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World TB Day 2025: Advancing the fight against tuberculosis through science and nature

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Editorial

World Tuberculosis (TB) Day, commemorated annually on March 24, highlights the critical need to eliminate TB.[1] According to the World Health Organization (WHO), TB is caused by the *Mycobacterium tuberculosis* bacterium, and it continues to represent the most fatal infectious disease globally. In 2023, the disease approximately affected 10.8 million individuals. It was responsible for approximately 1.25 million deaths, including 161,000 among people living with HIV. After three years during which COVID-19 temporarily overtook TB as the leading cause of infectious mortality, TB is once again expected to top the list in 2023, with a death toll nearly twice that of HIV/AIDS.[2] The global burden of TB remains disproportionately concentrated, with 30 high-burden countries accounting for approximately 87% of total cases reported in 2023. Notably, Indonesia ranks as the second-highest contributor to the global TB cases.[3] The Ministry of Health reported a significant increase in TB cases, with 821,200 detected in 2023 compared to 677,464 in 2022.[4]

The primary TB treatment approach follows the DOTS (Directly Observed Treatment, Short-Course) strategy, which lasts six months. Patients of TB undergo an intensive two-month phase with four key medications under close supervision, followed by a four-month continuation phase with two drugs. This regimen is recommended for all pulmonary and extrapulmonary TB cases, including children and the elderly.[5] However, Indonesia's TB treatment success rate in 2023 was 86.5%, slightly below the Ministry of Health's target of 90%.[4] Treatment adherence remains a challenge due to factors such as concerns over drug side effects, long waiting times at healthcare facilities, travel distance, transportation costs, limited awareness, forgetfulness, and psychological distress.[6] Poor compliance can increase the risk of relapse, treatment failure, and the development of resistance in TB strains to existing drug therapies.[7]

Drug resistance continues to be one of the biggest challenges in controlling TB. The WHO first identified TB drug resistance in 1990, and since then, multidrug-resistant TB (MDR-TB)—resistance to both rifampicin and isoniazid—has emerged as a critical global health issue.[5] In 2022, approximately 410,000 people worldwide were diagnosed with MDR or rifampicin-resistant TB (MDR/RR-TB). An even more dangerous form, extensively drug-resistant TB (XDR-TB), is resistant not only to first-line drugs, but also to fluoroquinolones and at least one additional second-line drug. XDR-TB cases have been reported in over 100 countries, and they have a high morbidity rate of 40–50%, posing a particularly severe threat in regions with high rates of HIV infection.[8] Indonesia is one of the 30 countries with the highest burden of MDR-TB, reporting approximately 11,000 new MDR-TB cases each year. National prevalence rates demonstrate that 2.8% of new TB cases and 16% of previously treated cases are MDR-TB.[9] This alarming situation is not only a consequence of microbial drug resistance but is also driven by broader social factors—such as limited access to medications, political instability, disruptions in

healthcare systems, and socioeconomic challenges—particularly among vulnerable populations.[10]

Historically, WHO-recommended treatment regimens for MDR-TB and XDR-TB were lengthy and complex, often requiring combinations of oral and injectable drugs administered over 18 to 20 months. However, the updated WHO guidelines released in 2022, based on clinical trials like STREAM and Nix-TB, now endorse shorter and more patient-friendly regimens that include newer drugs such as bedaquiline (Bdq), pretomanid (Pa), and delamanid (Dlm). These new approaches have significantly shifted the landscape of drug-resistant TB treatment. For example, the current recommendation includes a 6-month regimen using a combination of Bdq, Pa, linezolid (Lzd), and moxifloxacin (BPaLM). These shorter, all-oral treatments have demonstrated greater safety and effectiveness compared to older regimens that included injectable drugs. Some research has demonstrated that these new combinations are not only non-inferior but also often more effective, with fewer adverse events and better patient outcomes. This has been further supported by results from larger trials such as BEAT-TB and endTB, which tested 6- and 9-month regimens in broader patient populations.[11] However, where does herbal medicine stand in this context?

