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Bioprospecting Nigerian Ethnomedicinal Plants for Novel Anti-Tuberculosis Drug Development: Challenges, Opportunities, and Future Directions

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ABSTRACT

Tuberculosis (TB) remains a formidable global health threat, with Nigeria bearing a significant burden as Africa's highest-ranked TB-endemic country. Despite national interventions like the Directly Observed Treatment Short Course (DOTS) program, Nigeria's TB control efforts are undermined by factors including poor adherence, drug resistance, and limited resources. Complicating these challenges is the emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB, alongside high rates of TB-HIV co-infection. Recognizing these gaps, attention has turned to traditional medicinal plants as potential sources of novel anti-TB compounds. This paper explores the epidemiology of TB, the urgent need for new therapeutic agents, and the scientific basis for ethnomedicinal plants traditionally used in Nigerian communities to manage TB symptoms. Empirical data highlight the antimicrobial potential of various plant extracts and bioactive compounds, such as Licarin A from *Aegle marmelos* and Geraniol from *Costus speciosus*, which exhibit promising activity against mycobacteria. Despite these advances, challenges persist, including variable phytochemical profiles, potential toxicity, and the need for rigorous *in-vivo* studies to confirm therapeutic efficacy. This paper outlines a road-map for harnessing these natural resources through standardized extraction protocols, structural modification to reduce toxicity, and translational research to ensure clinical relevance. Ultimately, integrating ethnobotanical knowledge with modern scientific approaches could unlock innovative, affordable, and culturally acceptable solutions to combat TB in Nigeria and beyond.

Keywords: Medicinal plants, TB, Drug, Antimicrobial

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Introduction

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, remains one of the world's deadliest infectious diseases despite the availability of treatment (Olatunji *et al*., 2025a). Declared a global health emergency by the World Health Organization (WHO) in 1993, TB affects multiple organ systems, primarily the lungs, and is characterized pathologically by necrotizing granulomatous inflammation (Mbuh *et al*., 2019; Mathiasen *et al*., 2020). Transmission occurs mainly through inhalation of aerosols from individuals with active pulmonary disease, leading to either latent infection or active disease (Dheda *et al*., 2016). Globally, about one-quarter of the population harbors latent TB infection (LTBI), which can reactivate when immunity wanes (WHO, 2022). In 2021, approximately 10 million people developed active TB, with significant mortality especially among those co-infected with HIV. Nigeria, ranked 6th globally and 1st in Africa among high TB burden countries, reported 429,000 cases annually and about 154,000 deaths, underscoring the heavy toll of the disease (WHO, 2022).

Despite national efforts including the introduction of the Directly Observed Treatment Short Course (DOTS) program, TB control in Nigeria faces challenges such as poor treatment adherence, drug supply interruptions, stigma, and weak healthcare infrastructure, particularly in rural and under-resourced areas. The rising prevalence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB strains further complicates management, as these require prolonged, toxic, and costly chemotherapy regimens (Hannan *et al*., 2011; Sudhanshu *et al*., 2023). Additionally, TB-HIV co-infection exacerbates disease severity and treatment complexity. The urgent need for novel anti-TB therapies has led to increased interest in traditional medicinal plants as sources of bioactive compounds with potential therapeutic effects. Many communities in Nigeria rely on ethnomedicinal plants for symptom management, yet scientific validation of their efficacy and safety remains limited (Getachew *et al*., 2022). Exploring these natural products may offer safer, affordable, and culturally acceptable alternatives that could overcome resistance issues and improve treatment outcomes (Nasim *et al*., 2022; Qureshi *et al*., 2022).

2.0 Epidemiology of TB

TB affects all age groups worldwide but predominantly impacts adults in their most productive years, with over 80% of cases and deaths occurring in low- and middle-income countries (WHO, 2022). The WHO South-East Asian and African regions bear the highest burden, with 46% and 23% of new TB cases respectively in 2022. Thirty high-burden countries, including Nigeria, accounted for 87% of new TB cases globally. In 2022 alone, an estimated 10.6 million people fell ill with TB, resulting in 1.3 million deaths, including 167,000 among people living with HIV (WHO, 2022) (Table 1).

