Renaissance of Marine Natural Product Drug Discovery and Development

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The marine environment has been shown to be the source of chemical diversity structures with promising biological activities. Besides the chemical novelty associated with those compounds, some of them possess novel mechanisms of action as well. To date, eight marine drugs have been approved by the FDA or EMEA registered, they are Cephalosporin C, Cytarabine (Ara-C), Vidrabine (Ara-A), Ziconotide (Prialt), omega-3-acid ethyl esters (Lovaza), ET-743 (Yondelis), E7389 (Halaven), Brentuximab vedotin (SGN-35) [1,2] showed in Figure 1.

These success stories have had to overcome difficulties inherent to marine natural products-derived drugs, such as sustainable source and issues related to structural complexity. Nevertheless, five marine-derived agents are now approved, most as “first-in-class” drugs. Additionally, there is an abundant pipeline of clinical and preclinical marine compounds to suggest their continued application in human medicine.

The solidness of the marine pharmaceuticals pipeline is evident, clinical trials with Sob lidotin (TZT 1027), Tasidotin, Synthadotin (ILX-651), Bryostatin 1, Hemiasterilin (E7974), and Pseudopterosin (ASG-5ME) in Phase I trials have been completed, a compound (Plitidepsin) in Phase III trials, six derivatives (DMXBA(GTS-21), Plinabulin (NPI 2358), PM00104, Elisidepsin, PM01183, CDX-011) in Phase II trials, and four compounds (Marizomib (Salinosporamide A; NPI-0052), PM060184, SGN-75, ASG-5ME) in Phase I trials have been processed with multitudinous marine natural products being investigated preclinical as clinical candidates.

The global marine preclinical pharmaceutical pipeline remains very active. During the period 1998–2008, the global marine pharmaceutical preclinical pipeline included 592 marine natural products that showed antitumor and cytotoxic activity, and 666 additional chemicals which demonstrated other pharmacological activities (i.e. antibacterial, anticoagulant, anti-inflammatory, antifungal, anthelmintic, antiplatelet, antiprotozoal, and antiviral activities;) with actions on the cardiovascular, endocrine, immune, and nervous systems; and other miscellaneous mechanisms of action [3].

The unexplored marine organisms harbors the most biological and chemical diversity, it is the vastest resource to discover novel structures (to date, more than 21855 compounds were discovered [4]) with novel modes of action. In order to conduct preclinical and clinical trials and further develop a promising leading into a marketed drug, sustainable supply is necessary. The continuous supply problem is the major challenge for marine natural product drug discovery and development. However, modern approaches are available to overcome the obstacles. Proceedings in technologies such as sampling strategies, nanoscale NMR for structure determination, total chemical synthesis, fermentation, and biotechnology are all crucial to the success of marine natural products as drug leads. The high degree of innovation in the field of marine natural products, will lead to a new wave resurgence of new drugs in the coming future [5].

The potential of marine natural products to become new drugs is still on the horizon. With the prominent development of more marine natural products from the current pipeline, the contribution of marine natural products to the future pharmaceuticals seems to be promising. New technologies and efficient collaborations between multidisciplinary scientists will be essential to ensure the future success of marine natural products as new therapeutic chemical entities that can make a significant contribution to the cure of human disease.

References

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