International Journal of Pharmaceutical research and Applications
Volume 11, Issue 4, Jul.-Aug.2026, pp:1290-1296 www.ijprajournal.com ISSN:2456-4494

# Combination drug therapy in the management of Tuberculosis

Swati Nayak*[1], Vishal Pal[1], Vipul Gupta[1], Mukul Kumar[1]
[1]*Lecturer, Motherhood University , Roorkee, Uttarakhand*

Date of Submission: 03-08-2026 Date of Acceptance: 15-08-2026

**Abstract**
One of the most common infectious illnesses in the world and a significant public health concern is tuberculosis (TB). Mycobacterium tuberculosis's sluggish growth, intracellular survival, and growing antibiotic resistance make therapy challenging. Because combination medication therapy increases therapeutic efficacy, inhibits the development of drug resistance, and targets bacterial populations in various physiological stages, it has become the cornerstone of tuberculosis management. Treatment results have been greatly enhanced by standard first-line anti-tuberculosis medications, such as isoniazid, rifampicin, pyrazinamide, and ethambutol.However, the emergence of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) continues to complicate disease management worldwide. Recent advancements, including the discovery of innovative drugs like bedaquiline and delamanid, shorter treatment regimens, and supportive therapy techniques, have shown promising outcomes in the control of tuberculosis. This study highlights the mechanisms of action of the primary anti-tuberculosis drugs, the importance of combination drug therapy, the challenges presented by drug resistance, and new developments in the treatment of tuberculosis.

**Keyword:** Tuberculosis; Combination Drug Therapy; MDR-TB; XDR-TB; Anti-Tuberculosis Drugs; Drug Resistance; Bedaquiline; Delamanid.

## I. Introduction

One of the biggest causes of disease and mortality in the globe is still tuberculosis (TB) [1]. The World Health Organization estimates that there are 1.7 million fatalities and 9.4 million new cases of tuberculosis annually. When ideal treatment circumstances are maintained, the current recommended treatment regimen for drug-susceptible TB can achieve a cure rate of around 95%. However, it necessitates a lengthy course of therapy, usually lasting at least six months. However, the worldwide burden of the illness has increased due to the rising prevalence of TB-HIV coinfection and the appearance of drug-resistant strains. The World Health Organization (WHO) recommends the DOTS (Directly Observed Treatment Short-course) strategy as an effective approach for tuberculosis control, ensuring patient adherence and treatment success[2].Due to various traits of the causative organism, Mycobacterium tuberculosis, the treatment of tuberculosis requires the use of different medications. One significant reason is the organism's innate resistance to numerous therapeutic treatments, which is mostly due to its distinct cellular structure and metabolic characteristics. Mycobacterium tuberculosis can continue to exist within the host even in the face of immune system attacks or antimicrobial therapy. Its potential to quickly become resistant to specific medications when used alone is another significant worry.The treatment of tuberculosis has traditionally depended on the concurrent use of several antimicrobial drugs due to these biological features. Since the early days of medication therapy for tuberculosis, combination therapy has thus become the norm because it improves treatment efficacy and dramatically lowers the risk of developing drug resistance [3, 5]. Extensive study using two simultaneous scientific techniques led to the creation of the first combination medication therapy for tuberculosis. The first strategy concentrated on the development and discovery of antibiotics, starting with the discovery of Penicillin and culminating in the release of Streptomycin, the first antibiotic proven to be successful in treating tuberculosis brought on by Mycobacterium tuberculosis [21].The second strategy focused on the development of antimicrobial chemotherapy, which began with the synthetic antibacterial medication Arsphenamine (also called Salvarsan), which was used to treat syphilis. It continued with the creation of Para-aminosalicylic acid (PAS), the first synthetic antimicrobial agent that was effective against tuberculosis [22]. Due to these advancements, Streptomycin and Para-aminosalicylic acid became the first combination antibacterial therapy for tuberculosis. As other anti-tuberculosis medications were found, this original combination was expanded or modified to create subsequent tuberculosis

International Journal of Pharmaceutical research and Applications
Volume 11, Issue 4, Jul.-Aug.2026, pp:1290-1296 www.ijprajournal.com ISSN:2456-4494

treatment regimens. The development of combination therapy for tuberculosis was made possible by a variety of scientific breakthroughs, from basic studies in soil microbiology to carefully planned clinical trials, highlighting the significance of interdisciplinary scientific endeavors in enhancing the management of human illnesses.