Several risk factors, such as HIV infection, undernutrition, diabetes, smoking, and alcohol use disorders, increase susceptibility to TB and complicate treatment (Imtiaz *et al*., 2017; Hayashi and Chandramohan, 2018). Drug-resistant TB, worsened by antibiotic misuse, remains a critical challenge. The COVID-19 pandemic has further disrupted TB control efforts, causing an alarming increase in TB-related morbidity and mortality worldwide (Glaziou, 2020; Bai and Ameyaw, 2024).

In Nigeria, recent epidemiological reviews show stable TB notification rates around 50 cases per 100,000 population since 2014, largely due to

underdiagnosis and underreporting, particularly from private health sectors (WHO, 2023). However, improvements in case detection and reporting have raised treatment coverage from 24% in 2018 to 59% in 2022. Nearly all notified cases in 2022 were pulmonary TB, with a high rate of bacteriological confirmation, highlighting ongoing efforts to strengthen TB control despite persistent challenges. Table 2 presents the comparative characteristics of the types of TB.

Table 1: Epidemiology of TB (Global and Nigerian Data (2022–2023))

Parameter	Global Data (2022–2023)	Nigeria Data	Source
Total new TB cases	10.6 million (2022) / 10.8 million (2023)	429,000 cases annually (2022)	WHO (2022, 2023; Olatunji *et al*., 2025b)
TB deaths	1.3 million (2022) / 1.25 million (2023, incl. 161,000 with HIV)	154,000 deaths (2022)	WHO (2022, 2023)
TB as leading cause of death	Returned as leading cause from single infectious agent in 2023	Not specified	WHO (2023)
Latent TB infection (LTBI) prevalence	25% of global population (2022)	Not specified	WHO (2022)
TB burden by WHO region (%)	South-East Asia: 46%; Africa: 23%; Western Pacific: 18% (2022)	Nigeria ranked 6th globally; 1st in Africa (2022)	WHO (2022)
High-burden countries	30 countries (87% of new cases) (2022)	Nigeria included among high-burden countries	WHO (2022)
New TB cases by gender	Men: 5.8 million (2022) / 6.0 million (2023)	Not specified	WHO (2022, 2023)
	Women: 3.5 million (2022) / 3.6 million (2023)		WHO (2022, 2023)
	Children: 1.3 million (2022 & 2023)		WHO (2022, 2023)
Risk factors for TB incidence	Undernutrition: 2.2 million (2022)	Not specified	Imtiaz *et al*., 2017; WHO (2023)
	HIV infection: 0.89 million (2022)		
	Alcohol use disorders: 0.73 million (2022)		
	Smoking: 0.70 million (2022)		
	Diabetes: 0.37 million (2022)		
Case notifications	Not applicable	Increased from 103,018 (2018) to 285,561 (2022)	WHO (2023)

Table 2: Comparative characteristics of key *Mycobacterium* species highlighting their taxonomy, growth traits, pathogenicity, and virulence factors.

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Species	Taxonomy & General Traits	Growth & Morphology	Pathogenicity & Transmission	Virulence Factors & Research Importance
Mycobacterium tuberculosis	- Gram-positive bacillus- Family: *Mycobacteriaceae*- Order: *Actinomycetales*- Facultative intracellular parasite (monocytes, macrophages)- Member of *M. tuberculosis* complex (includes *M. bovis*, *M. africanum*, others)	- Slow grower: doubles once per day- Visible colonies in 4-6 weeks on Middlebrook's agar or Lowenstein-Jensen medium- Rough, dry, buff-colored colonies- Acid-fast due to thick lipid-rich cell wall	- Causes pulmonary /respiratory TB in humans- Survives for years despite immune response- Transmission via respiratory droplets- Resistant to antibiotics due to impermeable cell wall	- ESX Type VII secretion systems (ESX-1, ESX-3, ESX-5) critical for virulence- Outer membrane lipids: PDIMs, PGLs, sulfolipids prevent macrophage killing- Model for TB diagnosis via acid-fast staining
Mycobacterium bovis	- Member of *M. tuberculosis* complex- Slow-growing- Causes bovine and zoonotic TB- Shares many biochemical traits with *M. tuberculosis*	- Grows slowly- Difficult to cultivate compared to other bacteria- Environmental persistence in soil, feed, water	- Infects cattle primarily, but zoonotic to humans- Transmission via inhalation of droplets or ingestion of unpasteurized milk/dairy- Significant public health and economic impact globally	- Virulence factors similar to *M. tuberculosis*- Major concern in Africa due to co-infections (e.g., HIV)- Difficult eradication due to wildlife reservoirs- Studied for zoonosis control and livestock management
Mycobacterium smegmatis	- Saprophytic, non-pathogenic- Found in soil, water, plants- High Guanine-Cytosine (GC) content in genome- Fast-growing mycobacterium	- Rapid doubling time (3x faster than *M. tuberculosis*)- Velvety, yellow colonies with shiny, smooth, and wrinkled surface morphology- Forms biofilms	- Non-contagious in mammals- Environmental bacterium with no direct disease association	- Used extensively as a model organism for mycobacterial research- Studies on biochemical protection, antimicrobial properties- Cell wall rich in mycolic acids and hydrophobic lipids, similar to pathogenic mycobacteria

