An increasing incidence of deaths due to tuberculosis and the known drawbacks of the current existing drugs including the emergence of multi drug-resistant strains have led to a renewed interest in the discovery of new anti-tubercular agents with novel modes of actions. The recent researches focused on natural products have shown a useful way to obtain a potentially rich source of drug candidates, where alkaloids have been found more effective. The present review focuses on current epidemiology of tuberculosis, synergy of the disease with HIV, current therapy, available molecular targets and, highlights why natural products especially alkaloids are so important. The review summarizes alkaloids found active against mycobacteria from the mid-1980s to late 2008 with special attention on the study of structure–activity relationship (SAR).

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- Anti-tubercular activities
- Natural product
- Alkaloids
1. Introduction

The deadly infectious disease tuberculosis is caused by several species of Mycobacteria [1] including *Mycobacterium tuberculosis*, *M. bovis*, *M. africanum*, *M. microti*, *M. avium* and *M. leprae* that are intracellular, Gram-positive, non-motile, and rod-shaped obligate aerobic pathogens of higher vertebrates [2].

The distribution of tuberculosis is not uniform across the globe. About 80% of the population in many Asian and African countries test positive in tuberculin tests, while only 5–10% of the US population test positive [3]. Globally, 9.2 million new cases and 1.7 million deaths from TB occurred in 2006, of which 0.7 million cases and 0.2 million deaths were in HIV-positive people [4]. Among the infected individuals approximately 8 million develop active TB, and almost 2 million of these die from this deadly disease. Each year 95% of new TB cases occur in developing countries [5]. New infection, as well as reactivation of latent tuberculosis, is particularly prevalent in those that are HIV positive [6–8]. In addition, the emergence of drug-resistant strains of *M. tuberculosis* has led to increased pressure on current chemotherapy regimes [9,10]. The factors that contribute to MDR-TB are interrupted, erratic or inadequate therapy, as well as an inadequate public health system [11].

The rate at which new TB cases occur varies widely, even in neighboring countries, apparently because of differences in health care systems. The clinical symptoms include chest pain, coughing up blood, and a productive, prolonged cough for more than three weeks. Systemic symptoms include fever, chills, night sweats, appetite loss and weight loss. There is an urgent need to develop new TB drugs [12]. Although this disease can be cured with the current therapy, the treatments require six to nine months of time period that is too long, and accompanied by significant toxicity. These factors make patient compliance to therapy very difficult, and this noncompliance frequently selects for drug-resistant TB bacteria. The current TB problem clearly demonstrates the need for new and better drugs that are not only active against drug-resistant TB but also, more importantly, shorten the requirement for six months of therapy. The present review is focused to cover the entire formal and constant research on alkaloids against tuberculosis from the mid-1980s to late 2008 with special attention on structure–activity relationship (SAR) based activity. In order to highlight any possible SAR, the review is organized according to chemical structural class.

2. Current therapy

Treatment for tuberculosis uses antibiotics are also static to the bacteria. Rifampicin, isoniazid, pyrazinamide, ethambutol, and streptomycin are considered as the first line drugs against tuberculosis. A typical treatment for a non-drug resistant strains of TB involves two months of isoniazid, pyrazinamide,
ethambutol and rifampicin followed by four months of rifampicin and isoniazid [13]. However, the increasing emergence of drug resistant TB, and HIV infection, which compromises host defense and allows latent infection to reactivate or render individuals more susceptible to TB, poses further challenges for effective control of the disease [7].

New anti-tubercular drug regimens are clearly needed to reduce the therapy time required for a durable cure and to treat the expanding problem of drug- and multidrug resistant (MDR) \textit{M. tuberculosis} strains [14]. The need to develop less toxic and more potent compounds against tuberculosis has led to the discovery of diaryquinoline drugs that target mycobacterial F1F0 proton ATP synthase, a new drug target in mycobacteria. Among diaryquinolines, the modified form diaryquinoline R207910 has been identified as a promising anti-TB drug that not just shows \textit{in vitro} activity against \textit{M. smegmatis} (MIC of 0.003 µg/mL) and \textit{M. tuberculosis} (MIC of 0.030 µg/mL), but also display efficient activity against MDR-TB strains [15].

Oxazolidinones showing significant activity against \textit{M. tuberculosis} with an MIC of 2–4 µg/mL have been identified as a promising potential lead for development of anti-TB drugs. They are known to inhibit protein synthesis at an early stage by binding to 23S rRNA of the 50S ribosomal subunit [16].

