INTRODUCTION
1. INTRODUCTION

The marine environment is known as a rich source of chemical compounds with numerous beneficial health effects. Marine algae are recognized as rich sources of structurally diverse biologically active compounds with great pharmaceutical and biomedical potential. Among the marine organisms, the macroalgae occupy an important place as a source of biomedical compounds (Manilal et al., 2010). About 2400 natural products have been isolated from macroalgae belonging to the classes Rhodophyceae, Phaeophyceae and Chlorophyceae (Faulkner, 2001). Researchers have revealed that marine algal originated compounds exhibit various biological activities such as anticoagulant, anti-viral, antioxidant (Zou et al., 2008), anti-allergic (Li et al., 2008), anti-cancer (Kong et al., 2009), anti-inflammatory, anti-obesity (Kong et al., 2010) and others. Furthermore, several scientific studies have provided insight into neuroprotective properties of marine algae. Many species of marine algae have long been used in food diets as well as traditional remedies in eastern countries and more recently in Europe and America. Hence, marine algae have great potential to be used in neuroprotection. Macroalgae are the fascinating and diverse group of organisms living in the earth's oceans. We can find them attached to rocks in the intertidal zone, washed up on the beach, in giant underwater forests, and floating on the ocean's surface.

In Asian maritime areas, macroalgae extracts were used as curative or preventive agents for various maladies and can serves as antibiotics, antihelmintics, antihypertensive, antipyretic, antitumour, antidiarrhea, wound healings, upper respiratory tract infections, post operative infections (Ravikumar et al., 2002), treatment for gallstones and goiter (Chengkui and Chang, 1984).

Reports of Itoh et al. (1995) showed the lower incidence of breast cancer in the Japanese and Korean Populations has intrigued researchers. Researchers have found that dietary brown algae and their extracts inhibit carcinogen-induced breast cancers, lung metastases and leukemia in animal
models. Similarly tests on the macroalgal extracts in bacterial systems revealed that the extracts had a profound antimutagenic quality (Okai et al., 1993. Species of Sargassum were used for cooling and blood cleansing effect. Hypnea musciformis was employed as vermifuge or worm expelling agent and Centroceras clavulatum as cathartic agent. Macroalgae rich in iodine such as Asparagopsis taxiformis and Sarconema can also be used for controlling goitre, diseases caused by the enlargement of thyroid gland.

**Antioxidant**

Oxidative stress is the result of an imbalance between pro-oxidant and antioxidant homeostasis that leads to the generation of toxic reactive oxygen species (ROS). Compared to other parts of our body, the central nervous system (CNS) is more sensitive to oxidative stress due to its high oxygen consumption and lipid content. Increased oxidative stress in the CNS will further lead to lipid peroxidation, DNA and protein damage. Oxidative stress in the CNS has been demonstrated to involve excitotoxicity and apoptosis, the two main causes of neuronal death. Furthermore, oxidative stress has also been implicated the progression of Alzheimer’s disease (AD), Parkinson’s disease (PD), multiple sclerosis (MS) and other neurodegenerative diseases (Migliore et al., 2009). Antioxidants may have a positive effect in the CNS and seem to be a promising approach of neuroprotection therapy. Marine algae prove to be one of the useful candidates that can protect the CNS against oxidative degradation. Hence developing novel molecules derived from marine algae which promote antioxidant activity in the CNS may lead to the development of effective neuroprotective agents.

**Anti-Neuroinflammation**

Inflammation has been found to be the pathophysiological mechanism underlying many chronic diseases such as cardiovascular disease, diabetes, certain cancers, arthritis, and neurodegenerative diseases. Ecklonia cava, the “sea trumpet” has been reported to possess anti-
inflammatory activity (Jung et al., 2008). *E. cava* was able to suppress the levels of pro-inflammatory mediators.

**Cholinesterase Inhibitory Activity**

Alzheimer’s diseases (AD) is an irreversible, progressive neurodegenerative disease, which resulting in memory loss, behavior disturbances, personality changes and a decline in cognitive abilities. The serious loss of cholinergic function in the CNS contributes significantly to the cognitive symptoms associated with AD. AD was associated with deficiency in the brain neurotransmitter acetylcholine (ACh) (Pietrini et al, 2000). Several marine algal species are reported to have significant AChE inhibitory activity such as *Ulva fasciata*, *Caulerpa racemosa*, *Hypnea valentiae* and *Ulva reticulata*.