(**Source:** Vilcheze and Kremer, 2017; Ly and Liu, 2020; Sundarsingh *et al*., 2020; WHO, 2020; Montalla, 2021; Nawaz, 2023)

3.0 Bioprospecting Antimycobacterial Plants as Roadmap for Novel TB Drug Development

Current anti-TB therapies, both first- and second-line drugs, face considerable challenges, including prolonged treatment durations, significant toxicity, high pill burdens, and stringent adherence requirements (Olatunji *et al*., 2025a). These limitations contribute to treatment failure and the emergence of drug-resistant strains, underscoring the urgent need for alternative therapeutic strategies. Traditional medicinal plants, long used by Nigerian communities for alleviating TB symptoms, remain largely underexplored for their scientific validation and therapeutic potential.

Empirical data presented in Table 3 highlights the critical interface between traditional medicine and contemporary scientific research. Plants such as *Allium sativum*, with its notable 17.3 mm inhibition zone, and *Pterolobium stellatum*, exhibiting exceptional potency at a minimum inhibitory concentration (MIC) of 0.039 mg/mL, provide compelling evidence supporting their historical use in TB treatment. Furthermore, the data in Table 4 offers mechanistic insights, revealing how specific phytochemicals combat mycobacterial pathogens. For instance, Licarin A from *Aegle marmelos* compromises bacterial cell wall integrity, while 1′-acetoxychavicol acetate functions as a precise inhibitor of essential mycobacterial enzymes. These findings validate traditional remedies at a molecular level.

The profound mycobactericidal activity of natural compounds such as Geraniol (Table 4) suggests the potential to reduce current treatment durations of 6–9 months. Even more crucially, plants like *Costus speciosus* (Table 3) and bioactive compounds such as Carvacrol (Table 4) exhibit activity against mycobacteria through novel pathways, circumventing conventional resistance mechanisms and offering hope against multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB strains that render standard therapies ineffective.

4.0 Harnessing the Power of Antimycobacterial plants in Nigeria

Nature's inherent combinatorial chemistry provides promising avenues for therapeutic synergy (Kolawole *et al*., 2006; Suleiman *et al*., 2016). The properties of some medicinal plants such as *Crossopteryx febrifuga, Vitex doniana, Abrus precatorius, Detarium senegalense* is explored in this section however, despite the activities of these plants significant hurdles such as the need for standardization of protocols, moderation of toxic constituents to avoid compromise of antimicrobial efficacy and prioritization of *in-vivo* validation for top candidates remains.

i. ***Crossopteryx febrifuga*** (Figure 1a)***:*** It belongs to the family Rubiaceae, a monotypic genus of flowering plants with a wide distribution in Africa. It is widely distributed throughout the Savannah region, including Nigeria (West Africa). It is commonly called "Ayeye" (Ebiras) and "Ii-kwar" (Tiv) in North-Central Nigeria, and its English name is "Ordeal tree" (Khan *et al*., 2019). The different parts of the plants are used by traditional medicine practitioners in the treatment of upper respiratory infections such as cough, pneumonia, asthma, TB, and chest pain. Other therapeutic uses of the plant include pain, fever, gastrointestinal complaints, diabetes, wound infections, sleeping sickness, and epilepsy (Aristide *et al*., 2021; Ibekwe, 2022). Some phytochemical studies revealed the presence of alkaloids, phenols, flavonoids, tannins, triterpenes, saponins, and steroids in *C. febrifuga* extracts, thus explaining the origin of the observed biological properties (Nma *et al*.,

2018; Modjinan *et al*., 2019; Aristide *et al*., 2021). Secondary metabolites with high pharmacological potential isolated from Rubiaceae justify the growing interest in the scientific investigation of the species in this family corroborating its traditional therapeutic usage (Halilu *et al*., 2012; Ouedraogo *et al*., 2019; Aristide *et al*., 2021).

