VISVESWARAIAH TECHNOLOGICAL UNIVERSITY

Belgaum-590 010

Anti-Pathogenic Activity of Natural Products From Plants Against MRSA

A KSCST FUNDED PROJECT-2010

Submitted by

Mary Lidya & Vidya G

Under the guidance of
Dr. B.K.MANJUNATHA, Professor. Mr. DIVAKARA R and Dr. KUSUM PAUL
Professor and Head
Dept of Biotechnology

DEPARTMENT OF BIOTECHNOLGY, THE OXFORD COLLEGE OF

ENGINEERI NG

Bommanahalli, Hosur Road, Bangalore-560 068.

INTRODUCTION

Antimicrobial resistance is not new, but the number of resistant organisms, the geographic locations affected by drug resistance, and the breadth of resistance in single organisms are unprecedented and mounting[1]. Diseases and disease agents that were once thought to be controlled by antibiotics are returning in new leagues resistant to these therapies. In this review, we focus on the underlying principles and ecological factors that affect drug resistance in bacteria. It should be stressed, however, that antimicrobial resistance is also evident in other microorganisms—namely, parasites, fungi and viruses[2]. Drug-resistant strains initially appeared in hospitals, where most antibiotics were being used[3]. Sulfonamide-resistant *Streptoccoccus pyogenes* emerged in military hospitals in the 1930s[4]. Penicillinresistant *Staphylococcus aureus* confronted London civilian hospitals very soon after the introduction of penicillin in the 1940s[5]. Similarly, *Mycobacterium tuberculosis* with resistance to streptomycin emerged in the community soon after the discovery of this antibiotic[6]. Resistance to multiple drugs was first detected among enteric bacteria—namely, *Escherichia coli*, *Shigella* and *Salmonella*—in the late 1950s to early 1960s [7–9]. Such strains posed severe clinical problems and cost lives, particularly in developing countries. Nevertheless, the resistance problem was perceived by some, most notably those in the industrialized world, as a curiosity of little health concern confined to gastrointestinal organisms in distant countries. This attitude changed in the 1970s when *Haemophilus influenzae* and *Neisseria gonorrhoeae*, organisms that cause respiratory and genitourinary disease, respectively, emerged with resistance to ampicillin[10, 11] and, in the case of *Haemophilus*, with resistance to chloramphenicol and tetracycline as well[12,13]. Fueled by increasing antimicrobial use, the frequency of resistance escalated in many different bacteria, especially in developing countries where antimicrobials were readily available without prescription. Poor sanitation conditions aided spread and small healthcare budgets prevented access to new effective but more expensive antibiotics1. Since the 1980s, a re-emergence of tuberculosis has occurred that is often multidrug resistant (MDR) and enhanced by human immunodeficiency virus infection[14]. The severity of and difficulty in treating MDR strains necessitates the use of several, sometimes six to seven different, drugs[15]

The 20th century initially offered the promising prospect of penicillin and other antibiotics to fight bacterial infections, but ended with the gloomy scenario of emerging multiresistant bacteria. The efficiency of conventional antibiotics in preventing bacterial proliferation is the source of their success, but at the same time is also the cause of their failure. In many cases, selective pressure imposed by the use of conventional antibiotics leads to increased expression of degrading enzymes and development of drug-efflux systems which operate with increased efficiency and therefore actively reduce the internal concentration of the antibiotics. Furthermore, research over the last two decades has revealed that bacteria in the biofilm mode exhibit a higher tolerance to antimicrobial treatments[16] . The biofilm mode of growth also protects opportunistic pathogens, such as Pseudomonas aeruginosa, against the action of the host immune system, which in turn facilitates establishment of chronic infections[17]. In nature, eukaryotes live closely associated with virulent prokaryotes. This has forced mammals to evolve different defence systems. Plants and fungi, however, do not possess active immune systems; instead they have to rely on physical and chemical defaces. A well-studied example of this is the production of halogenated furanone compounds by the Australian alga Delisea pulchra[18].