New therapeutic applications of previously approved medications can frequently advance more quickly through clinical review since they already have documented pharmacokinetic characteristics and safety profiles. As a result, the approval process may be shortened from almost 14 years to almost 5 years, greatly reducing the overall development duration. Because it improves the prediction of drug compatibility in combination regimens and with antiretroviral drugs, drug repurposing is very useful in the creation of new tuberculosis treatment techniques. Additionally, doctors may think about using medications that are already approved for other medical diseases off-label when conventional treatments don't work. When treating extensively drug-resistant tuberculosis (XDR-TB), where there is few viable treatment alternatives, [11] this approach may be particularly pertinent.Mycobacterium tuberculosis's innate resistance to numerous clinically authorized medicines is one of the main obstacles to creating more potent treatments for the disease. A number of widely used antibiotics show little to no efficacy against this disease. Streptomycin was one of the first effective drugs against Mycobacterium tuberculosis, although resistance developed rapidly when used alone. Streptomycin inhibits bacterial protein synthesis by attaching to the 30S ribosomal subunit, just as other aminocyclitol antibiotics including streptomycin, kanamycin, and gentamicin. Streptomycin inhibits bacterial protein synthesis by binding to the 30S ribosomal subunit, similar to other aminoglycoside antibiotics such as kanamycin and gentamicin. However, streptomycin is associated with ototoxicity and nephrotoxicity. It is primarily used in the treatment of tuberculosis and certain other infections, although its use is limited due to toxicity and the development of resistance, especially in patients who cannot tolerate first-line drugs, despite its poor in vitro efficacy against several bacterial species, including M. tuberculosis. Streptomycin has been investigated in recent studies to assess if currently available medications with low efficacy against M. tuberculosis could still be helpful in the treatment of tuberculosis when used in conjunction with a synergistic companion molecule [8].

## 1. Stages of Tuberculosis

From initial exposure to active disease, tuberculosis (TB) goes through a number of stages. Comprehending these phases is crucial for prompt diagnosis, treatment, and disease transmission prevention.

### 1.1 Exposure stage

This is the initial stage where a person comes into contact with *Mycobacterium tuberculosis*, usually through inhalation of infected droplets from an active TB patient. At this stage, the bacteria enter the lungs, but infection may or may not develop. There are no symptoms, and the individual is not infectious [4].

### 1.2 Latent Tuberculosis Infection(LTBI)

In this stage, the bacteria remain alive in the body but are inactive. The immune system contains the infection, preventing the bacteria from multiplying. Individuals do not show any symptoms and are not contagious. However, latent TB can persist for years and may reactivate if immunity decreases [4].

### 1.3 Active Tuberculosis Disease

In this stage, the bacteria become active and begin to multiply, leading to clinical symptoms. Common symptoms include persistent cough (lasting more than 2–3 weeks), fever, night sweats, weight loss, and sometimes coughing up blood. At this stage, the person is infectious and can transmit the disease to others [4, 16].

### 1.4 Reactivation Tuberculosis

Reactivation occurs when latent TB becomes active again, usually due to weakened immunity caused by conditions such as HIV infection, diabetes, malnutrition, or aging. The symptoms are similar to active TB, and the disease becomes infectious again. This stage highlights the importance of monitoring and treating latent TB infection [4, 11].