Table 3: Selected Medicinal Plants with Anti-TB Properties

Plant Name	Extract/ Fraction	Activity Against *M. tuberculosis*	Key Findings	References
Allium sativum (Garlic)	Crude	Zone: 17.3 mm	Most active in Gupta *et al*. study	(Gupta *et al*., 2010)
Aloe vera	Crude	Zone: 12.1 mm	Moderate activity	(Gupta *et al*., 2010)
Acalypha indica	Crude	Zone: 2.5–8.4 mm	Mild activity	(Gupta *et al*., 2010)
Allium cepa (Onion)	Crude	Zone: 3.2 mm	Least active in study	(Gupta *et al*., 2010)
Costus speciosus	n-hexane fraction	MIC: 100 µg/mL; MBC: 200 µg/mL	Destroys cell structure	(Mohamad *et al*., 2018)
Cymbopogon citratus	n-hexane fraction	MIC: 200 µg/mL	Active against H37Rv	(Mohamad *et al*., 2018)
Tabernaemontana coronaria	n-hexane fraction	MIC: 200 µg/mL	Bactericidal effect	(Mohamad *et al*., 2018)
Pterolobium stellatum	Chloroform	MIC: 0.039 mg/mL	Highly potent	(Kahaliw *et al*., 2017)
Aegle marmelos	Methanolic	MIC: 0.8–100 µg/mL	Dose-dependent	(Kaur & Kaur, 2015)
Glycyrrhiza glabra (Licorice)	Methanolic	MIC: 1.6 µg/mL	Most active in Kaur & Kaur study	(Kaur & Kaur, 2015)
Lawsonia inermis (Henna)	Methanolic	MIC: 6.25 µg/mL	Significant activity	(Kaur & Kaur, 2015)
Senna occidentalis (L.)	n-hexane	MIC:156 µg/mL	Significant activity	Olatunji *et al*., 2025b
B. grandiflora	n-hexane	MIC 313 µg/mL	Significant activity	Olatunji *et al*., 2025b

Table 4: Selected Natural Products with Anti-TB Activity

Compound/Plant Source	Class	Activity	Mechanism	References
Licarin A	Lignan	MIC: 3.12–12.5 µg/mL	Targets MDR strains	(León-Díaz *et al*., 2010)
1′-Acetoxychavicol acetate (*Alpinia galanga*)	Phenylpropanoid	MIC: 0.1 mg/mL	Direct mycobacterial inhibition	(Roy *et al*., 2012)
Carvacrol (*Lantana hispida*)	Monoterpenoid	Growth inhibition (low concentrations)	Membrane disruption	(Dubey *et al*., 2013)
Citronellol/Geraniol	Monoterpenes	Not specified (general anti-mycobacterial)	Cell wall interference	(Chinsembu, 2016)
Iridoids (*Crossopteryx febrifuga*)	Iridoid glycosides	Antibacterial (e.g., *P. aeruginosa*)	Virulence factor suppression	(Ouedraogo *et al*., 2019)
5,7,2′-Trihydroxyflavone (*Bridelia micrantha*)	Flavonoid	Active *in-vitro*	Enzyme inhibition	(Dubey *et al*., 2013)

