Over the past decade, there has been a significant increase in the incidence of Tuberculosis (TB) worldwide (Frieden, 2003). Thirty-two percent of the world's populations (i.e., 1.86 billion people) are infected with *Mycobacterium tuberculosis*. Most of these people have latent *M. tuberculosis* (Denis, 2004). In 1997, there were about 1.87 million deaths, with an average mortality rate of 23%. In 2000, there were between 8 and 9 million new cases of TB, with up to 50% of patients being smear positive (Frieden, 2003). The incident is high in Africa, with 290 cases per 1,000,000 populations (Dye, 1999), although the greatest prevalence is in the most populous countries, such as India, Bangladesh and Pakistan. Each year, 6,36,000 new incident cases (80%) occur in the top 23 TB countries (Samaan, 2003). TB is the second commonest cause of death worldwide (Frieden, 2003). In some African countries the mortality rate was as high as 50% (Samaan, 2003). Australia is fortunate to have a low incidence of TB. In 2002, there were 1028 cases reported, representing an incidence of 502 per 1,000,000 population (Lumb, 2003). The large majority of the cases and deaths are from the poor nations. India is one of the countries worst affected. More than 40 percent of the populations are infected and some 15 million suffer from tuberculosis in the country, of which over three million are highly infectious open cases. Half a million people die from the disease every year in India (Raviglione et al., 1992).

Four first line drugs (FLD’s) form the basis of current therapy for drug sensitive *M. tuberculosis* are isoniazid, rifampicin, pyrazinamide and ethambutol. Second line drugs (SLD’s) are ethionamide, cycloserine, capreomycin, amikacin, kanamycin, PAS, Thioacetazone, ofloxacin, ciprofloxacin, sparofloxacin, clarithromycin, clofazimine, amoxicillin and clavulanic acid (Wayne et al., 1994). The standard regimen for active TB is to treat with all four first line drugs, using isoniazid and rifampicin for 6 months, concurrently with pyrazinamide and ethambutol for the first two months of treatment. Ethambutol can be discontinued once the organism is known to be susceptible to both.
isoniazid and rifampicin (Wayne et al., 1994). Therapy does not necessarily require daily administration and regimens have been designed to allow administration two or three times a week. Most forms of active TB can be treated with six months of medication. Latent TB is generally treated with six months of isoniazid monotherapy.

Unfortunately, the very success of the drug treatment of tuberculosis has been the catalyst for the emergence of a new wave of drug resistance. Beginning in 1990, outbreaks of multi drug resistant Tuberculosis have been reported in hospitals and prisons in the eastern United States (Kent, 1993). It has been estimated that 3.2% of the world’s new cases of TB, in 2000, were Muti Drug Resistant Tuberculosis (MDR-TB), defined as resistant to at least isoniazid and rifampicin (Espinal, 2003). Tuberculosis patients in part of Eastern Europe and Central Asia are 10 times more likely to have multi drug resistant TB (MDR-TB) than in the rest of the world according to a World Health Organization (WHO) report into the deadly infectious disease. China, Ecuador, Israel and South Africa are also identified as key areas. WHO’s leading infectious disease experts estimates there are 3,00,000 new cases per year of MDR-TB worldwide. There is also evidence providing drug resistant strains are becoming more resistant, and unresponsive to current treatment. 79% of MDR-TB cases are now “super strains”, resistant to at least three of the four main drugs used to cure TB. The proportion of tuberculosis cases co-infected with Human Immuno Deficiency virus (HIV) was also found to be raising, being 2 – 10 times greater for the 1997 estimates, than for 1990 (Dye, 1999). The association with HIV and increasing multi drug resistant tuberculosis (MDR-TB) appears to be a serious issue, especially for the developing nations. In addition, approximately 12% (2,26,000) of deaths from TB was attributed to co-infected with M. tuberculosis and Human Immuno Deficiency Virus (TB-HIV). Immune deficiency patients with HIV are at increased risk of latent M. tuberculosis infections progressing to active disease, and being transmitted to others (Murray et al., 1993). MDR-TB is a global problem menacing the poor and the rich nations alike. When first line drugs become ineffective, second line drugs are being used aminoglycosides, macrolides, para amino salicylic acid, ethanbutol, ethionamide, cycloserine, capreomycin, thiocetazone and others. They are unsatisfactory, being much less effective, costlier, and more toxic and requiring prolonged treatment.
The recent increase in the number of MDR clinical isolates has created an urgent need for the discovery and development of new antituberculosis leads. Natural products form one avenue in the search for new antituberculosis agents. Nature has continuously provided humankind with a broad and structurally diverse of pharmacologically active compounds that continue to be utilized as highly effective drug to compact a multitude of deadly diseases. Natural products and their derivatives have traditionally been the most common source of drugs, and still represent more than 30% of the current pharmaceutical market (Kirkpatrick, 2002). Of the 877 small molecule new chemical entities (NCEs) introduced between 1981 and 2002, roughly half (49%) were natural products, semi synthetic natural product analogues or synthetic compounds based on natural products pharmacophores (Newman et al, 2003).