**Cytotoxic activity**

The cytotoxic activities of organic solvent extracts of three brown algal species (*Sargassum swartzii*, *Cystoseira myrica* and *Colpomenia sinuosa*) were investigated by Khanavi et al (2010). The results showed that extracts had some effects on different cancer cells. Two novel trihydroxylated diterpenes were isolated from the brown algae *Bifurcaria bifurcate*. Both compounds were tested in vitro for their cytotoxicity and proved to be active against the NSCLC-N6 cell line. Two novel cyclized meroditerpenoid satomarianones derived from the brown algae *Taoniaatomaria* were found to exhibit significant cytotoxic activity against two lung cancer cell lines. De Inés et al (2004) investigated the cytotoxic effects of nine halogenated monoterpenes isolated from the red algae *Plocamium cartilagineum* against different tumor cell lines. The results showed that some compounds had strong and interesting cytotoxic activities.

**Anticancer properties of Macroalgae**

The anticancer properties of macroalgae have been well documented. Since ancient times, the Chinese and Egyptians used brown algae to treat breast cancer (Luis J. Villarreal-Gómez et al.,
Macroalgae derived oligo and polysaccharides have been demonstrated to induce apoptosis (programmed cell death) in cancer cell lines and some including carrageenan and alginate can inhibit the growth of tumours in rodents through immunomodulating activity. Japan produces a range of macroalgae based products that are active against leukemia, stomach and colon cancer. The active ingredient is cl-fucoidanTM, a guluronic rich polysaccharide extracted from kelps. The active components are fucoidan, laminaran, and alginate.

Fucoxanthin (photosynthetic Pigment) extracted from the kelp Undaria can significantly reduce the viability of human prostate cancer cells and colon cancer cells. Japanese women typically suffer from very low levels of estrogen related cancers (breast and cervical) and it is thought that this is due to the high levels of brown algae that they ingest. Macroalgae are also a good source of the trace element selenium which is currently attracting a lot of attention regarding its potential anticancer properties.

**Anticoagulant activity of Macroalgae**

Thrombosis is a health problem that affects many people in the world. Researches has been done in anticoagulant activity of polysaccharides and glycosaminoglycans of diverse sources such as Ascidians, Sea Cucumber and Tunicates. In recent years, sulphated polysaccharides from marine algae have been demonstrated to have many biological activities such as anticoagulants, antiviral, antitumour, hypolipidemic etc.. Heparin is used as an anticoagulant which has some disadvantages as it is extracted and purified from internal organs of higher animals making its production difficult and also it exhibits haemorrhagic side effects. These disadvantages associated with heparin have opened up a new area of antithrombotic research for anticoagulant activity of SPS from marine algae was first reported in 1936.
Antibacterial substances from algae

Many compounds of marine algae show anti-bacterial activities such as polysaccharide (Laurienzo, 2010), lyengaroside (Ali et al., 2002), polyhydroxylated fucophlorethol (Sandsdalen et al., 2003), bromophenols, guaianesesquiterpene (Chakraborty et al., 2010), lactone malyngolide (Cardelina et al., 1979), cycloeudesmol (Sims et al., 1975), polyphenolic compound (Devi et al., 2008), halogenated compound (Vairappan, 2003) and quinone metabolite (Horie et al., 2008).

Antiviral Effects

Brown macroalgae, including the commonly eaten Undaria have inhibitory effects on herpes viruses. Herpes viruses are important human pathogens and include Herpes simplex (HSV1), genital herpes (HSVII), Varicella/chicken pox/shingles, Cytomegalo virus, Epstein-Barr virus (EBV), herpes 6, Herpes7 (Roseola, post-transplant infections), and Herpes8 (associated with Kaposi’s sarcoma). Ingestion of Undaria led to inhibition of herpes and amelioration of active infections in a patient study. kahalalide F from a species of Bryopsis as a possible treatment of lung cancer, tumours and AIDS.