ii. ***Vitex doniana*** (Figure 1b)***:*** This is a deciduous flowering tree of Verbernaceae family. *Vitex doniana* is known locally as "Oori nla" in Yoruba, "Dinya" in Hausa, and "Ucha Koro" in Igbo (Owolabi *et al*., 2022). This plant is a deciduous evergreen tree widely found in the middle belt of Nigeria, particularly Niger, Kogi, Benue, and parts of savannah regions of Kaduna, Sokoto, or Kano State (Mohammed *et al*., 2023). The leaves, fruits, stem bark and root of *V. doniana*, are widely used as ingredient for herbal medicine in many parts of Africa for jaundice, anemia, dysentery, cancer, malaria, mental illness, gastrointestinal disorders, and urinary conditions among others (Barry *et al*., 2022; Odoom *et al*., 2023). The presence of certain secondary metabolites has been reported such as saponin, tannins, phenols, cardiac

glycosides, flavonoids, sterols, and triterpenes as well as a high concentration of sodium, potassium, calcium, iron, phosphorus, and sulfur (Sulaiman *et al*., 2021; Udeani *et al*., 2021; Barry *et al*., 2022). Its antifungal and antibacterial properties have also been adduced to presence of alkaloids, tannins, and flavonoids (Agbafor and Nwachukwu, 2011; Bunu *et al*., 2021; Ayoka and Nnadi, 2022).

iii. Abrus precatorius (Figure 1c)***:*** Also known as rosary pea, is a medicinal plant belonging to the family Fabaceae. It is a woody twining plant with characteristic toxic red seeds with a black mark at the base growing in tropical climates (Madaki *et al*., 2020). *Abrus precatorius* is mainly considered a poisonous plant due to the presence of the most lethal toxin, Abrin, a toxalbumin in seeds that inhibits protein synthesis, causing cell death (Tripathi and Mishra, 2023). It is used traditionally as a remedy for canker sores, tonsillitis, and eye inflammation. It also contains vitamins A, B1, B6, C, protein, calcium oxalate, and many other minerals needed by the body (Perkasa, 2024). A wide range of *in-vitro* and *in-vivo* pharmacological functions of *A. precatorius* have reported its antitumor, antimicrobial, insecticidal, antiprotozoal, antiparasitic, anti-inflammatory, antioxidant, immunomodulatory, antifertility, antidiabetic, and other pharmacological activities (Qian *et al*., 2022; Izebe *et al*., 2023; Perkasa, 2024). The plant has also been explored for antimicrobial activity on multidrug-resistant bacteria at varying success such as *Klebsiella pneumoniae, Escherichia coli*, and *M. tuberculosis* (Santhosam *et al*., 2023).

iv. Detarium senegalense (Figure 1d)***:*** It is commonly called tallow tree, sweet detar and belongs to the family Caesalpiniaceae, which produces globular fruits. It is a dicotyledonous angiosperm that grows from thick and scattered branches (Dossa *et al*., 2020). *Detarium senegalense* is found growing in western and central tropical Africa in both closed forests and savannah. It is commonly known as 'Taura' in Hausa, it is called 'Ofo' in Igbo, and it is known as 'Ogbogbo' in Yoruba. The leaves are eaten as vegetables and are used traditionally as a wash for itch, enema for dysentery, and eye wash for conjunctivitis. A bark decoction is given to women at childbirth to expel the placenta. It is macerated in the palm for bronchitis, pneumonia, and all internal complaints (Trekpo *et al*., 2024). The stem bark, seeds, leaves, and roots of *D. senegalense* are widely used in herbal medicine in Nigeria (Agada *et al*., 2018). It has been traditionally reported in the treatment of diarrhea, cough, antirheumatic, antihelmintic, antiepileptic, antipyretic, and anti-cancer. It is also used in treating intestinal and hepatic diseases. Pharmacological studies also revealed that the extract of *D. senegalens*e was found to possess antidiarrheal activity, antimicrobial activity, antiproliferative activity, anthelminthic, antiepileptic, and antihyperglycemic (Nwachukwu *et al*., 2022; Ekene *et al*., 2023; Igbudu *et al*., 2024). Presence of secondary metabolites such as alkaloids, tannins, flavonoids, terpenes and steroids, saponins, and glycosides alongside mineral and vitamin compounds such as Riboflavin, Thiamin, Niacin, and Ascorbic acid has reported to play an important role in its activities (Ekene *et al*., 2023; Dassou *et al*., 2023).

5.0 Charting a Path Forward

Based on insights from available studies, the development of a road-map for novel plant-based TB therapies (Figure 2) should prioritize the clinical evaluation of the most promising candidates. Innovative combination therapies pairing phytochemicals with existing anti-TB drugs could help overcome resistance and shorten treatment duration.