Nitroimidazopyran PA824A derived from 5-nitroimidazole is another promising candidate for treatment of tuberculosis. It shows activity against \textit{M. tuberculosis} and MDR TB with MIC as low as 0.015–0.250 µg/mL [17]. The drug is currently being evaluated in clinical trials by the Global Alliance for TB Drug Development [13].

A new semisynthetic rifamycin derivative, rifalazil (RLZ; also known as KRM1648) has been shown to have significant activity against \textit{M. tuberculosis} and \textit{M. avium}. A preliminary safety study in humans has shown that the drug at doses of 10 mg and 25 mg was safe. However, at a dose of >100 mg, RLZ produces flu-like symptoms and a transient dose-dependent decrease in white blood cell and platelet counts [18]. Currently, no information is available for the clinical trial of RLZ for the treatment of mycobacterial infections [13].

3. Available molecular targets

Many well known anti-TB drugs are known to target the biosynthetic pathways that involve the production of macromolecules such as proteins, nucleic acids, or cell wall polymers. In selecting targets for antitubercular agents, it is advantageous to avoid targets that are close to the counterparts in mammalian cells [19]. The new targets should be
specific to Mycobacteria to limit the transfer of resistance factors from other bacteria. New drugs must act on a target essential for bacterial survival and ideally be active against Mycobacterium throughout its growth cycle both inside and outside the mammalian cells during infection [20].

The intensive efforts of medicinal chemists to develop anti-tubercular agents based on inhibition of protein synthesis have suggested that the ribosome may not be an efficient target for novel anti-TB drugs [21]. Many of the inhibitors of protein synthesis like tetracycline, chloramphenicol, and macrolides do not show activity against M. tuberculosis. An aminoglycoside, streptomycin being used for widespread treatment of TB, is known to disrupt bacterial protein synthesis. However, mutation altering the 16s ribosomal subunit in RNA, results in drug resistance to M. tuberculosis [22].

A detailed study of enzymes involved in tetrahydrofolate biosynthesis may lead to a rational design of new and novel anti-TB drugs [23]. The anti-TB drug p-amino salicylic acid initially designed as competitive inhibitor of salicylic acid has been reported to act on the tetrahydrofolate pathway as well as salicylate dependent biosynthesis of mycobactins, required for iron transport. Sulphonamides, the structural analogs of p-amino benzoic acid, inhibit biosynthesis of tetrahydrofolic acid, and thereby block the production of purine and pyrimidine bases required for nucleic acid biosynthesis in microbes. A type II topoisomerase, DNA gyrase, involved in many reactions including ATP-dependent negative supercoiling of closed circular double stranded DNA, ATP-independent relaxation of negatively supercoiled DNA is a promising target for development of novel antituberculosis drugs [20]. Recently, gyr A and gyr B have been cloned from M. tuberculosis and M. smegmatis. A stretch of 165 amino acids found in E. coli gyr B is absent from mycobacterial gyr B and thus any drug acting against gyr B would be specific to Mycobacteria. Inhibition of its activity prevents supercoiling, as subsequent process such as replication and transcription are DNA topologically dependent.

Nucleotide biosynthesis has been reported to be a good target particularly for TB in HIV cases [22]. In this regard, thymidine monophosphate kinase (dTMKase) has been suggested as validated target to develop new anti-tubercular agents particularly for the treatment of MDR TB and TB in HIV infected patients [24]. This enzyme is an essential enzyme of nucleotide metabolism that catalyzes the reversible phosphorylation of thymidine monophosphate (dTMP) to thymidine diphosphate (dTDP). Detailed structural elucidation of this enzyme is known and the well-known anti-HIV drug AZT has low affinity and this has led to the design and synthesis of more potent nucleoside analogs to develop new anti-TB agents [25].

Based on recent advances in ultra structure and biochemistry, the three basic structural components of the M. tuberculosis cell, the plasma membrane, the cell wall, and the capsule have been identified as the most important target to develop new anti-TB drugs [26,27]. The two layered cell wall in M. tuberculosis and M. leprae is very complex and poorly permeable. Classical studies carried out over many years identified that the peptidoglycan, the arabinogalactan, and the mycolic acids are the main structural components of the M. tuberculosis cell wall [28]. Beyond the membrane peptidoglycan (PG) layer is covalently linked to arabinogalactan (AG), which in turn, is attached to large mycolic acids with their long meromycolate and short α-chains. These three constitute the cell wall core, the mycolyl arabinogalactan–peptidoglycan (mAGP) complex [29]. Moreover, D-amino acids are important constituents of the mycobacterial cell wall. A cytoplasmic enzyme d-alanine racemase is required in the initial step of peptidoglycan biosynthesis to convert natural L- to D-alanine and has been identified as a novel target for antitubercular drug development [30,31].