Natural products are still major source of innovative therapeutic agents for infectious diseases, cancer, lipid disorders and immunomodulation (Moore et al., 1998). It has long been recognized that natural product structures have the characteristics of high chemical diversity, biochemical specificity, and other molecular properties that make them favorable as lead structures for drug discovery, and which serve to differentiate them from libraries of synthetic and combinational compounds (Noaman et al., 2004). During the past 20 years, a core group of marine natural products chemists from several countries, in collaboration with both academic pharmacologists and the pharmaceutical industry, has reported a very large number of novel metabolites from organisms exist in terrestrial and marine environments. The oceans are the source of a large group of structurally unique natural products that are mainly accumulated in marine organisms. Several of these compounds show pronounced pharmacological activities and are interesting candidates for new drugs primarily in the area of cancer treatment (Faulkner, 2002). Other compounds are currently being developed as an analgesic or to treat inflammation. Among the many phyla found in the oceans, the best source of pharmacologically active compounds are bacteria (including cyanobacteria), fungi, certain group of algae, sponges, soft corals and gorgonians. Prokaryotic and eukaryotic micro algae produce a wide array of compounds with biological activities (Kreitlow et al., 1999). These include antibiotics, algicides, toxins, pharmaceutically
active compounds and growth regulators. The micro algal toxins is either important as material for useful drugs or one of the great mysteries in the world of biotoxicology.

Recently, microalge have become targets for screening programmers in search of novel compounds of potential medicinal value. Numerous compounds have been isolated from prokaryotic and eukaryotic marine microalgae, and have been tested for different types of bioactivity with positive effects. The future role of micro algal compounds in drug discovery is especially in the priority areas for the development of new medicines, namely to fight viral infections and cancer, and to combat infections from antibiotic resistant bacteria and fungi. Discovering new therapeutic molecules is becoming increasingly important as more and more bacteria resistant to the usual antibiotics. Traditionally used Asiatic medicines, algae, since the second half of the 20th century, are screened for their biological activities. Thus, antibacterial effects have been noticed in all the algal classes (Brkholder et al., 1960; Aubert and Gauthier, 1966; Duff et al., 1968; Aubert and Gambarotta, 1977; Berland et al., 1972; Aubert et al., 1968; Gauthier, 1980; Cooper et al., 1983; Reichelt and Borowitska, 1984; Viso et al., 1987; Pesando, 1990). However, most of these antibiotic actions have only been tested against human pathogens and the active molecules were rarely purified.

The role of marine micro algae in the discovery of drugs which could reach the pharmaceutical market has increased notably in recent years, due to substantial improvement in biological screening methods. Only a small percentage of the microbial species have been examined and explored thoroughly for their pharmaceutical potential. Considering these aspects the current study was initiated with the following objectives:

- Isolation and identification of MDR Mycobacterium tuberculosis from collected specimens.
- Screening of antibacterial compounds from chosen marine micro algal extracts and partial characterization of active principles.
- In-vivo acute and sub acute toxicity study of antimycobacterial compounds from marine micro algal extracts in albino mice as animal model.