Seaweeds: A novel, untapped source of drugs from sea to combat Infectious diseases

S. Chanda*, Dave R, Kaneria M and Nagani K

Phytochemical, Pharmacological and Microbiological Laboratory, Department of Biosciences, Saurashtra University, Rajkot 360 005, Gujarat, India

* author for correspondence email: svchanda@gmail.com

The discovery and development of antibiotics are among the most powerful and successful achievements of modern science and technology for the control of infectious diseases. Prolonged usage of broad – spectrum antibiotics has led to the emergence of drug resistance. There is a tremendous need for novel antimicrobial agents from different sources. The biodiversity of marine ecosystem provides an important source of chemical compounds which have many therapeutic applications. Seaweeds or marine algae have been reported to contain many important compounds which act as antibiotics, laxatives, anticoagulants, anti-ulcer products and suspending agents in radiological preparations. Many substances obtained from marine algae such as alginate, carrageenan and agar as phycocolloids have been used for decades in medicine and pharmacy. More and more chemist and biologist pay attention to the constituents of the algae; if their natural products are explored, they may lead to an efficient lead for the discovery of new drug molecules against several pathogens causing infectious diseases.

Key words: Infectious diseases; seaweeds; antimicrobial; marine algae

1. Synthetic dominance: growing threat of antimicrobial resistance

Mankind's discovery of antibiotics ushered in a new age of medicine during the 19th century, an age wherein many predicted an end to diseases that had plagued the mankind for centuries with the appearance of penicillin during World War II as the first miracle drug [1]. From 1940s to almost 1980s many classes of antibiotics discovered have helped tame many of the terrors of human health. The use of these "wonder drugs", combined with improvements in sanitation, housing, nutrition, and the advent of widespread immunization programmes, led to a dramatic drop in deaths from diseases that were previously widespread, untreatable, and frequently fatal. Over the years, antimicrobials have saved the lives and eased the suffering of millions of people.

Advances in synthetic chemistry for identification of many key chemical molecules offered more opportunities to develop novel compounds. Numerous drugs like sulphonamides, isoniazid, anti-psychotics, anti-histamines and penicillin were developed from thousands of chemicals [2]. Emergence of modern pharmaceutical industry is an outcome of all these different activities that developed potent single molecules with highly selective activity for a wide variety of ailments. These successes resulted in reduced interest in natural products drug discovery. Thus, herbal medicines became the domain of ‘old wives tales’.

It was not until the 1970s that antibiotic resistance was considered to be a real threat. In the past, medicine and science were able to stay ahead of this natural phenomenon through the discovery of potent new classes of antimicrobials, a process that flourished from 1930-1970 and has since slowed to a virtual standstill, partly because of misplaced confidence that infectious diseases had been conquered, at least in the industrialized world. In just the past few decades, the development of resistant microbes has been greatly accelerated by several concurrent trends like urbanization, pollution, AIDS epidemic, etc. These have worked to increase the number of infections and thus expand both the need for antimicrobials and the opportunities for their misuse.

Recently, infections have become the leading cause of death world-wide which has led to an increase in antibacterial resistance, making it a global growing problem [3]. More and more bacteria are developing resistance to antibiotics conferred by randomly mutated genes [4]. Each year infectious diseases cause 14 million deaths worldwide, with mortality increasing even in the United States at an annual rate of 4.8 percent. In 2000, the World Health Organization (WHO) estimated that pneumonia, diarrhoeal disease, and tuberculosis accounted for more than half the deaths due to infectious disease worldwide. The problem is worsened by antibiotic resistance, as well as the emergence of new pathogens with the potential for rapid global spread [5]. In addition to this problem, antibiotics are sometimes associated with adverse effects on the host including hypersensitivity, immune-suppression and allergic reactions [6]. Now, Scientists accepted that antibiotics will leave healthcare professionals without effective therapies for bacterial infections for example *Staphylococcus aureus*. It is estimated that about half of all strains found in many medical institutions are resistant to antibiotics such as methicillin [7]; or enterococci, which are resistant to widely effective antibiotic, vancomycin [8]. Thus, there is an urgent need to discover new antimicrobial compounds with diverse chemical structures and novel mechanisms of action for new and re-emerging infectious diseases. The new therapeutic agents should be effective and have a novel mode of action that render them impervious to existing resistance mechanisms. Not only drugs from natural sources have new structural features, with novel biological activity but
phytochemicals derived from them are also extremely useful as lead structures for synthetic modification and optimization of bioactivity.