The ability of M. tuberculosis to survive within an inhospitable environment has been attributed to its robust cell wall that comprises complex glycolipids including mycolyl-arabinogalactanpeptidoglycan (mAGP) and lipoarabinomannan (LAM) [32]. LAM facilitates the entry of bacterium into macrophages, prevents macrophage activation, and protects M. tuberculosis from damage by superoxide and hydroxyl radicals. Although macrophages also produce H2O2 during a respiratory burst, the effect of H2O2 on LAM was not reported alongside the studies on superoxide and hydroxyl radicals [33]. Many other extractable lipids including glycolipids (glycopeptidolipid, GPL; lipooligosacharide, LOS) [34,35], phenolic glycolipids (PGL), and other classes of free lipids (sulpholipids, SL; phthiocerol dimycocerosate, PDM) are very important in pathogenesis and survival of M. tuberculosis in the host macrophages [36].

4. Why phytochemicals?

Natural products are evolutionary shaped molecules with a profound impact on human health. Nature’s biosynthetic engine produces innumerable secondary metabolites with distinct biological properties that make them valuable as health products or as structural templates for drug discovery. However, there are several practical aspects to consider while trying to explain the difficulties associated with natural products research: (a) compound availability is very low (low yield, one-sample-one-source problem), (b) relative structural complexity is very high and includes the occurrence of multiple stereoisomers, (c) follow-up studies are mostly lacking, since most efforts (e.g. in academic environments) are not the part of focused drug development programs and simply lack the opportunity for synthetic follow-up of promising leads; (d) the isolated active principles rarely exhibit potent activity themselves, but require follow-up improvement in order to be attractive.

A common finding in the natural products literature, in particular with regard to well-established natural compounds, is that the same compound is reported to act on a myriad of targets, with very different potential, and with an inconsistent activity pattern. Natural product literature provides a growing research on plant derived antimycobacterial alkaloids and many groups are actively engaged in screening of natural product extracts as the preliminary step to finding new lead compounds. Several natural products have reportedly displayed promising activity against different species of Mycobacteria. Some lead compounds that have shown in vitro activity towards M. tuberculosis include aminoglycoside antibiotics, e.g. streptomycin (MIC of 0.5 µg/mL), isolated from Streptomyces griseus, and related compound kanamycin (MIC of 6 µg/mL), cyclic peptides, e.g. capreomycin 1A and 1B (MIC of ~5 µg/mL), isolated from Streptomyces capreolus NRRL 2773, and viomycin.
(MIC of 4 µg/mL) are used in combination with other antituberculars as either front-line or second line drugs [37].

5. Alkaloids

5.1. Pyrrole alkaloids

The pyrrole alkaloid solsedomine A (1), isolated from the plant *Solanum sodomaeum*, inhibited the growth of *M. intracellulare* with an MIC of 10 µg/mL [38]. Similarly, bangeasine (2) isolated from the eubacteria *Aristabacter necator* exhibited antitubercular activity against *M. smegmatis* with MIC 0.5 µg/mL [37]. SAR studies on nitropyrrrole analogues like pyrrolnitrin (3) did not show significant improvements in MIC values (4–16 µg/mL) observed against *M. tuberculosis*, *M. avium* and *M. smegmatis* but a mixture of 2 and 3 showed activity with MIC value of 0.075 µg/mL [39]. A structurally related dichloropyrrole metabolite celastramycin A (4), isolated from *Streptomyces* strain fermentations, exhibited potent antimycobacterial activity with MIC values of 0.05–3.1 µg/mL against *M. smegmatis*, *M. aurum*, *M. vaccae* and *M. fortuitum* [40]. Likewise, the metabolite (5) obtained from actinomycete *Streptomyces rimosus*, inhibited the growth of *M. aurum* and *M. phlei* at a loading of 20 µg/disc [41,42].