## 2. Pathogenesis and Biology of Tuberculosis

Mycobacterium tuberculosis, an aerobic, slow-growing bacterium that mainly affects the lungs but can also infect other organs, is the cause of tuberculosis [4]. When an infected person coughs, sneezes, or speaks, airborne droplets are generated that spread the virus. After being inhaled, the bacteria travel via the respiratory system and enter the lungs' alveoli, where immune cells called macrophages consume them. Mycobacterium tuberculosis, in contrast to many other bacteria, has

International Journal of Pharmaceutical research and Applications
Volume 11, Issue 4, Jul.-Aug.2026, pp:1290-1296 www.ijprajournal.com ISSN:2456-4494

a distinct cell wall that is rich in lipids and mycolic acids and offers defense against numerous antimicrobial drugs and host immunological defence[5]. Because of this structural characteristic, the bacteria can live and proliferate inside macrophages without being immediately destroyed by the host immune system. A granuloma forms when the immune system reacts to the infection by attracting more immune cells to the affected area. Granulomas serve as a barrier that keeps the bacteria contained and stops them from spreading widely. Latent TB, in which the bacteria remain dormant without producing symptoms, occurs when the immune system effectively suppresses the infection in certain people [4]. However, if the immune system is compromised, the bacteria may reactivate and become active tuberculosis, which manifests as symptoms like fever, night sweats, weight loss, and a persistent cough. The complexity of tuberculosis therapy and management is greatly increased by Mycobacterium tuberculosis's capacity to remain latent and then reactivate. Mycobacterium tuberculosis's biological traits, such as its slow growth, intracellular survival, and persistence inside granulomas, are important aspects that contribute to the disease's progression and make long-term combination medication therapy necessary for successful treatment[3,5].

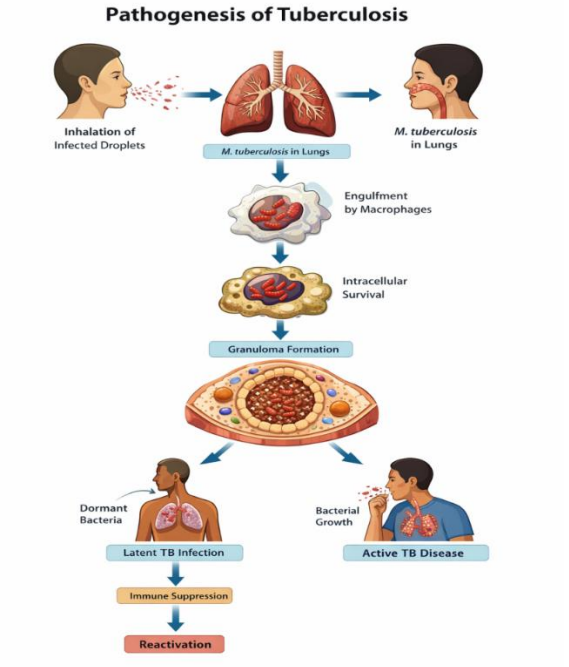


**Figure 1: Pathogenesis of Tuberculosis**

## 3. Current Status of Tuberculosis Treatment Approaches

Tuberculosis remains one of the most prevalent infectious disease-related causes of death worldwide. According to estimates from the World Health Organization (2025), 10.7 million people globally developed tuberculosis in 2024, with an anticipated 1.23 million deaths reported annually [25]. Despite being a preventable and curable disease, tuberculosis remains a major global health concern, particularly in low- and middle-income countries. The incidence and mortality rates of tuberculosis have been gradually declining in recent years, indicating significant progress. Nevertheless, the drop rate is still not high enough to achieve the End TB Strategy's goals [1].Since 2015, the prevalence of tuberculosis has only dropped by roughly 12% worldwide, falling well short of the 50% reduction aimed for by 2025.When properly followed, the traditional 6-month combination regimen employed in modern drug-susceptible tuberculosis treatment methods is still quite effective, with success rates of roughly 85–90% [2, 3]. However, treatment adherence remains a major challenge due to long duration, medication toxicity, and patient-related factors. The emergence of drug-resistant tuberculosis, especially extensively drug-resistant (XDR-TB) and multidrug-resistant (MDR-TB) strains, has made treatment strategies more difficult [6, 11].

Access to these treatments is still limited in many places, despite the fact that shorter all-oral regimens and more recent drugs like bedaquiline and delamanid have improved outcomes. Moreover, only a tiny portion of patients with drug-resistant tuberculosis receive the appropriate treatment globally [8, 9]. About 25% of all cases of tuberculosis worldwide are found in high-burden countries like India [17]. Underdiagnosis, poor adherence, and a lack of healthcare resources persist despite improvements in diagnosis, treatment coverage, and national initiatives. Even while advancements in diagnosis, drug development, and treatment strategies have improved tuberculosis control, the current state of affairs demonstrates that substantial efforts are still required to fulfill global elimination targets. Continued research, improved medical facilities, and patient-centered treatment approaches are necessary for effective tuberculosis management.

