Screening of Bioactive peptides from marine microbes

The Ocean, which is called the ‘mother of origin of life’, is also the source of structurally unique natural products that are mainly accumulated in living organisms. The marine environment continues to provide a wealth of microorganisms from which to discover structurally unique bioactive secondary metabolites. Several of these compounds show pharmacological activities and are helpful for the invention and discovery of bioactive compounds, primarily for deadly diseases like cancer, acquired immunodeficiency syndrome (AIDS), arthritis, etc., while other compounds have been developed as analgesics or to treat inflammation, etc. Today, approximately one-half of all cancer drug discovery focuses on marine organisms, and forecasts for the future are bright. In fact, some of the most important recent discoveries have been made from the marine environment.

With the enormous potential for discovery, development, and marketing of novel marine bioproducts comes the obligation to develop methods by which these products can be supplied in a way that will not disrupt the ecosystem or deplete the resource. Supply of most marine-derived compounds is a major limiting factor for further pharmaceutical development. Often, the metabolite occurs in trace amounts in the organism, and a steady source of supply from wild harvest cannot provide enough of the target compound for preclinical studies. Some options for sustainable use of marine resources are chemical synthesis, in vitro production through cell culture of the microorganism or microorganism source, and transgenic production.

In the past century, an increasing role has been played by microorganisms in the production of antibiotics and other drugs for the treatment of some serious diseases. In recent years, many bioactive compounds have been extracted from various marine animals like tunicates, sponges, soft corals, sea hares, nudibranchs, bryozoans, sea slugs and marine microbes. The search for new metabolites from marine organisms has resulted in the isolation of more or less 10,000 metabolites, many of which are endowed with pharmacodynamic properties. Between 1977 and 1987, around 2500 new metabolites (Marine Natural Products) were reported from marine organisms ranging from microbes to fish, which accounts for less than 1.0% of the total marine organisms. Marine microbes provided numerous novel compounds with sensational multiple pharmacological properties ranging from antiviral to anticancer have been isolated from various marine sources. The marine pharmacy currently holds more than 35,000 marine derived biological samples, with approximately 150 compounds to be cytotoxic against the tumor cells.

India is one among 12 mega-biodiversity countries and 25 hot spots of the richest and highly endangered eco-regions of the world. Among the Asian countries, India is perhaps the only one that has a long record of inventories of coastal and marine biodiversity dating back to at least two centuries. In terms of marine environment, India has a coastline of about 8000 km, an Exclusive Economic Zone (EEZ) of 2.02 million km² adjoining the continental regions and the offshore islands and a very wide range of coastal ecosystems such as estuaries, lagoons, mangroves, backwaters, salt marshes, rocky coasts, sandy stretches and coral reefs, which are characterized by unique biotic and abiotic properties and processes. Whereas, adequate efforts are yet to be made by
Indian scientists to explore the marine microbes towards harnessing them for isolation of potential bioactive molecules for therapeutic applications.

Marine natural products have attracted the attention of biologists and chemists the world over for the last five decades. To date approximately 16,000 marine natural products have been isolated from marine organisms and several bioactive compounds had antiviral, antibacterial, antimalarial, anti-inflammatory, antioxidant, and anticancer potentials. But till date only few anticancer drugs (cytarabine, vidarabine) have been commercially developed from marine compounds while several others are currently in different clinical trials. Pharmacological investigations of marine organisms are relatively new and have been founded on the establishment of unprecedented "scientific bridges" between the marine and pharmaceutical sciences. The ocean is considered to be a source of potential drugs. Various species of bacteria, fungi, actinomycetes, dinoflagellates, algae, coelenterates, sponges, corals, soft bodied molluscans, echinoderms, fishes etc are expected to have potential bioactive molecules that require serious attention. Although sporadic attempts are being pursued around the world to screen drugs from sea the efforts are mainly focused on screening organisms from the neritic and coastal environments. The recent appearance of a growing number of bacteria resistant to conventional antibiotics has become a serious medical problem. To overcome this resistance, the development of antibiotics with novel mechanisms of action is a pressing issue. Endogenous antimicrobial peptides are exciting candidates as new antibacterial agents due to their broad antimicrobial spectra, highly selective toxicities, and the difficulty for bacteria to develop resistance to these peptides. The ocean covers 71% of the surface of the earth and contains approximately half of the total global biodiversity, with estimates ranging between 3 and 500 x 10^6 different species. Therefore, the marine environment, especially marine microbes, is a spectacular resource for the development of new antimicrobial compounds.

In the present research programme it is proposed to target marine microbes, bacteria and fungi towards screening bioactive molecules including bioactive peptides with varied bioactivities such as antibacterial, antifungal, antiviral, antitumor, analgesic, anti-inflammatory and antidiabetic. Once the active molecules are recognized the bioactive molecules will be purified, characterized and the gene encoding them will be isolated towards further cloning and expression in domesticated hosts so that they can be produced at industrial level. Further, once the molecular structures of the bioactive molecules are recognized the same could be also utilized for synthesis of similar bioactive molecule towards therapeutics application.

**Objectives**
The present proposal primarily aims at screening and isolation of bioactive molecules from microbes isolated from marine environments around Indian subcontinent.

Specific objectives include the following:
1. Screening of marine microbes (bacteria and fungi) for various bioactive molecules with potential for antibacterial, antifungal, antiviral, anti-tumour, anti-inflammatory, anti-diabetic activities and other bioassays.
2. Purification of the potential molecules with bioactivity.
3. Physical, chemical and immunological characterization of the potential molecules with bioactivity.
4. Isolation of genes coding for bioactive peptides.
5. Construction of genomic library for the bioactive peptides towards further utilization of the genes for cloning and expression in domesticated hosts of subsequent industrial production of the bioactive molecules.

**Anticipated output from the proposal**
The present project is anticipated to contribute the following:
- Recognition of bioactive molecules with antibacterial, antifungal activity against well known pathogens, anti-diabetic activity, anti-tumour activity, anti-inflammatory activity, anti-viral activity, analgesic activity which could be patented.
- Isolation of genes encoding bioactive peptides, which could be adopted for the transgenic production of the bioactive molecules by pharmaceutical industry in our country.
- Recognition of structure of the bioactive molecules could enable chemical synthesis of them and consequent industrial production by pharmaceutical industries.