5.2. Pyridine alkaloids

Pyridine alkaloids e.g. metabolite (6), isolated from the fermentation of *Streptomyces* species and the corresponding synthetic derivatives (7–13), displayed antitubercular activity with MIC values 10–14 µg/mL. Among these, octyl ester 12 exhibited optimal activity with an MIC 8 µg/mL [43,44].

5.3. Cyclostellettamine alkaloids

Cyclostellettamines A–F (14–19), isolated from sponges of *Pachychalina* sp. have shown excellent antimycobacterial activity (i.e. 14: 32, 15: 4.0, 16: 4.0, 17: 8.0, 18: 11.0 and 19: 8.0 µg/mL, respectively) against *M. tuberculosis* H37Rv. The other structurally related synthetic analogues G–K (20–24) also significantly inhibited the growth of *M. tuberculosis* i.e. compound 20: 4.6, 21: 9.3, 22: 6.6, 23: 5.3 and 24: 4.6 µg/mL, respectively. Results based on comparison of activity among compounds 14–19 were suggestive that the cyclostellettamines with larger alkyl chains, such as compounds 17 (MIC 8.0 µg/mL), 18 (MIC 11.0 µg/mL) and 19 (MIC 8.0 µg/mL), were less active than compounds with smaller alkyl chains as linkers of the two pyridinium moieties, although compound 14 (MIC 32 µg/mL) is an exception [45].

5.4. Indole alkaloids

Among pentacyclic indole alkaloids, ibogaine (25) and voacangine (26), isolated from *Tabernaemontana citrifolia*, exhibited activity with MIC values of 50–100 µg/mL against *M. tuberculosis*, *M. avium* and *M. kansasii* [46].

5.5. Quinoline alkaloids

The alkaloids 27–32 were isolated from plant *Galipea officinalis*, exhibited antimycobacterial activity with MIC values
5.5. Imide alkaloids

Substituted maleimide and succinimide derivatives himanimides A-D (36–39) obtained from liquid cultures of the fungus Serpula himantoides, growing on the plant Eucalyptus globulus, have been shown to inhibit the growth of M. phlei. Among these only metabolite 37 inhibited significantly the growth of M. phlei, with an MIC of 25 µg/mL [49].

The hirsutellones possess unique structural features: a highly strained 12- or 13-membered ring containing a γ-lactam or succinimide, a para-substituted phenyl ether, and tricyclic polyketide moieties have been shown to exhibit
promising antimycobacterial activity. Among these hirsutellones A–D (40–43), isolated from the Thai insect pathogenic fungus *Hirsutella nivea* BCC 2594 inhibited the growth of *M. tuberculosis* H₃₇Rv with MICs of 0.78, 0.78, 0.78 and 3.125 µg/mL, respectively. Furthermore, compound 42 also showed *in vitro* cytotoxic activity with an IC₅₀ of 3.2–12 µg/mL [50].

5.7. Azaanthraquinone alkaloids

Among azaanthraquinones, the metabolite (44) isolated from the plant *Mitracarpus scaber* [51] exhibited activity against *M. intracellular* with MIC values of 6.25 µg/mL. A structurally related alkaloid cleistopholine (45), isolated from the plant *Cleistopholis patens* [52], inhibited the growth of *M.*
intracellular at an MIC value of 12.5 µg/mL [53]. In an extensive SAR study of the related tetracyclic plant metabolites sampangine (46) and 3-methoxysampangine (47), reported from *Canna odorata* [54] and *C. patens* [55] respectively, the presence of substitution at the 3-position (47) or 4,5-benzo ring fusion led to enhanced activity towards *M. intracellulare* (MIC 0.39–25 µg/mL) [42]. A complex pentacyclic marine alkaloid ascididemin (48), occurring in the Ascidian *Didemnum* species displayed antimycobacterial activity against *M. aurum* [56]. The metabolite with an MIC of 0.25 µg/mL significantly inhibited the growth of *M. aurum* A+ [57].

5.8. Indoloquinazolinone alkaloids

An indoloquinazolinone alkaloid, tryptanthrin (49), isolated from the plant *Strobilanthes cusia*, with MIC values of 1, 4 and 6 µg/mL inhibited the growth of *M. tuberculosis*, *M. avium* complex and *M. smegmatis*, respectively [58,59]. An SAR study
led to the identification of a potent analogue (50) that unfortunately failed to show in vivo activity [42]. Cryptolepine (51), neocryptolepine (52) and bicryptolepine (53), isolated from the African climbing liana Cryptolepis sanguinolenta, exhibited significant activity against M. fortuitum. However, against M. fortuitum the metabolite 53 was more potent with an MIC of 6.25 µg/mL while 51 and 52 exhibited MIC values of 25 and 31 µg/mL, respectively [60]. Among these the alkaloid 51 showed activity towards a panel of fast-growing myco-

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65 &: R = \text{alkyl} \\
66 &: R = \text{aryl} \\
67 &: R = \text{aryl} \\
68 &: R_1 = R_2 = OCH_3 \\
69 &: R_1 = R_2 = OCH_2O \\
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bacteria including *M. aurum*, *M. phlei* and *M. fortuitum* with MIC values of 2, 4, and 16 µg/mL, respectively [61].

