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Ashima Gakhar
Head of Department, Department of Botany, Faculty of Science, KVA DAV College for Women, Karnal, Haryana, India

Corresponding Author:
Ashima Gakhar
Head of Department, Department of Botany, Faculty of Science, KVA DAV College for Women, Karnal, Haryana, India

Insights into the recently discovered botanical products with anti-tuberculosis potentials

Ashima Gakhar

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Abstract
Tuberculosis (TB) is a dangerous bacterial infection. The illness is extremely infectious and is normally spread from person to person by inhaling bacteria-carrying air droplets. TB is a disease that mostly affects the lungs, although it may also affect other organs. It has culminated in a progressive rise in the number of orphans owing to parental deaths, and is projected to be 10 million, with maternal mortality accounting for 6%-15% of the total, or 15%-34% if only indirect factors are included. TB screening is performed using a clinical procedure that looks for current cough, sputum intake, temperature, weight loss, and night sweats. The pursuit of fresh, urgently required anti-TB drugs from natural sources necessitates a multidisciplinary approach. The usage of allopathic medications in such a complicated disease leads to more serious complications such as cross-resistance, whereas natural drugs have been seen to be more effective in this situation. The key criterion is the exploration of new remedies for the effective weakening of the unstable disease associated with TB.

Keywords: tuberculosis, botanicals, anti-tubercular, natural, phytoconstituents, therapy

Introduction
Tuberculosis (TB) is an infectious bacterial illness that is the world's second leading cause of death. In 1882, Robert Koch, a German microbiologist, found the bacteria that trigger TB, *Mycobacterium tuberculosis*, of the Mycobacterium family [1]. Following his findings, the development of effective prescription treatments and vaccinations offered the disease's eventual remedy. Indeed, the United Nations made predictions of TB being eradicated globally by 2025 at one stage [2]. TB was once considered to be a minor infection that could be treated with antibiotics. The first antibiotic was developed in 1944 and it worked wonders, but due to drug tolerance, streptomycin monotherapy started working, teaching us the importance of defining a modern therapy using a multiple drug system to deter bacteria from being more resistant. Soon after, a multi-drug protocol was implemented, along with a variety of anti-TB medications [3]. Nevertheless, a new form of antibiotic resistance arose, known as multidrug-resistant tuberculosis (MDR-TB), which is triggered by bacteria resistant to at least rifampicin and isoniazid, the first-line drugs for TB care. TB strains that are extensively drug-resistant tuberculosis (XDR-TB) are resistant to both first-line and second-line TB treatments [4]. Antibiotic resistance has become a serious topic of debate among doctors, academics, governments, and the general public. The past of antibiotic research, as well as modern knowledge of cell biology and antibiotic function, have the ability to be used to create drugs that can control infection [5].

Current Drug Therapy
Current medication therapy employs a cocktail of medications to improve the body's capacity to adapt to care and shorten the duration of treatment. Rifampicin and isoniazid are two of the most often prescribed first-line therapies currently.[6] Rifampicin is more important in the protocol since it shortens the recovery time and ensures the optimal effects. Rifampicin and isoniazid, as well as streptomycin and ethambutol, are included in a nine-month treatment [7]. According to one of the studies conducted by the Medical Research Council of the United Kingdom, using pyrazinamide in the first two months of the therapy regimen will shorten the treatment time to six months while also maintaining a cure rate of 95% or better [8]. To eradicate TB, the most effective method is to stop the virus from transmitting, and this can be accomplished by prioritizing care with sputum smear-positive patients, or others that can transmit the disease. DOTS, which stand for Directly Observed Treatment, may be used to test and manage these people.

The short course is an extremely useful and cost-effective TB management approach that is widely recommended around the world.[9] DOTS is made up of five components: ongoing political and financial commitment, quality-assured diagnostic protocols, reliable delivery of superior anti-TB medications, supervised documentation and reporting, and systematic short-course (SCC) anti-TB care offered under clear and supportive observation (DOT) [10].

Problems with The Current Drug Therapy

Owing to the long duration of TB therapy, patient compliance is limited, and the vast number of medications used will make it difficult for patients to administer their normal doses. The current therapy is still prone to adverse effects and has shown antagonistic interactions with other medications. Furthermore, the prolonged procedure necessitates a significant financial investment in the medications used for the care. The new multidrug treatment has little if no impact on latent TB. It has also resulted in MDR-TB [11] Drug tolerance happens when the wrong or ineffective medications are used, and may be attributed to the confusion of drug delivery, leaving the procedure in-between, or leaving only one of the medicines administered in the protocol (standard treatment is at least two drugs) [12]. Second-line medications, such as fluoroquinolones, aminoglycosides, and others, may be used to treat MDR-TB, although they are ineffective, harmful, and expensive. Second-line drugs are more expensive than first-line drugs, but the main issue is their treatment duration, which is almost double that of standard TB treatment, making it much more difficult for certain patients to afford treatment, continue treatment for the full duration, and increase the risk of disease spread, leading to the development of further resistance [13].