International Journal of Pharmaceutical research and Applications
Volume 11, Issue 4, Jul.-Aug.2026, pp:1290-1296 www.ijprajournal.com ISSN:2456-4494

## 4. Current Tuberculosis Treatment Approaches

When streptomycin, the first successful drug for treating tuberculosis caused by Mycobacterium tuberculosis, was taken alone after it was discovered in 1944, clinical investigations immediately revealed that the organism swiftly developed resistance [21, 24]. To solve this issue, combination therapy was created, which makes use of other anti-tuberculosis drugs such isoniazid and Para-amino salicylic acid.Although this approach improved treatment efficacy and reduced the development of resistance, there were still several problems [3, 5]. One of the major obstacles was ensuring patient commitment to the protracted treatment regimen, which often required several months of therapy and was accompanied by painful injections as well as potentially dangerous ill effects. The best drugs for eliminating tubercle bacilli in different physiological conditions are isoniazid, pyrazinamide, and rifampicin. As a result, these medications form the basis of modern tuberculosis therapy regimens [18, 19]. Standard therapy usually consists of two steps.These three medications are used in conjunction with a fourth medication, usually ethambutol, during the initial intensive phase, which usually lasts two months. The bulk of rapidly reproducing bacilli found in various physiological conditions are successfully eliminated by this combination. Isoniazid and rifampicin are given during the continuation phase, which typically lasts four months, following the intense phase. While isoniazid stops the emergence of rifampicin-resistant mutations that could occur during treatment, rifampicin aids in the removal of any remaining latent bacilli [3].

## 5. Combination Drug Therapy in Tuberculosis

Combination medication therapy is the cornerstone of modern tuberculosis treatment. Multiple antimicrobial medicines are required to effectively remove the causative organism, Mycobacterium tuberculosis,, which shows slow growth, intracellular survival, and a significant tendency to acquire resistance when exposed to single-drug therapy[5,7]. The administration of medications with various modes of action guarantees the eradication of bacterial populations that exist within the host in a variety of physiological situations.For drug-susceptible tuberculosis, first-line anti-tuberculosis medications such isoniazid, rifampicin, pyrazinamide, and ethambutol are frequently used in combination therapy. These medications work in several ways: pyrazinamide operates especially on latent bacilli in acidic settings, isoniazid inhibits the manufacture of mycolic acid, rifampicin inhibits the synthesis of bacterial RNA, and ethambutol interferes with the formation of cell walls. When combined, these medications have a synergistic bactericidal action and greatly lower the chance of developing resistance [5].The potential of combination therapy to target several bacterial populations present during illness is another significant benefit. Some bacilli are dormant or metabolically inert, whereas others are actively dividing. Utilizing a variety of medications guarantees the successful elimination of various bacterial populations, which lowers treatment failure and recurrence rates and enhances total treatment results [6].In recent years; there has been growing interest in integrating Ayurvedic and herbal approaches with conventional combination drug therapy. Herbal remedies like Ashwagandha (Withania somnifera), Guduchi (Tinospora cordifolia), and Turmeric (Curcuma longa) may be used as supportive therapy because of their immunomodulatory, anti-inflammatory, and antioxidant qualities, even though conventional anti-tuberculosis medications continue to be the mainstay of treatment. Tuberculosis-like disorders are referred to as "Rajayakshma" in Ayurveda, where the goal of treatment is to improve nutritional status, restore physiological balance, and strengthen the body through Rasayana therapy. These integrative methods may increase patient adherence throughout long-term medication, boost immunity, and lessen drug-related toxicity. However, these treatments should not take the place of conventional anti-tuberculosis medication regimens; rather, they should be utilized as supplemental methods under appropriate physician supervision [20].Combination therapy may have several disadvantages despite its efficacy, such as medication toxicity, adverse effects, and the requirement for rigorous adherence to extended treatment schedules. However, it continues to be the most dependable method for managing and controlling tuberculosis, and it is crucial for total infection eradication and relapse prevention [3, 6].