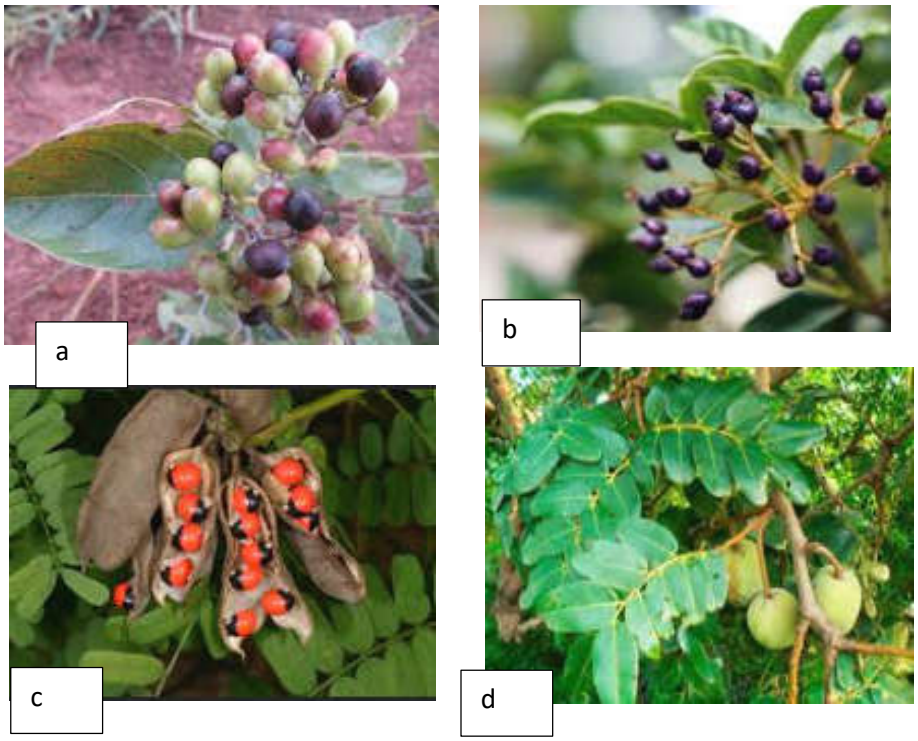


Figure 1: (a.) *Crossopteryx febrifuga* (b.) *Vitex doniana* (c.) *Abrus precatorius and* (d.) *Detarium senegalense*

(**Source:** Ejeje *et al.,* 2024; West african plants available at: http://www.westafricanplants.senckenberg.de/root/index.php?)

Additionally, the sustainable cultivation of high-value species is essential to ensure the long-term availability of these bio-resources. The convergence of whole-plant evidence and molecular-level data represents an unprecedented opportunity to develop safer, more effective, and ecologically responsible TB therapies, while also honoring and validating traditional medicinal knowledge.

The chart further presents a breakdown of workflow to achieve TB drug candidate but can be adapted for other antimicrobial studies. This begins with exploration of the traditional repositories and knowledge as a source of time-tested remedies to narrow the workload. These medicinal plants are carefully identified and selected, to form the backbone of drug discovery journey. The next step is to extract bioactive compounds from these plants through various bioassay techniques. The extracts are can then be screened for their anti-TB activity, typically by measuring the minimum inhibitory concentration (MIC) or observing zones of inhibition (ZOI) in laboratory tests. Promising extracts should not be left but use to undergo phytochemical analysis to pinpoint the specific components driving their potent activity. The crude stage of antimicrobial activity is where most of available research halts either due to scope of study or funding to explore further.