2. Need of the hour
We are now at the crucial stage where it is essential to explore new strategies in order to combat infectious diseases. The oceans represent virtually untapped resource from which novel bioactive compounds can be discovered. The marine environment representing approximately half of the global biodiversity, is an enormous resource for new compounds. Sea weeds or marine algae are potentially prolific sources of highly bioactive secondary metabolites that might represent useful leads in the development of new pharmaceutical agents. Many reports have been published about isolated compounds from algae with biological activity, demonstrating their ability to produce metabolites, with high complexity and unlimited diversity of pharmacological and/or biological properties.

3. Seaweeds
Seaweeds belong to a group of plants known as algae. Seaweeds are classified as Rhodophyta (red algae), Phaeophyta (brown algae) or Chlorophyta (green algae) depending on their nutrient, pigments and chemical composition. Like other plants, seaweeds contain various inorganic and organic substances which can benefit human health [9]. Seaweeds are considered as a source of bioactive compounds as they are able to produce a great variety of secondary metabolites characterized by a broad spectrum of biological activities. Compounds with antioxidant, antiviral, antifungal and antimicrobial activities have been detected in brown, red and green algae [10, 11]. Some promising red, brown and green algae of Gujarat coast region are shown in Fig. 1.

The environment in which seaweeds grow is harsh as they are exposed to a combination of light and high oxygen concentrations. These factors can lead to the formation of free radicals and other strong oxidizing agents but seaweeds seldom suffer any serious photodynamic damage during metabolism. This fact implies that seaweed cells have some protective mechanisms and compounds [12].

In recent years, several marine bacterial and protoctist forms have been confirmed as important source of new compounds potentially useful for the development of chemotherapeutic agents. Previous investigations of the production of antibiotic substances by aquatic organisms point to these forms as a rich and varied source of antibacterial and antifungal agents. Over 15,000 novel compounds have been chemically determined. Focusing on bioproducts, recent trends in drug research from natural sources suggest that algae are a promising group to furnish novel biochemically active substances [13].

Seaweeds or marine macro algae are the renewable living resources which are also used as food and fertilizer in many parts of the world. Seaweeds are of nutritional interest as they contain low calorie food but rich in vitamins, minerals and dietary fibres [14]. In addition to vitamins and minerals, seaweeds are also potentially good sources of proteins, polysaccharides and fibres [15]. The lipids, which are present in very small amounts, are unsaturated and afford protection against cardiovascular pathogens.

4. Seaweeds - Diversity in marine ecosystem
Algae are known to be comparatively sensitive to chemicals [16]. Their ecological position at the base of the aquatic food chain and their essential roles in nitrogen and phosphorus cycling are critical to aquatic ecosystems [17]. Moreover, the alternation of species composition in an aquatic community as a result of toxic stress may affect the structure and function of the whole aquatic ecosystem [18].

The diversity of life in the terrestrial environment is extraordinary; the greatest biodiversity is in the world’s oceans, with 34 of the 36 phyla of life represented. The oceans cover more than 70% of the earth’s surface and contain more than 300,000 described species of plants and animals [19, 20]. The marine environment represents a treasure of useful products awaiting discovery for the treatment of infectious diseases. Ecological pressures, including competition for space, the fouling of the surface, and predation have led to the evolution of unique secondary metabolites with various biological activities [21]. The important role of these secondary metabolites in the control of infectious microorganisms was for many years largely unnoticed.