## 6. Effects of Combination Medication for Tuberculosis

### 6.1 Prevention of Drug Resistance

Using several medications with various modes of action decreased the likelihood that Mycobacterium tuberculosis would become resistant [5, 7].

International Journal of Pharmaceutical research and Applications
Volume 11, Issue 4, Jul.-Aug.2026, pp:1290-1296 www.ijprajournal.com ISSN:2456-4494

### 6.2 The Synergistic Effect
When drugs are used in combination, their bactericidal activity is increased more than when they are used separately [18].

### 6.3 Focus on Various Bacterial Population
It affects bacilli in many physiological states, both dormant and actively dividing [3].

### 6.4 Increase the Success Rate of Treatment
When medications work together, the cure rate rises and treatment failure decreases [2, 6].

### 7.5 Shorten the Duration of Therapy
The right medication combination shortens the duration of treatment and aids in achieving complete bacterial clearance [2].

## 7. Drawbacks of Combination medication therapy for tuberculosis

### 7.1 Enhanced Toxicity of Drugs
Hepatotoxicity, neurotoxicity, and gastrointestinal disturbances are among the side effects that are more likely to occur when numerous drugs are used [19].

### 7.2 Inadequate Patient Compliance
Treatment outcomes may be impacted by non-adherence brought on by long treatment durations and several drugs [16].

### 7.3 Exorbitant Medical Expenses
Due to the use of second-line medications, combination therapy, particularly for drug-resistant tuberculosis, can be costly [14].

### 7.4 Need for Continuous Monitoring
The burden of healthcare is increased when patients need to be continuously monitored for drug toxicity and treatment response [11].

### 7.5 Interactions between Drugs
When several medications are administered at the same time, there may be interactions that increase toxicity and decrease efficacy [18, 19].

## 8. Mechanism of Action of Major Anti –Tuberculosis Drugs

| Drug Name | Target | Mechanism of action | Genes involved in resistance |
|---|---|---|---|
| Isoniazid | Enoyl - [acyl- carrier protein] reductase (InhA) | Inhibitsmycolic acid biosynthesis and affects the metabolism of DNA, lipid, carbohydrate, and NAD | katG, inhA, ahpC, ndh |
| Rifampicin | RNA polymerase, β subunit | InhibitsRNA synthesis | rpoB |
| Ethambutol | Arabinosyl transferase | Arabinogalactan biosynthesis inhibition | embCAB |
| Pyrazinamide | Pyrazinamidase (pncA), PanD | Converted to pyrazinoic acid (POA), disrupts energy metabolism, lowers intracellular pH, inhibits coenzyme A synthesis | pncA, FAS-I |
| Streptomycin | S12 and 16S rRNA component of 30S ribosomal subunit | Inhibition of protein synthesis | rpsL, rrs |
| Para-aminosalicylic acid(PAS) | Thymidylate synthase(ThyA)and dihydropteroate synthase | Inhibits folic acid and iron metabolism | thyA,folC |

**Table 1: Mechanism of Action and Resistance Genes of Anti-Tuberculosis Drugs**

The several biological activities of Mycobacterium tuberculosis, such as cell wall production, RNA synthesis, and protein synthesis, are targeted by the anti-tuberculosis medications

International Journal of Pharmaceutical research and Applications
Volume 11, Issue 4, Jul.-Aug.2026, pp:1290-1296 www.ijprajournal.com ISSN:2456-4494

used in combination therapy. These medications increase bactericidal action and lessen the possibility of resistant bacterial strains emerging by acting on several targets at once [5, 18, 19].