Natural Botanical Anti-Tubercular Products

If the number of cases of XDR-TB and MDR-TB rises, a new antibiotic is needed to fight the resistant bacteria to deter and eradicate TB around the world. Natural sources are attractive starting points in the quest for innovative and improved anti-TB medicines since they are rich in chemical complexity and have a lot of antimicrobial action [14]. Owing to a lack of understanding and analysis of the chemical compositions of herbal products, they are not used to their maximum extent. This sector will grow by developing effective standardization approaches to ensure product consistency and transparency. Allopathic medications are evidence-based and offer the best treatments for a suffering individual, but medication is often symptomatic, expensive, and treatment with chronic illnesses often results in negative side effects [15]. Natural drugs have greater chemical diversity, higher hit rates in high throughput screening, and greater capacity to approach their target cells' site of action. Natural products were traditionally the pedigree of various medicinal agents from which possible leads of heterocycles such as pyrans, flavones, chalcones, coumarins, pyrimidones, and oxzolidines were architected to assign the sources of potential candidates for the reduction of various ailments such as anti-cancer, anti-inflammatory, anti-microbials, anti-viral, and anti-TB [16]. This has reignited interest in natural resource discovery in the quest for new anti-TB agents. Several experiments have also shown that natural tools may be used to create modern drug design models. They have not, however, been thoroughly investigated in any area. Recently, few botanical products have been identified by scientists that have noteworthy anti-TB properties.

(+)-Calanolide A

(+)-Calanolide A is a naturally occurring compound that can be derived from the Malaysian plant *Calophyllum lanigerum*. It is an anti-HIV-1 agent known as a non-nucleoside reverse transcriptase inhibitor (NNRTI). The research found that the compound is effective against all strains of *M. tuberculosis*, including resistant strains. (+)-Calanolide A functions by inhibiting DNA, RNA, and protein synthesis at a rapid pace. This compound has related results to the regular TB medication Rifampicin, which prevents RNA synthesis as well [17].

1,10-di-epi-cubenol

An active ingredient of the essential oil derived from the plant *Salvia aratocensis* is 1,10-di-epi-cubenol, a naturally occurring compound belonging to the Sesquiterpenes family that accounts for 14.2%. It has been shown to be effective against *M. tuberculosis* strains as well as bacteria immune to normal anti-TB medicines [18].

Alpha-terpineol

Alpha-terpineol is a monoterpene alcohol that is generally made from alpha-pinene, which is more readily available. *Eucalyptus citriodora* is the source of this oil. It is a popular ingredient in cosmetics, perfumes, and flavorings. It has been shown to have anti-TB properties and is effective against MDR-TB and TB with XDR-TB [19].

Artemisinin

Artemisinin is derived from the *Artemisia annua* herb. It is a Chinese herb used in herbal medicine. According to a review, artemisinin has the potential to cure TB while still increasing the effectiveness of normal medicines. It works as an anti-TB agent by keeping the TB bacteria from going inactive. Dormancy is a hard-to-kill condition in which bacteria defend themselves from low-oxygen conditions, which are normally created by the immune system to regulate bacteria growth and avoid infection. Dormant bacteria, on the other side, develop a strong level of opioid tolerance. Artemisinin binds to the heme molecule in bacteria, stopping it from detecting oxygen levels and, as a result, from entering dormancy and dying. This could both reduce recovery time and delay the emergence of opioid resistance [20].

Citronellol

Citronellol, also known as dihydrogeraniol, is a naturally occurring acyclic monoterpenoid obtained from the *E. citriodora*, also known as lemon eucalyptus, a member of the Myrtaceae family. Citronellol has been found to have anti-TB properties in the air, both neat and in various artificial mixtures, and it may be used as an inhalation drug to reduce the number of infected people and avoid TB spread [21].

Drima-7,9(11)-diene

Drima-7,9(11)-diene is extracted from the essential oil of *Turnera diffusa*, also known as damiana, a member of the Passifloraceae family native to southern Texas. According to a report, the essential oil includes several substances, including drima-7,9(11)-diene, which could be effective in the treatment of TB and MDR-TB. Hydrodistillation may be used to extract the essential oil from this vine [22].

Epi-alpha-cadinol

Epi-alpha-cadinol is a sesquiterpenoid alcohol that can be derived from the Columbian plant *Salvia aratocensis*, which

belongs to the Lamiaceae family. According to a report, the essential oil extracted by hydrodistillation from this plant has anti-TB properties and is also effective against MDR-TB [23].

Germacrene D

Sesquiterpenes are the naturally occurring volatile compounds known as germacrenes. Germacrene D can be derived from the Columbian plant *Lippia Americana*. The insecticidal and anti-microbial properties of this compound are well established. According to a report on the impact of essential oil from *L. Americana* on *M. tuberculosis* variant strains, germacrene D has the capacity to suppress TB-causing bacteria as well as MDR-TB-causing bacteria [24].

