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Advances in anticancer drug research from marine organisms: an overview

Abstract

Over 70% of Earth's surface is covered with sea/salty water. World's oldest, most revered and holiest texts, the Vedas, term the Ocean as 'Ratnakar', or the bestower of immense riches. From times immemorial the oceans/seas have been a source of inspiration, awe & adventure for Humankind. Modern science for the first time in the nineteen fifties discovered for the first time, potent bioactive, chemical compounds from marine organisms. Today, several potent cytotoxic and anticancer drug leads, from secondary metabolites biosynthesized in Marine invertebrates, have been identified. In order to tide over the problem of supply, even artificial culture of Marine organisms is being attempted. Such vital aspects are discussed herewith.

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Abbreviations: HPLC, high–performance liquid chromatography; NMR, nuclear magnetic resonance spectroscopy; IR, infrared radiation; UV, ultraviolet radiation; QSAR, quantitative structure–activity relationship

Introduction

Anticancer drug research, has now centered around Marine Drug Research, as secondary metabolites from marine organisms, have proved to possess remarkable cytotoxic properties. Ara–C, & related nucleotides, were the foremost discoveries of cytotoxic metabolites from marine fauna. These secondary metabolites are bio–synthesized in the organisms, as a means for offense &/or defense, in order to sustain their existence in an otherwise highly hostile marine environment. Umpteen number of cytotoxic compounds have been isolated from marine organisms, particularly marine fauna. Some of these like, the Bryostatins, are in final stages of pre–clinical trials, and are on the way of becomes potent drug leads in the future. The unfortunate trend of global warming has dealt a severe blow to the natural habitats, threatening the very existence of most of economically valuable marine organisms, which can be a gold mine of priceless chemicals.[1] Marine environment is complex in nature, which is a challenge to the organisms, & it only permits the survival of the fittest. Most small–sized marine organisms are filter–feeding in nature. In the highly hostile marine environment, predation is the main source of survival. Thus, the offensive & defensive mechanisms are very advanced in marine organisms. The biochemical processes in these organisms are specially designed to synthesize potent cytotoxic chemicals, to boost their weaponry of offence & defence. These cytotoxic compounds help them prey, & also save their lives & defend themselves, when attacked by a stronger predator.[2–5] The fact that these organisms produce & store such cytotoxic chemicals, as secondary metabolites, make them favourite & lucrative destinations for scientific investigation, targetted towards Anticancer Drug discovery. Research in exploring bioactive secondary metabolites, from the ocean has yielded several promising compounds, & as much as, even some QSAR studies have also been attempted on these cytotoxic compounds.[6]

Apart from Marine Drug research, several anticancer compounds have also been obtained via the synthetic route. Prominent among such synthetic compounds, are Vascular Disruptive agents, which destroy cancer cells, by blocking their nutrition supply, from adjoining healthy tissue, surrounding the tumor vasculature. Due to this extraordinary mechanism of action, & resulting comparatively lesser adverse effects, these compounds hold immense promise for the future.[7,8] In addition to these, somewhat well acclaimed sources of anticancer compounds, even some heterocycles active as anti–fertility agents, can also be found active as anticancer agents. Although development & usage of such compounds, is more likely to be focused at anti–breast cancer therapy.[9]

Material and methods

Marine organisms, specially marine fauna are preferably preserved in deep freeze, at sub–zero temperatures, immediately after their collection from their natural marine habitat, to prevent any microbial degradation, & production of undesirable artefacts; till they finally reach the laboratory, for further processing & chemical investigation. Marine fauna are more prone to microbial degradation, and production of chemical artefacts, than marine flora. Deep–freezing the organisms ensures preservation of the chemical constituents, in exactly the natural form.

In cases where deep–freezing is practically impossible, soaking of organisms in solvents such alcohol, n–butanol, etc. is generally preferred, during their travel to the laboratory. Upon arrival in the laboratory, marine organisms are thoroughly washed, in order to remove all undesirable materials, such as silt, sand, salts, etc. Thereafter, their chemical processing is commenced, mainly by cold percolated solvent extraction, followed by successive fractionation of the crude extract. The exact extraction/fractionation protocol to be followed depends upon factors like, the organism, the biological activity sought, the chemical constituents to be isolated, etc. The isolated bioactive compounds are then purified by various chromatographic methods, including HPLC. Purified compounds are then characterised & identified, using spectroscopic methods like, NMR, IR, UV, and Mass Spectrometry, along with necessary elemental analysis, and other physico–chemical data, depending upon the nature of the compound isolated.

Results and discussion

The best among the bioactive compounds, are characterised for their

chemical structure determination, with the help of physico–chemical and spectroscopic data obtained mainly by 2D NMR, CNMR, etc. Thus, any new bioactive chemical entities present in the constituents are carefully identified. Studies like QSAR may also be attempted, in case sufficient number of structurally related bioactive compounds, making a library are available. This enables the researchers to identify the pharmacophores, or the most active chemical portion/ functional groups, present in the molecule.

Conclusion

To sum up, there are umpteen number of possibilities, regarding search of potent anticancer compounds, both via the marine/natural, as well as the synthetic routes. Marine sources can prove to be the most economical sources, if the problems related to a regular supply of marine organisms, and losses due to climate change, are taken care of. Despite tremendous advances, the scarce supply of marine organisms still continues to be the biggest challenge. An attempt towards artificial farming/harvest of marine organisms has been initiated in California, where Bryozoans like, Bugula neritina are being artificially harvested for extraction of cytotoxic Bryostatins. Bryostatins form the group of macrolide secondary metabolites, possessing potent bioactivity. If such artificial harvests succeed, the supply problem of marine organisms will be addressed to a great extent. Then, we will have the liberty to extract the quantities of required compounds, almost at will. Recent advances hold great promise for anticancer drug development in the future.

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Conflict of interest

The author declares no conflict of interest.

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