### 9. Drug-Resistant Tuberculosis

Globally, drug-resistant tuberculosis has emerged as a significant public health issue [11, 24]. When Mycobacterium tuberculosis develops resistance to the two most potent first-line medications, isoniazid and rifampicin, it is known as multidrug-resistant tuberculosis (MDR-TB) [14]. Extensively drug-resistant tuberculosis (XDR-TB), a more severe variant, shows further resistance to second-line injectable medications including Amikacin and fluoroquinolones [10]. The rise of these resistant strains has made treating tuberculosis much more difficult, underscoring the critical need for better therapeutic approaches and the creation of novel anti-tuberculosis medications. Compared to drug-susceptible tuberculosis, managing multidrug-resistant tuberculosis (MDR-TB) is more difficult and complex. It necessitates the use of second-line anti-tuberculosis medications, which are frequently more costly, toxic, and ineffective. Additionally, the length of treatment is lengthier, usually lasting between nine and twenty-four months, depending on the intensity and treatment plan. Fluoroquinolones like levofloxacin and moxifloxacin, as well as more recent medications like bedaquiline and linezolid, are frequently utilized in MDR-TB. For positive results and to stop additional resistance, proper patient adherence, frequent monitoring, and customized treatment plans are crucial. Drug resistance is largely caused by insufficient treatment, incorrect drug use, and poor patient compliance [12].

### 10. New and Emerging Anti-Tuberculosis Drugs

A number of novel and repurposed medications for the treatment of drug-resistant tuberculosis have been developed as a result of recent developments in tuberculosis research [8, 9]. Under certain circumstances, novel drugs like bedaquiline and delamanid are currently advised due to their notable effectiveness against multidrug-resistant tuberculosis (MDR-TB). By blocking mycobacterial ATP synthase, bedaquiline prevents Mycobacterium tuberculosis from producing energy [8]. Delamanid inhibits mycolic acid synthesis, thereby affecting the cell wall development of Mycobacterium tuberculosis [9].Additionally; treatment plans for extremely resistant cases are increasingly incorporating repurposed medications like linezolid, clofazimine, and carbapenems like meropenem. The World Health Organization's development of shorter multidrug-resistant tuberculosis regimens has improved treatment accessibility by reducing cost and duration. Nevertheless, despite these advancements, developing successful combination regimens is challenging due to drug toxicity, potential drug-drug interactions, and the emergence of novel resistance [1, 14]. Therefore, continued research and innovation are necessary to develop safer, faster, and more effective tuberculosis treatment approaches. These advancements represent a significant step toward improving patient outcomes and reducing tuberculosis globally [15].

## 11. Conclusion

Even with the availability of contemporary therapeutic methods, TB remains a significant worldwide health concern. Mycobacterium Tuberculosis has distinct biological traits, such as slow growth, intracellular survival, and the capacity to acquire drug resistance, which make treatment difficult. Since combination medication therapy increases therapeutic efficacy, inhibits the development of drug resistance, and targets bacterial populations in various physiological stages, it has been shown to be the most successful approach for managing tuberculosis [3, 5].

First-line medications including isoniazid, rifampicin, pyrazinamide, and ethambutol make up the conventional multidrug regimen, which has greatly increased treatment results and cure rates. Global tuberculosis control initiatives are still severely hampered by the rising incidence of extensively drug-resistant tuberculosis (XDR-TB) and multidrug-resistant tuberculosis (MDR-TB). Successful disease management is further complicated by elements such medication toxicity, poor patient adherence, extended treatment duration, and restricted access to healthcare [11, 14].Recent developments in tuberculosis research, such as the creation of more recent medications like bedaquiline and delamanid as well as shorter, all-oral treatment plans, have demonstrated encouraging outcomes in terms of increasing treatment success. Supportive strategies like medication repurposing and complementary therapy may also improve patient outcomes and treatment efficacy [8, 9, 15]. In conclusion, combination medication therapy continues to be the cornerstone of successful tuberculosis management, but ongoing research, stronger healthcare infrastructure, early diagnosis, and greater patient compliance are crucial for

reaching global tuberculosis elimination targets [1, 17].