Isopulegol

Isopulegol is a naturally occurring monoterpene alcohol derivative that can be isolated from a variety of plants, including *E. citriodora* of the Myrtaceae genus. It is used as a scent and flavoring agent, but according to a report, it has additional benefits such as anti-TB action. It is an inhalation therapy that can be used to control and avoid TB and a variety of other airborne diseases [25].

Linalool

Linalool is an agricultural terpene alcohol compound present in a variety of plants, including *E. citriodora*. Linalool has a wide range of commercial uses, the most well-known of which is its delightful fragrance. According to a review, linalool has the capacity to combat *M. tuberculosis* by inhalation therapy and plays a key role in TB prevention as well as other bacterial, fungal, and viral diseases [26].

Phenazine

Many organisms of the actinobacteria phylum produce phenazines, which are aromatic compounds. Riminophenazines, which are extracted from lichens, were first developed as a possible anti-TB agent many years ago. Because of clofazimine's anti-TB efficacy, these compounds are once again being studied as lead compounds for TB therapy. Clofazimine is used to treat leprosy and has been shown to be effective in controlling the disease. It has also shown clinical effectiveness in TB, especially in MDR-TB. Clofazimine does not cause tolerance and therefore stops it from developing against isoniazid in the treatment of TB. Several novel riminophenazine derivatives, such as B746 and B4157, have been synthesized and tested with the aim of lowering lipophilicity and increasing activity [27].

Propolis

Propolis, a complex resinous material also known as bee glue, is a natural product produced by honeybees for the construction of hives. This glue is made by bees gathering plant secretions or sticky exudates on cone-bearing tree buds. Propolis' chemical structure varies depending on when it is harvested. Propolis has long been used to heal sores, burns, respiratory infections such as HIV, and gastrointestinal issues, and it is still a common method for treating TB. Propolis extracts have been shown *in vitro* to suppress the development of TB bacteria while increasing the effectiveness of anti-TB medications such as rifampicin, isoniazid, and streptomycin. Propolis has been shown to prevent the growth of TB by reducing the production of granulomas in infected persons. Enzymes involved in the bacteria's essential physiological functions may be attractive candidates for the discovery of new anti-TB medicines [28].

Spathulenol

Spathulenol is a viscous aromatic organic tricyclic sesquiterpene alcohol compound with a slightly bitter and spicy flavor. It comes from the herb *E. citriodora*, also known as lemon eucalyptus, which belongs to the Myrtaceae family. Despite its ability to cure and avoid airborne bacterial diseases such as TB and MDR-TB, it is used as a flavoring agent and scent [29].

Trans-beta-Caryophyllene

Trans-beta-Caryophyllene is a bicyclic sesquiterpene with a cyclobutane and a 9-membered ring that occurs naturally. It is made from the herb *L. americana*, which belongs to the verbenaceae family. This phytoconstituent makes up around 11.3 percent of the hydrodistillation extract, has been shown to be effective against *M. tuberculosis* strains and MDR-TB strains [30].

Viridiflorene

Virdiflorene is a sesquiterpenoid compound made up of 5,10-cycloaromadendrane. It can be collected from a variety of plant types, such as the damiana shrub, which can be found in the United States and Mexico. According to one report, virdiflorene has the potential to combat TB and MDR-TB. In this analysis, the essential oil obtained by hydrodistillation was evaluated against *M. tuberculosis* strains.[31]

Conclusion

The escalating strain of TB tolerance, along with the lack of competent drug production, is wreaking havoc on the nation. With little chance of eliminating this deadly disease very soon, there is an immediate need to halt this extinction. Natural sources seem to be the safest option, since they provide a strong degree of anti-microbial activity against a wide number of pathogens and a large chemical variety. A large number of naturally occurring candidates have progressed to the late stages of growth. To overcome, new natural drugs with advanced mechanisms of action are needed. It is preferable to prevent rather than heal. Negligence is not a choice, particularly when dealing with a fatal illness that has no cure for a certain period of time. TB may be avoided by using the right vaccinations and stopping the spread of the disease to healthy individuals. To offer sufficient care to patients with MDR-TB and XDR-TB, a nation's government must control its finances in order to deliver adequate services to all who are financially disadvantaged. Both policymakers must work with all service suppliers to render MDR-TB monitoring and prevention as simple as possible. The DOTS, as well as other TB care agencies and clinics, must strengthen XDR-TB and MDR-TB monitoring and ensure the supply of high-quality anti-TB medications. To eradicate this lethal epidemic from the planet, everybody must come together and collaborate as a squad, putting down all obstacles. The government must solve the challenge of limited anti-TB medication supply by prioritizing TB infection prevention, which would deter disease spread and, in turn, more resistance. Surveillance technologies must be improved, and further funds must be allocated to the discovery, development, and commercialization of novel medical mechanisms, drugs, and vaccinations.

Conflict of Interest

The author declares no conflict of interest.

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Author's Contribution
The author did the literature survey from standard databases, collected all essential elements, and wrote this manuscript.

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