5. Seaweeds – an anti infectious agent
The revolutionized therapy of infectious diseases by the use of antimicrobial drugs has certain limitations due to changing patterns of resistance in pathogens and side effects they produce. These limitations demand for improved pharmacokinetic properties, which necessitates continued research for the search of new antimicrobial compounds for the development of drugs. Seaweeds are used in traditional remedies in many parts of the world. The production of inhibitory substances by seaweed was noted as early as in 1917.

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Fig 1. Some promising marine macro algae
6. Seaweeds – biological activities and bioactive compounds

The extracts and active constituents of various algae have been shown to have antibacterial activity \textit{in vitro} against Gram-positive and Gram-negative bacteria; some examples are given in Table 1. The production of antimicrobial activities was considered to be an indicator of the capacity of the seaweeds to synthesize bioactive secondary metabolites [22]. There are numerous reports of compounds derived from macroalgae with a broad range of biological activities, such as antibacterial [23], antivirals [24], antitumorals [25], anticoagulant [26] and antifouling [27]. Compounds with cytostatic, antiviral, antihelminthic, antifungal and antibacterial activities have been detected in green, brown and red algae [28]. Also, considering their great taxonomic diversity, investigations related to the search of new biologically active compounds from algae can be seen as an almost unlimited field.

Among the different compounds with functional properties, antioxidants are the most widely studied. Moreover, the important role of antioxidants in human health has been demonstrated thus increasing the interest in such products and their demand by consumers. Marine algae serve as important resources for bioactive natural products [29]. Brazilian red algae have been found to have phenolic substances. \textit{Kappaphycus alvarezi} has nutritive and antioxidant property; different parts of the thalli are also known to differ in their antimicrobial potential [30].

Similarly, some microalgae contain and/or excrete pharmacologically active compounds. For example, the dinoflagellates \textit{Gymnodinium} sp. and \textit{Gonyaulax} sp. produce an alkylguanidine compound that affects the central nervous system. Brominated bi-indoles of \textit{Rivularia firma} show pharmacological activity. \textit{Gracilaria lichenoides}, a red alga, excretes prostaglandins and the compound C\textsubscript{20} [31]. Seaweeds are known to contain reactive antioxidant molecules, such as ascorbate and glutathione (GSH) when fresh, as well as secondary metabolites, including carotenoids (\(\alpha-\) and \(\beta-\)carotene, fucoxanthin, astaxanthin), mycosporine-like amino acids (mycosporine-glycine) and catechins (e.g., catechin, epigallocatechin), gallate, phlorotannins (e.g., phloroglucinol), eckol and tocopherols (\(\alpha-\), \(\gamma-\), \(\delta-\)tocopherols) [32]. Brown-algal polyphenols phlorotannins worked as antioxidants and antibacterial compounds [33].

7. An attempt at integration — Conclusion

Research is a crucial part of the response to new and emerging diseases. A sustained, forward-thinking applied research programme would enable scientists to identify the weak links in the armour of emerging microbes, create novel ways to fight microbial foes, and evaluate the preventive power of new approaches. The priority for the next decades should be focused in the development of alternative drugs and/or the recovery of natural molecules that would allow the consistent and proper control of pathogen-caused diseases. The general trend to more widespread antibiotic resistance is relentless and if it continues unabated, deaths from what were previously treatable infections will occur with increasing frequency. The initiatives must be implemented now because the battle against antibiotic resistance is being lost. Complacency and delay will have major detrimental effects on future public health. Seaweeds may be an answer to unsolved and growing problem of resistance, a novel untapped source to combat infectious diseases.
<table>
<thead>
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<td>2</td>
<td>Corallina officinalis, Cystoseira barbata, Dictyota dichotoma, Halopteris filicina, Cladostephus spongiosus f. verticillatus, Ulva rigida</td>
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