According to the findings of Witvrouw et al., (1994) sulphated polysaccharides from macroalgae Aghardhiella tenera and Nothogenia fastigiata show antiviral activities against human immunodeficiency virus, Herpes simplex virus, human Cytomegalo virus and respiratory syncytial virus. Carlucci et al (1997) reported that carrageenan isolated from the red algae Gigartina skottsbergii showed antiviral activity against herpes simplex virus types 1 and 2. Feldman et al (1999) isolated three fractions of fucoidan from the brown algae Leathesia difformis and investigated their antiviral activities. They reported that these compounds showed selective antiviral activities against Herpes simplex virus types 1 and 2 and human Cytomegalo virus.
Effects on Plasma Cholesterol and Hypertension

Many foods are known to reduce cholesterol levels and brown algae fall into this category. *Undaria* ingestion results in lower cholesterol levels in rats. *Undaria* fucogalactan fractions were shown to reduce lipid clearance dramatically when introduced intravenously. The fucoidan component may block the macrophage scavenger receptor that is involved in low-density lipoprotein uptake. It contains substantial amounts of laminine and similar tetrapeptides, which have been shown to have angiotensin-converting enzyme inhibitory qualities both in vitro and in vivo. Ingesting 3.6 g per day of *Undaria* (wakame) for 4 weeks resulted in a 14 mm Hg drop in systolic blood pressure in Asian patients who had hypertension.

Bioactivity of Fucoidan

Fucoidans and their oligosaccharides have attributed several different bioactivities. These include anti-tumoral, anti-coagulant (Silva *et al.*, 2005), anti-viral and antiinflammatory activities. It is postulated that sulphate groups are essential for the antiviral activity and that a higher sulphation degree is beneficial for the antiviral and anti-tumoral activity and that structure plays a major role in the biological activity. Algal polysaccharides have been suggested to affect the virus adsorption and penetration. The antitumour activity relies on the inhibition of the proliferation and the induction of apoptosis. Wound healing processes are accelerated because of the activity of fucoidan.

Use of Macroalgae as fertilizers

In India, large quantities of macroscopic marine algae and seagrasses have been utilized directly as manures or in the form of compost. In recent years the use of natural macroalgal products as substitutes to the conventional inorganic fertilizers assumed importance. Due to the presence of potassium chloride (KCl) in macroalgae, they are used as fertilizers in many countries such as Japan, France, United States, England and South India. Macroalgae are used in different parts of the world as fertilizer for various land crops. In India, freshly collected and cast ashore macroalgae are used as
manure for coconut plantation either directly or in the form of compost in coastal areas of Tamil Nadu and Kerala. Macroalgae manure has been found superior to farm yard manure. Macroalgal liquid fertilizers promote seed germination, shoot length, root length and leaf area (Thankam et al., 2003). The liquid macroalgal fertilizer obtained from macroalgal extract is used as foliar spray for inducing faster growth and yield in leafy and fleshy vegetables, fruits, orchards and horticultural plants.

Bioactive compounds from macroalgae

Algal pheromones, caulertpenyne from green algae Caulerpa taxifolia, diterpenes from brown algae, triterpenes and sterols from green algae Tydemania, Cytotoxic sesquiterpene peroxide-majapoleneA from Laurencia majuscule, Cytotoxic polyether isodehydrothyrsiferol from Laurencia viridis, Anti HIV brominated biprenyl quinol peyssonol A from Peyssonnetia sp. antifouling brominated furonones from Delisea pulchra and antibacterial dipeptide almazole D from red algae Senegalese.

Other uses

Macroalgae is currently under consideration as a potential source of bioethanol. Macroalgae is an ingredient in toothpaste, cosmetics and paints. Alginates are used in industrial products such as paper coatings, adhesives, dyes, gels, explosives and in processes such as paper sizing, textile printing, hydro-mulching and drilling. The present uses of macroalgae such as extraction of industrial gums and chemicals. They have the potential to be used as a source of long- and short-chain chemicals with medicinal and industrial uses. Marine algae may also be used as energy-collectors and potentially useful substances may be extracted by fermentation and pyrolysis. Rotting macroalgae is a potent source of hydrogen.
Bioactive potential of macroalgal associated bacterial species

Animals and plants typically exist in association with specific microbial biota (Bry et al., 1996). Bacteria grow and feed partly or wholly on the metabolic products of the host (Shib and Taga, 1980). In recent years marine organisms have become more important in the study of novel microbial products exhibiting antimicrobial, antiviral, antitumour, anticoagulant and cardioactive properties. The intertidal macroalgae belongs to the group of green marine algae known to require the presence of bacteria for normal growth and also for the defence against fouling organisms. In many cases the populations found are specific, with changes occurring throughout the year or throughout the life of basibiont. Epibiotic bacteria protect them from infections by the production of antimicrobial compounds.

