and HIV. Nat Prod Rep 2013 ;30(8):1098-1120.
16. Efange SMN. Natural products: a continuing source of inspiration for the medicinal chemist, in Advances in Phytomedicine, Ethnomedicine and Drug Discovery, ed. M. M. Iwu and J. C. Wootton, Elsevier Science, Amsterdam, The Netherlands, 2002; 1:61–69.
17. Green E, Samie A, Obi CL, Besong PO and Ndip RN. Inhibitory properties of selected South African medicinal plants against Mycobacterium tuberculosis. Journal of Ethnopharmacology 2010; 130: 151-157.
18. Chin YW, Mdee LK, Mbwambo ZH, Mi Q, Chai HB, Cragg GM, et al. Prenylated flavonoids from the root bark of Berchemia discolor, a Tanzanian Medicinal Plant. Journal of Natural Products 2006; 69: 1649–1652.
19. Ngemenya MN, Mbah JA, Tane P and Titanji VPK. Antibacterial effects of some Cameroonian medicinal plants against common pathogenic bacteria. African Journal of Traditional Complementary and Alternative Medicine 2006; 3: 84–93.

Authors Contribution: **PIA-**Concept and design of the study, reviewed the literature, manuscript preparation, critical revision of the manuscript, collected data and review of study; **BBN-**Concept and design of the study, reviewed the literature, manuscript preparation, critical revision of the manuscript, collected data and review of study; **JB-** Conceptualized study, literature search, prepared first draft of manuscript and critical revision of the manuscript; **FEA-**Conceptualized study, literature search, prepared first draft of manuscript and critical revision of the manuscript; **LNO-** Conceptualized study, literature search, prepared first draft of manuscript and critical revision of the manuscript; **ECO-** Conceptualized study, literature search, prepared first draft of manuscript and critical revision of the manuscript; **ACO-** Concept, collected data and review of literature and helped in preparing first draft of manuscript.

Work attributed to: 1. TB/HIV/AIDS Research Group, Philip Nelson Institute of Medical Research, Lagos, Nigeria. 2. Chemical Bioactivity Information Centre (CBIC) Cameroon. Department of Chemistry, University of Buea, South West Region, Cameroon. 3. Fundación centro de investigación de bioprospección y biotecnología de la biodiversidad BIOLABB, Colombia. 4. Center for Health and Development, University of Port Harcourt Teaching Hospital, University of Port Harcourt, Nigeria. 5. Department of Haematology, Blood Transfusion and Immunology, University of Port Harcourt Teaching Hospital, University of Port Harcourt, Nigeria.

Orcid ID:
Dr. Philip Anochie - http://orcid.org/0000-0003-2057-9163
Dr. Boa Bakoh Ndingkokhar - http://orcid.org/0000-0002-8011-6585
Dr. Juan Bueno - http://orcid.org/0000-0002-0915-0908
Dr. Felix Emeka Anyiam - http://orcid.org/0000-0003-2774- 7406
Dr. Linus Ndidi Ossai-Chidi - http://orcid.org/0000-0002-5385-0389
Dr. Edwina Chinwe Onyeneke - http://orcid.org/0000-0001-7830-837X
Dr. Anthony Chidiebere Onyeozirila - http://orcid.org/0000-0002-7859-1336

Source of Support: Nil; **Conflict of Interest:** None declared.