## References

[1]. World Health Organization. *Global Tuberculosis Report 2024*. Geneva: WHO; 2024.
[2]. World Health Organization. *WHO Consolidated Guidelines on Tuberculosis: Module 4 – Treatment*. Geneva: WHO; 2023.
[3]. Nahid P, Dorman SE, Alipanah N, et al. Official American Thoracic Society/CDC/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. *Clin Infect Dis.* 2016; 63(7):e147–e195.
[4]. Pai M, Behr MA, Dowdy D, et al. Tuberculosis. *Nat Rev Dis Primers.* 2016;2:16076.
[5]. Zhang Y, Yew WW. Mechanisms of drug resistance in *Mycobacterium tuberculosis*. *Int J Tuberc Lung Dis.* 2015;19(10):1276–1289.
[6]. Pontali E, Raviglione MC, Migliori GB. Regimens to treat multidrug-resistant tuberculosis: past, present and future perspectives. *Eur Respir Rev.* 2019;28(152):190035.
[7]. Singh R, Dwivedi SP, Gaharwar US, Meena R, Rajamani P, Prasad T. Recent updates on drug resistance in *Mycobacterium tuberculosis*. *J Appl Microbiol.* 2020;128(6):1547–1567.
[8]. Diacon AH, Pym A, Grobusch M, et al. Multidrug-resistant tuberculosis and culture conversion with bedaquiline. *N Engl J Med.* 2014;371:723–732.
[9]. Conradie F, Diacon AH, Ngubane N, et al. Treatment of highly drug-resistant pulmonary tuberculosis. *N Engl J Med.* 2020; 382:893–902.
[10]. Lange C, Chesov D, Heyckendorf J, et al. Drug-resistant tuberculosis: an update on disease burden, diagnosis and treatment. *Respirology.* 2018;23(7):656–673.
[11]. Dheda K, Gumbo T, Gandhi NR, et al. Global control of tuberculosis: from extensively drug-resistant to untreatable tuberculosis. *Lancet Respir Med.* 2014;2(4):321–338.
[12]. Fox GJ, Schaaf HS, Mandalakas AM, et al. Preventing the spread of multidrug-resistant tuberculosis and protecting contacts of infectious cases. *Clin Microbiol Infect.* 2017;23(3):147–153.
[13]. Ma Z, Lienhardt C, McIlleron H, Nunn AJ, Wang X. Global tuberculosis drug development pipeline: the need and the reality. *Lancet.* 2010;375(9731):2100–2109.
[14]. Migliori GB, Tiberi S, Zumla A, et al. MDR/XDR-TB management of patients and contacts: challenges facing the new decade. *Int J Infect Dis.* 2020;92:S15–S25.
[15]. Zumla A, Nahid P, Cole ST. Advances in the development of new tuberculosis drugs and treatment regimens. *Nat Rev Drug Discov.* 2013;12(5):388–404.
[16]. Centers for Disease Control and Prevention. *Tuberculosis (TB) Treatment Guidelines*. Atlanta: CDC; 2023.
[17]. National Tuberculosis Elimination Programme. *India TB Report 2024*. New Delhi: Ministry of Health and Family Welfare; 2024.
[18]. Goodman LS, Brunton LL, Hilal-Dandan R, Knollmann BC. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*. 14th ed. New York: McGraw-Hill; 2023.
[19]. Katzung BG. *Basic & Clinical Pharmacology*. 15th ed. New York: McGraw-Hill; 2021.
[20]. Tripathi KD. *Essentials of Medical Pharmacology*. 9th ed. New Delhi: Jaypee Brothers Medical Publishers; 2020.
[21]. Mandell GL, Bennett JE, Dolin R. *Principles and Practice of Infectious Diseases*. 9th ed. Philadelphia: Elsevier; 2020.
[22]. World Health Organization. *Treatment of Tuberculosis: Guidelines*. 4th ed. Geneva: WHO; 2010.
[23]. Diacon AH, Donald PR, Pym A, et al. Randomized pilot trial of eight weeks of bedaquiline treatment for multidrug-resistant tuberculosis. *Am J Respir Crit Care Med.* 2012;186(7):640–645.
[24]. Gandhi NR, Nunn P, Dheda K, et al. Multidrug-resistant and extensively drug-resistant tuberculosis: a threat to global control of tuberculosis. *Lancet.* 2010;375(9728):1830–1843.
[25]. World Health Organization. *Global Tuberculosis Report 2025*. Geneva: WHO; 2025.