Many plants have been used for centuries across cultures to treat a range of diseases, including TB. Traditional remedies such as infusions, decoctions, macerations, and tinctures prepared from various plant parts have long been employed by indigenous communities for managing TB. Recent scientific reviews reveal that over 350 plant species from different regions have shown potential in treating TB. Numerous bioactive compounds derived from these plants have demonstrated activity against *Mycobacterium tuberculosis*, as well as MDR-TB and XDR-TB strains.[5]

Conventional antibiotics typically work by disrupting bacterial processes like protein synthesis, transcription, and translation. However, *Mycobacterium tuberculosis* has developed resistance to many of these drugs, prompting researchers and medicinal chemists to seek new therapeutic agents that act through different biological pathways. Among these, plant-derived compounds such as coumarins have pointed out promising anti-tubercular and antibacterial effects. Coumarins function by inhibiting protein production and blocking carbonic anhydrase enzymes. Recent findings also suggest that they influence microbial communication systems like quorum sensing and hinder biofilm development.[12]

Beyond their inherent antimicrobial properties, herbal remedies may play a supportive role in tuberculosis treatment by acting as adjunct therapies. These natural agents can potentially amplify the effectiveness of conventional anti-TB medications, reduce adverse drug reactions, and contribute to mitigating antimicrobial resistance.[5,13] For example, bergenin—a plant-derived secondary metabolite—has been reported to activate Th1 and Th17 immune pathways and suppress *Mycobacterium tuberculosis* replication in murine models. When administered in combination with isoniazid, bergenin not only alleviates the immunotoxic effects of the drug but also enhances the development of long-lasting immune memory and accelerates bacterial clearance. Similarly, silymarin, a bioactive compound extracted from *Silybum marianum* seeds, can enhance the Th1 immune response in both drug-sensitive and drug-resistant strains of TB. Additional phytochemicals with immunomodulatory effects include allicin (from garlic), curcumin (from turmeric), and gingerol (from ginger). These natural substances exhibit strong antioxidant and anti-inflammatory properties and have potential as adjuncts to DOTS therapy, offering an alternative to corticosteroids in the management of TB-induced inflammation.[12]

The World TB Day 2025 theme, "Yes! We Can End TB: Commit, Invest, Deliver," highlights the urgency for global commitment, funding, and accountability for combating TB. At the 2023 UN High-Level Meeting, world leaders pledged to intensify TB eradication efforts. To fulfil this promise, we must accelerate the implementation of WHO guidelines, enhance national TB programs, and ensure complete financial support. Fulfilling these commitments means expanding access to proven WHO-recommended measures, including early detection, prompt diagnosis, preventive therapies, and high-quality care—especially for drug-resistant TB strains. This effort relies heavily on community engagement, civil society participation, and multi-sector

collaboration. The "Invest and Deliver" component underscores the need for sufficient investment to close existing gaps in TB care and to push forward research and innovation.[1] Utilizing natural products in TB therapy aligns with this year's World TB Day campaign.

While numerous natural compounds have been identified with notable antimycobacterial activity, some research on this case remains largely concentrated on the development and assessment of synthetic agents. A significant limitation in advancing phytochemicals for TB therapy is the lack of in vivo validation. This is primarily due to several constraints: (1) limited availability of Biosafety Level 3 (BSL-3) facilities required for conducting animal studies on tuberculosis, (2) poor solubility profiles of many natural products, (3) inadequate data on their pharmacokinetics, pharmacodynamics, and toxicological properties, (4) challenges in isolating sufficient quantities of pure active constituents, and (5) the considerable financial burden associated with in vivo experimental procedures. These barriers collectively hinder the translational progress of promising plant-based compounds in TB drug development.[13] More research is needed to fully understand the mechanisms, bacterial clearance capabilities, and immune-modulating properties of medicinal plants. Exploring how herbal medicine can enhance or support current TB therapies, particularly in reducing drug resistance or side effects, is an area that warrants further scientific investigation.

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