Epiphytic bacterial communities on the surface of marine algae have diverse origin (Wang Zifeng et al., 2009). With the rapid development of molecular community analysis technologies, it is now possible to obtain a more comprehensive picture of microbial populations on living surfaces. Rosenfeld and Zobell (1947) demonstrated that marine bacteria produce anti-microbial substances. The first documented identification of bioactive marine bacterial metabolite was the highly brominated pyrrole antibiotic isolated by Burkholder from a bacterium obtained from the surface of the Caribbean sea grass Thalassia (Burkholder et al., 1960). Marine natural products serves as a tool for drug discovery. Endosymbiosis is a relationship in which a member of one species lives not just near or even permanently on a member of another species. Production of antibacterial compounds by the surface flora of the macroalgae was demonstrated by Lemos et al (1985). The Secondary metabolites produced by marine bacteria serves as antibiotics. Identification of bacterial groups in marine environment has been made possible in the past decade by the application of molecular techniques (Giovannoni et al., 1990).
Icthyoprotective properties of marine macroalgae

Fish diseases may occur due to many reasons such as nature of water, type of feed, salt content and external infectious agents such as parasites, bacteria, fungus and viruses. The oxygen content and pH plays a major role. Similarly the parasites attached to the gill and the body of the fish creates a lot of problems to the fish farms (Faruk et al., 2004). Many bacteria cause infections in fish and cause ulcers, blood spots or misty eyes on susceptible fishes. Similarly, fungal infections can also be noted on the skin of infected fishes. Viral infection may cause sudden death of fish masses. The bioactive compounds isolated from the macroalgae showed remedial measures against fish infections caused by Vibrio parahaemolyticus, Aeromonas hydrophila, etc and gradually increased the resistant property and prolonged the survival rate of the fishes. Macroalgae are used in traditional remedies in many parts of the world. The production of inhibitory substances by macroalgae was noted as early as in 1917. Macroalgae serve as a potent reservoir of many bioactive metabolites. These bioactive compounds have the potential to treat many plant, animal, human and fish pathogens (Seenivasan et al., 2010).

Microbe-Macroalgal Interaction

Marine macroalgae have been challenged throughout their evolution by microorganisms and have developed in a world of microbes. Therefore, it is not surprising that a complex array of interactions has evolved between macroalgae and bacteria which basically depends on chemical interactions of various kinds. Bacteria specifically associate with particular macroalgal species and even to certain parts of the algal body. Although the mechanisms of this specificity have not yet been fully elucidated, ecological functions have been demonstrated for some of the associations. Though some of the chemical response mechanisms can be clearly attributed to either the alga or to its epibiont, in many cases the producers as well as the mechanisms triggering the biosynthesis of the biologically active compounds remain ambiguous (Thevanathan et al., 2000). Positive macroagal-
bacterial interactions include phytohormone production, morphogenesis of macroalgae triggered by bacterial products, specific antibiotic activities affecting epibionts and elicitation of oxidative burst mechanisms. Some bacteria are able to prevent biofouling or pathogen invasion or extend the defense mechanisms of the macroalgae itself. Deleterious macroalgal bacterial interactions induce or generate algal diseases. To inhibit settlement, growth and biofilm formation by bacteria, macroalgae influence bacterial metabolism and quorum sensing and produce antibiotic compounds. There is a strong need to investigate the bacterial communities living on different coexisting macroalgae using new technologies, but also to investigate the production, localization and secretion of the biological active metabolites involved in those possible ecological interactions. Ubiquitous epiphytic bacteria have been observed among the thallus surfaces of many macroalgae (Shiba, 1992). Phylogenetic analysis of bacterial sequences derived from the macroalgae have been documented (Meusnier et al, 2001).

Today one of the thrust areas in biomedical research is bioprospecting for novel bioactive compounds from marine resources. The current research is oriented towards the study of interaction that exist between the macroalgae and their associated microbes, both ectosymbionts and endosymbionts, their potential to inhibit potent medically important bacterial pathogens isolated from clinical samples and also to prove the immune modulating effects of macroalgae against fish pathogen *Aeromonas hydrophila* under invivo conditions.