5.9. Aerothionin alkaloids

Marine Verongid sponges are rich sources of brominated spiro-cyclohexadienylisoxazoline alkaloids [62]. The alkaloid aerothionin (54) exhibited antituberculotic activity [63] against *M. tuberculosis*, while derivatives (55–57) exhibited mild activity or were inactive [64]. The structurally related bromotyrosine alkaloid (58) and a guanidine derivative (59), isolated from an Australian non-verongid sponge, *Oceanapia* species has been identified as a potent inhibitor of the mycobacterial enzyme mycothiol S-conjugate amidase [65,66]. The ability of either compound to effect growth inhibition of mycobacteria has not been reported [42].

5.10. Oxaquinolizidine alkaloids

The bis-1-oxaquinolizidine alkaloid (−)-araguspongine C (60), isolated from the marine sponge *Xestospongia exigua*, exhibited activity with an MIC of 1.9 µg/mL against *M. tuberculosis* H37Rv [67].

5.11. Quinolones alkaloids

Quinolones 61–65, isolated from unripe fruit of *Evodia rutaecarpa*, have been shown to inhibit the growth of mycobacteria, with MICs of 2–32 µg/mL [68].

5.12. Isoquinoline alkaloids

The alkaloid berberine (66), an active constituent of many plant families (Annonaceae, Menispermaceae, Berberidaceae) exhibited antituberculotic activity against *M. intracellulare* with MIC of 0.78–1.56 µg/mL [69]. Moreover, at MIC of 25 µg/mL the metabolite also inhibited the growth of *M. smegmatis* and *M. tuberculosis* [58,70]. SAR studies on some structurally related benzo[c]-phenanthridine plant alkaloids like nitidine (67), chelerythrine (68), sanguinarine (69), chelirubine (70) and macarpine (71) demonstrated the significant inhibition on growth of *M. tuberculosis* H37Rv by ≥94% at 12.5 µg/mL [71]. Conclusively, the alkoxy substitution, either in the form of methoxy or methylenedioxy functional groups, plays an important role in the antituberculotic potency of this family of alkaloids [42].
5.13. Agelasine alkaloids

Agelasine E (72) isolated from the marine sponge Agelas nakamura[72], has been synthesized along with its analogues and tested against M. tuberculosis H37Rv [73]. Among these compounds 72 was found to be inactive, while compounds 73–75 exhibited MIC values of 3.13, 1.56 and 3.0 µg/mL, respectively. Another simple analogue 9-methyladenine (76) displayed an MIC of 6.25 µg/mL [37]. Agelasine F (77), isolated from Philippine sponge Agelas species significantly inhibited the growth of tuberculosis H37Rv with MIC of 3.13 µg/mL. The metabolite was also equally potent towards a range of single drug resistant strains including isoniazid, rifampicin, ethambutol and ethionamide resistant strains. With an IC50 33.8 µg/mL the compound 77 showed mild cytotoxicity towards Vero cells [74,75].

5.14. Carbazole alkaloids

A number of carbazole alkaloids occurring in Clausena excavata and Micromelum hirsutum have shown significant antimycobacterial activity. The compound (78) isolated from roots and rhizomes of C. excavata inhibited the growth of M. tuberculosis with MIC 50 µg/mL [76]. The substituted carbazoles 79, 80, 81 and 82 isolated from stem bark of M. hirsutum exhibited significant antimycobacterial activity with MIC value of 31.5, 14.3, 42.3, and 15.6 µg/mL, respectively [77].

5.15. Piperidine alkaloids

The methylenedioxybenzene alkaloid chabamide (83), isolated from Piper chaba, displayed activity towards M. tuberculosis H37Ra with MIC of 12.5 µg/mL [78]. The alkaloids eceainasidin (84) and analogue (85) isolated from Thai ascidian Ecteinascidia thurstoni, inhibited the growth of M. tuberculosis H37Ra with MIC values of 0.1 and 1.6 µg/mL respectively [42].