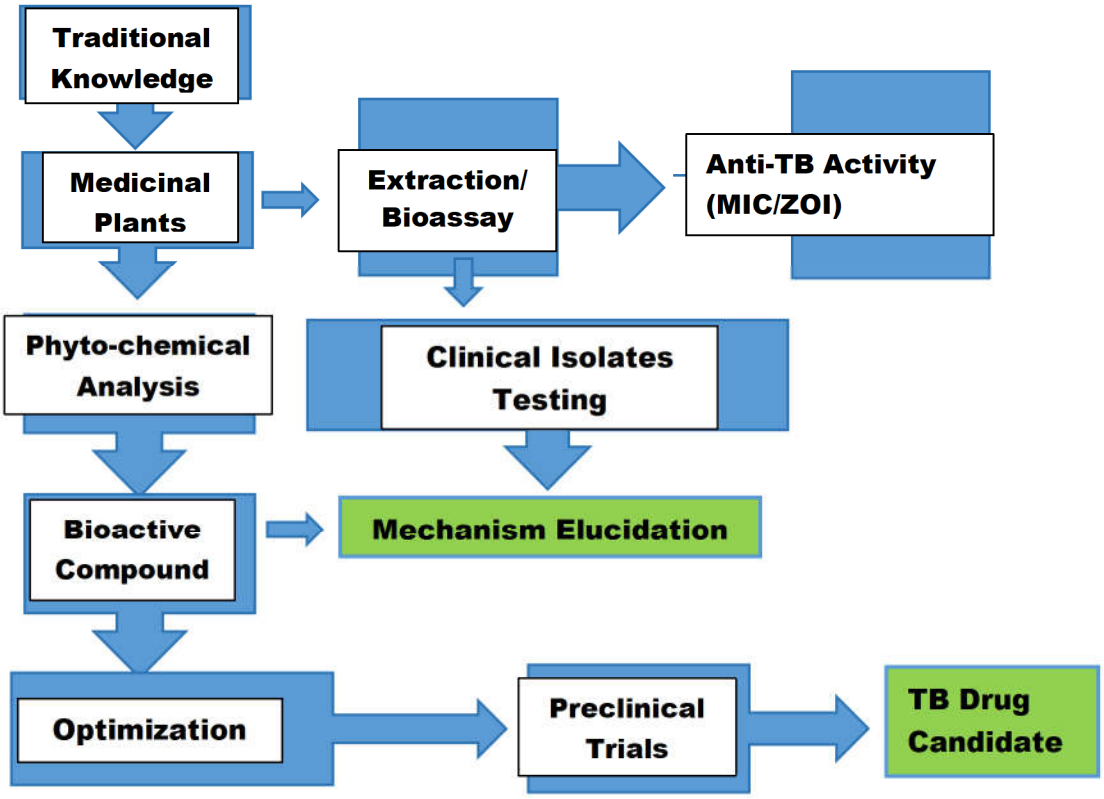


Figure 2: A Roadmap for Novel TB Drug Development

These extracts are always tested against clinical isolates of *M. tuberculosis* to validate their efficacy in real-world bacterial strains. Once active compounds are confirmed, researchers isolate the bioactive molecules and seek to understand how these molecules work through mechanism elucidation. This crucial step uncovers how the compounds inhibit or kill TB bacteria, offering insights into their potential as therapies. To bring these natural compounds closer to the clinic, scientists should engage in optimization to refine structures and boost efficacy, reduce toxicity, and improve how the body handles them. The optimized compounds can then enter preclinical trials, where they're tested for safety and effectiveness in animal models.

The ultimate goal is to produce TB drug candidates or in other cases, drug candidate for other organisms including fungi (Durowade *et al*., 2008) and viruses (Ogah *et al*., 2021) which will be a powerful and effective treatment that not only tackle the disease but also overcome the limitations of current therapies. This approach posit to bridges the gap between ancestral healing knowledge and modern science, offering new hope in the fight against TB.

Conclusion

The persistent burden of TB in Nigeria, coupled with the threat of drug-resistant strains and the inadequacy of existing therapies, highlights an urgent need for alternative, effective treatment strategies. Bioprospecting of ethnomedicinal

plants offers a promising avenue, as demonstrated by in vitro evidence of potent antimycobacterial activity in several Nigerian species. However, realizing this potential requires addressing critical challenges such as standardizing extraction techniques, ensuring safety through toxicity mitigation, and conducting *in-vivo* validation to confirm efficacy. Bridging the gap between traditional medicine and modern scientific rigor, present an opportunity to develop novel anti-TB therapies that are both culturally resonant and scientifically robust, contributing meaningfully to global TB control efforts and offering hope to the millions affected by this deadly disease.

Conflict of Interest: None

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