Control of microbial infections by inhibition of microbial growth or quorum sensing has been the base of antimicrobial chemotherapy[19]. However, an emerging problem associated with misuse of antibiotic therapy is the worldwide emergence of higher level tolerance of target organisms against available broad spectrum antibiotics.[20] As a result, and in the light of the rapid spread of multidrug resistance, the development of new antimicrobial or antipathogenic agents that act upon new microbial targets has become a very pressing priority[21]. In view of the fact that quorum sensing is involved in microbial pathogenesis, research efforts have focused recently upon developing antipathogenic agents to control bacterial diseases by inhibiting quorum sensing[23,24]. Antiqourum sensing agents would offer a way of controlling microbial infections with the advantage of reducing risks of resistance development [25]. The continuing search for new and novel antimicrobials and antipathogenic agents has focused on exploiting the fact that plants surviving in an environment with high bacterial density have been seen to possess

protective means against infections[26]. Using this argument, researchers are increasingly looking at herbal products in the quest for new therapeutic and antipathogenic agents which might be nontoxic inhibitors of quorum sensing, thus controlling infections without encouraging the appearance of resistant bacterial strains[27]. Current literature estimates that 10% of all terrestrial flowering plants on earth have been used by different communities in treating diseases, however, only around 1% have gained recognition and validation[28]. Controlled studies indicate the great potential of phytochemicals to be the richest reservoir of new and novel therapeutics[29]. Although the antimicrobial activities of plant extracts are beyond doubt, in many instances their exact mechanism of antimicrobial functionality is not well understood[30].

Butea superba Roxb., a member of Papilionaceae is a rare, endangered medicinal plant, found sparsely distributed in Western Ghat's region of Karnataka state. The plant is commonly known as Lathapushpa (Sanskrit) and Muttugada balli (Kannada). Leaf juice is used in treating heat eruptions in children, stembark is used in the preparation of tonics, elixire and in poultice and stem is known to contain flavonoids and flavone glycosides. Root contains oestrogenic substance, two glycosides[1]and is used against erectile dysfunction.

The plant *Vernonia arborea* Hk., is a moderate sized tree of Asteraceae, it is sparsely distributed in the costal districts of Karnataka state, especially in South Canara district. The plant is used medicinally viz., leaf juice is used to treat worms in children's eyes, infusion of roots or a decoction of bark is given in fever. In Southern Sumatra, the bark is chewed at the first sight of sprue, also chewed as a substitute for pan by Nagas. The plant contains sesquiterpene, Zaluzanin D, which is a potent anti fungal agent. The plant is potent against hepatitis and septic wounds.

Pterocarpus santalinus L.f. (Fabaceae) is commonly called as Red sander (English), Kempu honne (Kannada) and Raktachandan (Sanskrit). It is an endangered plant species, endemic to the state of Andrapradesh in India. The plant is renowned for its

characteristic timber of exquisite color, beauty and superlative technical qualities and ranks among the finest luxury in Japan. Wood is used as astringent, tonic, as external application for wounds, cuts and inflammations, in treating headache, skin diseases, fever, boils, scorpion sting and to improve sight. The red wood yields a natural dye santalin which is used as a coloring agent in pharmaceutical preparations, food stuffs; fruit extract is used as astringent, diaphoretic, in inflammations, headache, skin diseases, bilious infections and chronic dysentry. Heart wood is known to possess isoflavone glucosides, savinin, calocedrin[8] and triterpene. The lignan isolated from the heartwood is known to inhibit tumor necrosis factor–alpha production and T-cell proliferation [8]thanolic stem bark extract is known to possess antihyperglycemic activity.

The plant *Myristica malabarica* L., (Myristicaceae) is known for many medicinal properties such as indigestion, ulcers, wounds, aphrodisiac, as rejuvenator, in bladder, inflammation, cough, diarrhea, dropsy, liver disorders, paralysis, rheumatism, urinary calculi, vomiting, in bronchitis, fever, burning sensation, relief of pain in muscles, sprains and sores. The plant contains many active constituents like 7, 4-dimethoxy-5 hydroxyl isoflavone, biochanin A, prunetin, 1,3-diarylpropanol and alpha-hydroxyldihydrochalcone, 2-acylresorcinol, diarylnonanoids, malabaricone, malabaricone A, Malabaricones A-D, diarylnonanoids. The plant is known for its antioxidant activity.