5.16. Manzamine alkaloids

Several alkaloids based on manzamine skeleton have been isolated from marine sponges [79–81]. Among these, the
metabolites (86–94) exhibited activity towards _M. tuberculosis_ H37Rv with MIC values of 1.53, 0.91, 3.76, 2.56, 3.13, 12.5, 1.77, 30.2 and 1.93 µg/mL, respectively.

SAR based study have shown that the stereochemistry of the alkaloid is significant for activity (87: MIC 0.91 µg/mL vs. 90: MIC 3.13 µg/mL) while the β-carboline moiety is not essential for activity, as evidenced by 94 with an MIC 1.93 µg/mL.

Similarly, manadomanzamines A (95) and B (96) isolated from sponge *Acanthostrongyliphorora* species exhibited activity against _M. tuberculosis_ H37Rv with MICs of 1.9 and 1.5 µg/mL, respectively [84]. The metabolite 6-hydroxymanzamine E (97), and 8-hydroxymanzamine J (98), isolated from same species [85], exhibited an MIC of 0.4 µg/mL against _M. tuberculosis_ H37Rv and an IC₅₀ of 3.5 µg/mL against _M. intracellularare_.

5.17. Aporphine alkaloids

Bidebiline E (99), isolated from the roots of *Polyalthia cerasoides* showed _in vitro_ antimycobacterial activity against _M. tuberculosis_ with an MIC value of 6.25 µg/mL [86].

Similarly, Cepharadione B (100), isolated from the stem and leaves of *Piper sanctum* exhibited activity against _M. tuberculosis_ H37Rv with an MIC value of 32 µg/mL [87].
N-methylouregidione (101), liriodenine (102) and oxostephanine (103), isolated from Pseuduvaria setosa displayed in vitro activity towards *M. tuberculosis* with MIC values of 100, 12.5, 25 µg/mL, respectively [88].

5.18. Diterpene alkaloids

Homopseudopteroxazole (104), pseudopteroxazole (105) and ecopseudopteroxazole (106), isolated from sea plume...
Pseudopterogorgia elisabethae inhibited the growth of *M. tuberculosis* H37Rv by 80, 97 and 66%, respectively at a concentration of 12.5 µg/mL [89].

5.19. Other alkaloids

Cepharanone B (107), piperolactam A (108), isolated from the stem and leaves of *P. sanctum* exhibited activity against *M. tuberculosis* H37Rv with MIC values of 12 and 8 µg/mL, respectively [88]. The metabolite vasicine (109), isolated from the *Adhatoda vasica*, and related semi-synthetic derivatives bromhexine (110) and ambroxol (111) were found to inhibit the growth of *M. tuberculosis* with MIC values of 6–64 µg/mL [90]. Two benzylized semi-synthetic derivatives 112 and 113 of aaptamine (114), a cytotoxic sponge metabolite, inhibited the growth of *M. tuberculosis* H37Rv by 98% and 97%, respectively at a concentration of 6.25 µg/mL [91]. The alkaloid ingenamine G (115), isolated from the marine sponge *Pachycladina* species showed antimiobacterial activity with an MIC value of 8 µg/mL against *M. tuberculosis* H37Rv [92].

Halicyclamide A (116), isolated from Indonesian marine sponge of *Haliclona* sp. 05A08 displayed significant growth inhibition against *M. smegmatis, M. bovis* BCG, and *M. tuberculosis* H37Ra with MICs in the range of 1.0–5.0 µg/mL under both aerobic conditions and hypoxic condition inducing a dormant state [93].

6. Conclusion

Significant advances in parasitological and biochemical research on various species of tuberculosis has been made in the past few decades, but the available treatment options are far from satisfactory. To eliminate this problem from every corner of the world, a safe, non-toxic and cost-effective drug with novel mode of action is urgently required. Natural products covering a wide diversity of promising structural skeletons would serve as useful scaffolds or templates for the development of new specific and selective anti-mycobacterial drugs. Plant products as a source of anti-tubercular drugs are effective treatment and would involve a non invasive alternative to the invasive method of parasitological diagnosis, identification of the most cost effective surveillance system and control strategies to reduce the mortality rate, identification and quantification of risk factors to better focus the control activities, are the most important aspect for the control and complete eradication of the disease from world.

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