e-ISSN: 2321-6182 p-ISSN: 2347-2332

Marine Pharmacology: A Promising Hand for New Drug Development

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Research Article

ABSTRACT

Received: 12/10/2016 Revised: 26/11/2016 Accepted: 30/11/2016

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Keywords: Marine drugs, Marine organism, Pharmacology, Organic compounds

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Lots of work is going on to develop new drugs for human kind. Earlier our researches were mainly based on natural organic compound. Later we shifted our focus towards synthetic organic compound. Unfortunately synthetic drugs causing side effects. With change in our lifestyle we face new challenge in medical science which can be resolve by natural resources obtained from terrestrial and marine organism. Over thousands of new drugs launched in last decades originating from marine microbes, plants as well as animals. Now marine drugs either directly or indirectly play a vital role in pharmacology. Hence, this review provides baseline information of new discoveries in marine pharmacology and highlights the topics required attention.

INTRODUCTION

Ocean occupied 70% of earth surface with diversity of plants, animals and microbes. Ocean house millions of marine organisms which are source of unique chemical compounds. We merely exploit the marine organism for medicinal purpose. With the emergence of new and fatal human diseases marine pharmacology comes in lead role. Many marine invertebrates release toxic compound to defend themselves against predators. These secondary metabolites attracted the scientist all over the word for anaesthetic substitute ^[1].

Marine ecosystem comprises taxonomically diverse algae, fungi, bacteria, seaweeds, mangrove vegetation, and other planktons. The marine flora is rich in various secondary metabolites such as peptides, polysaccharides, terpenes, tannins, and fatty acids ^[2].

Drug demands and their continuous supply is an important matter for medical field which might be resolved by new innovation in pharmaceutical sciences based on marine organism ^[3]. Antibiotic properties of certain marine product give us an opportunity to exploit our vast marine biota for medicinal purpose ^[4].

In last five decades we discovered more than 20,000 compounds from different marine organism ^[5]. For systematic analysis of drugs derived from marine organism we divided the whole review paper in three subtopics:

- Marine microorganism
- Marine algae and plants
- Marine invertebrates

Marine Microorganism

Marine bacteria Pseudoalteromonas produce toxic proteins, ployanionic exopolycahharides, substituted phenolic, and pyrolle containing alkaloids, cyclic peptides and a range of bromine-substituted compounds. These biomaterials showed antimicrobial, anti-fouling, algicidal and various pharmaceutically-relevant activities ^[6,7]. Fungal infections are generally caused morbidity and mortality in marine mammals. The genus candida consists of 200 pathogenic species ^[8-10]. Chan et al. isolated six strains of halophilic bacteria from sea coast of China. These bacteria were found to be potential agent for extracellular proteases ^[11-14].

Marine Algae

Marine algae are the source of many bioactive compounds with antioxidant activity. Both microalgae and microalgae contain pharmacologically important compounds. These biomaterials are utilized in cosmetics and pharmaceuticals. Scientist evaluated the mechanism of action, disinfection, and efficacy, potential application of product obtained from red, brown, and green algae in laboratory ^[15-17].

Some marine flora produced antioxidant and antiradial activities (e.g. Spirulina platensis) as reported by Shalaby and Shanab ^[18,19]. Lakshmi et al. have selected C. hornemanni to evaluate its antileishmanial potential ^[20]. A

Research and Reviews Journal of Pharmacognosy and Phytochemistry e-ISSI

study was designed to evaluate the lipid lowering potential of total extract as well as several fractions from Pseudobryopsis mucronata by Lakshmi and Puri^[21]. This alga has been selected for lipid lowering activity because it showed lipid lowering effect in our random screening programme of marine flora. Kappaphycus alvarezii is red seaweed rich in polysaccharides. Sakthivel et al. were attempted to isolate polysaccharide from K. alvarezii and also tested for immunostimulatory effects on Asian seabass (Lates calcarifer) using Vibrio parahaemolyticus as a test pathogen ^[22].

Marine cyanobacteria have been extensively used in cancer research. It produces chemically diverse compounds which induce anti-inflammatory effect and used as template for development of anticancer drugs. Besides this it causes cytotoxic effect in tomor cell line. The most important effect is cell cycle arrest, mitochondrial dysfunction, oxidative damage, and alternation in membranes sodium dynamics ^[23,24].

An investigation carried out by scientist about most abundant phytosterol in brown algae. They found it showed cytotoxic effect on breast and colon carcinoma cell lines. Anticancer compound fucosterol, which was derived from brown algae, is effective against breast cancer and colon carcinoma cell line ^[25]. Many polysaccharides derived from marine products show promising therapeutic application. Marine polysaccharides are species specific and having great chemical diversity ^[26-28].

Several scientists reported that sulphated polysaccharides and oligosaccharides isolated from marine algae have antiviral, immunoinflamatory, antithrombotic, antilipidemic, and antioxidant activities ^[29]. Another example was reported from brown algae carotenoid fucoxanthin. In laboratory experiment it was found that fucoxanthin expresses antitumoral, ant metastatic, and antiangiogenic activities ^[30].

Mangrove Vegetation

Mangroves ecosystem provides unique environmental conditions and harbor rich microbial communities. Among these fungi is one of the most important components. Simultaneously studies have revealed that endophytes are recognized as a source of novel metabolites and produce a wide range of biologically active compounds. Studies suggested that marine mangrove fungi serve as a source of biologically active natural products and a large number of antimicrobial compounds have been isolated from these endophytes belonging to several classes like alkaloids, peptides, steroids, terprnoids, phenols, quinines and flavonoids. It has been reported that metabolites isolated from endophytes acts as anti-carcinogenic agents and as an alternate source of plant originated compounds ^[31]. Scientist isolated anti-tumor compound from actinomycetes inhabited in mangrove. They isolated biologically active metabolites from fungi in vicinity of mangrove vegetation ^[32].

Marine Invertebrate

Marine invertebrate produce unique chemical compounds in their vicinity to protect against predators. These secondary metabolites are now considered as potent drug in disease cure. Some of them already launched in market such as Prialt (ziconotide;potent analgesic) and Yondelis (trabectedin or ET-743;antitumor) while others have entered clinical trials, e.g., alpidin and kahalalide ^[33]. Aiello et al. reported 130 antitumor alkaloids from marine invertebrates. These alkaloids belongs to different structural families e.g. indole,pyrrole, quinolines, and pyridoacridines etc. ^[34]. Grosso et al. summarized the potential of marine invertebrates in neuroscience particularly neurotoxins and neuroprotective drugs ^[35]. Marine natural product sarcophine was isolated from soft coral Sarcophyton glaucum. Sarcophine was showed remarkable chemopreventive activity for skin cancer ^[36].

Asian people are familiar with use of sea cucumber in traditional medicine. They use sea cucumber as dietary supplement for long time. The important secondary metabolite in sea cucumber is triterpene glycosides ^[37]. Sea cucumber (*Holothuria scabra*) was processed to produce high protein biscuits and jam ^[38].

Now Knottins play a crucial role in oral peptide drug development. Some plant knottins showed long term stability, high temperature resistance, and well in extreme pH condition. Conotoxins, sponges, horse shoe crabs, and sea anemone Knottins were found to be possible marine organism for clinical and industrial application ^[39,40].

Putra et al. (2014) isolated variety of alkaloids from Indonesian marine sponge. These biologically active alkaloids are mainly isolated from Leucteta chagosensis, Agelas linnaei, and Acanthostrongylophora species ^[41].

Relevance of marine organism in Cancer treatment

Nature provided many anticancer drugs like bleomycin, dactinomycin, bleomycin, and doxorubicin, vinblastine, irinotecan, topotecan, etoposide, and paclitaxel. The wealth of natural resources cannot be completely utilized without exploitation of marine organism ^[42]. Naturally derived anticancer agents play a vital role against tumors and haematological malignancies. These discoveries providing proof that nature as a valid tool to discover new innovative anticancer agents ^[43].

Tricone compared the enzymes from terrestrial and marine organism. He discussed the stereochemistry and usefulness of marine biocatalyst. He reported that sustainability of collection methods and availability of organism are two important aspects for their commercial use ^[44]. Some other groups of scientist also tried to find out new drugs for cancer treatment ^[45-51].

Research and Reviews Journal of Pharmacognosy and Phytochemistry e-ISSN: 2321-6182

p-ISSN: 2347-2332

Alzheimer's disease is a neurodegenerative disorder with incurable symptoms. Current drugs show temporary effect for restricted time period. Some marine derived organic compound (example Cytarabine, Trabectedin, Eribulin and Ziconotide) found effective in neurodegeneration ^[52].

CONCLUSION

Ancient civilization has been using natural medicine for long time around the globe. Ocean comprises diverse species of plants and animals. These produce unique compound having antimicrobials activity. These antimicrobials act either directly by killing the bacterial pathogen or through parallel mechanism similar to antibiotics [14].

Marine environment generate a stressful condition where inhabitants acclimate to survive. Most of the survivors are rich in secondary metabolites which are medically useful for human kinds. Mostly these biomaterials are directly applied as drugs substitute or used as template for synthetic drug development ^[53].

Marine drugs are new hope for future drug development. But pharmaceutical industries facing problem in many cases like continues supply and sustainable production. Due to molecular complexity and low yield their commercial production is not economically feasible. This can be sort out by gene manipulation and Mari-culture. Advanced biomedical research is carried out before large scale commercial application ^[54-63]. Marine organisms are helpful in clinical trials [64-83]. The pharmacokinetic of norfloxacin following single intravenous and oral administration in healthy goldfish were investigated [84].

Modern sophisticated techniques like computer added drug designing should play a significant role in marine drug development ^[85-89]. But sustainable management of natural resources is main challenge in present scenario ^{[90-} ^{100]}. Overall conclusion of this review is to present a new opportunity in marine pharmacology especially incurable cancer disease.

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