"Saving the oceans? They could save us!"

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INTRODUCTION

Life emerged from oceans more than 3500 milion years ago. Over years of evolution, marine organisms have developed complex biological and chemical mechanisms to survive, mainly with the biosynthesis of potent chemical weapons. The pharmaceutical industries recognized this opportunity as new potential ways to obtain drugs. Recent progress has resulted in compounds that are being used to treat so important pathologies as cancer or inmunosuppressive disorders.
Firstly, the main source to obtain active compounds to treat our pathologies was the soil (specifically, from the bacteria and plants), but it is very relevant that whereas only 1 over 10.000 earth species is useful to develop new drugs, 1 over 70 marine species is adequate to develop them. It is not surprising so, that in the last twenty years, the sea had become the main bioactive molecules source.

OBJECTIVE: The main purpose of the present job is to intensify the awareness of preserving the oceans, presenting a very promising application of marine biology: the discovery of new marine drugs against the major human pathologies on the eve of the 21st century.

RESULTS

HIGHLIGHTS

- 23-79 dC: First quotes about the topic on Pliny the Elder's book "Naturalis Historia". Pliny presented the use of the sea-wormwood *Seriphum* against gastrointestinal disturbances.
- 1900: First marine product *sensu stricto* is commercialized: kainic acid. Obtained from a seaweed, kainic acid is a potent central nervous system excitant used in epilepsy research.
- The gorgonian *Plexaura homomalia* contains the highest concentrations of prostaglandins in nature.
- Cephalosporin C was isolated from a marine-derived fungus. It is used as antibiotic and let to synthesize analogs that had became some of the first marketed cephalosporin antibiotic drugs.
- Aequorin is a photoprotein osolated from the hydrozoan *Aequorea victoria* that lets to follow protein pathways allong different organisms.
- Iota-Carrageenan is the only broad band antiviral therapeutic option available for the treatment of respiratory infections. It is obtained by a seaweed.
- GTS21, designed basing upon a toxin of a nemertin worm (anabasein) is being investigated for the treatment of Alzheimer's disease, nicotine dependence and for schizophrenia.
- Bryostatins are a group of macrolide lactones isolated from bryozoans. To date 20 different bryostatins have been isolated. These promising molecules are currently under investigation as anti-cancer agents and as a memory enhancing agent.
- RefirMAR™: Daily skincare cream. Inhibits the release of acetylcholine at the synapse of the motor neuron. In contrast to the well known botulinum toxin (BOTOX®), RefirMAR™ does not have a permanent action and shows dermal penetrating capacity, avoiding the inconvenience of administration by injection.
- 2004: The First International Symposium on Marine drugs was celebrated in Qingdao.
- There are mainly three obstacles on developing a new marine drug: budget (it involves around 500 million Euros), time (it requires 10 years from the discovery to the aproval of a new drug) and synthetic production on a large scale (for example, 1000 kg of bryozoans are needed to obtain 1 g of bryostatin, which is naturally unstaintable).
- Present: A high number of marine drugs are in full development. For example, recently, researchers have discovered cnidarins; proteins obtained from corals, capable of blocking the HIV virus from penetrating T-cells.

MARINE DRUGS AS A BOOMING SECTOR

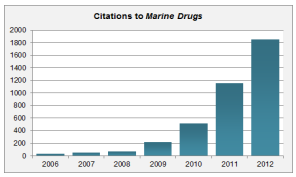


Fig.1: Citations to *Marine Drugs*
Image obtained by: https://dl.dropboxusercontent.com/u/165068305/marinedrugs-if.png

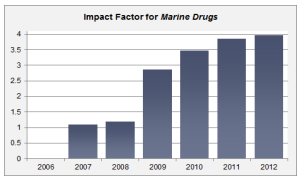
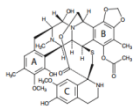


Fig.2: Impact Factor for *Marine Drugs*
Image obtained by: https://dl.dropboxusercontent.com/u/165068305/marinedrugs-if.png

"Marine Drugs" is an open-access journal publishing on the research, development and production of therapeutic agents from marine natural products. In recent years it has been observed a sudden increase in its number of citations and its impact factor (currently it has a value of 3,978).

TRABECTEDIN: A UNIQUE MECHANISM OF ACTION TOWARDS METASTATIC SOFT TISSUE SARCOMA



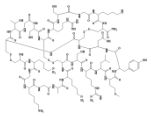
Trabectedin (Yondelis®)

Trabectedin, which is also known as ET-743 is an alkaloid isolated from the Caribean ascidian *Ecteinascidia turbinata*. It received firstly marketing authorisation for the treatment of advanced metastatic soft tissue sarcoma, and two years later for the treatment of relapsed platinum-sensitive ovarian cancer in combination of other drugs.

Relevance: It was the first antitumoral marine drug to be approved. Currently, is the only way to treat advanced or metastatic soft tissue sarcoma. Trabectedin also presents a unique mechanism of action binding to the minor groove of the DNA and interfering with cell division and the gene transcription processes and repair machinery of the DNA.

Ecteinascidia turbinata

ZICONOTIDE: AN ANALGESIC 1000 TIMES MORE POTENT THAN MORPHINE!



Ziconotide (Prialt®)

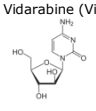
Ziconotide, which is also known as SNX-111, is a powerful non.opioid analgesic drug approved for the treatment of severe chronic pain. It is a synthetic version of ω-conotoxin MVIIA, which is a peptide that is found in the venom of the fish-hunting marine snail *Conus magus*.

Relevance: Ziconotide is 1000 times more potent than morphine. Unlike opiates, prolongate administration of ziconotide does not lead to the development of addiction nor tolerance.

Conus magus

VIDARABINE AND CYTARABINE: A TURNING POINT IN THE STORY OF AIDS

Vidarabine (Vira-A®)



Cytarabine (Cytosar-U®)

Vidarabine is an antiviral drug that inhibits DNA polymerase and DNA synthesis of herpes, vaccinica and varicella zoster viruses.

Cytarabine is a chemotherapy agent that kills cancer cells by interfering with DNA synthesis. It is mainly used for the treatment of cancers of white blood cells.

Relevance: Vidarabine and Cytarabine, commonly known respectively as Ara-A and Ara-C, inspired zidovudine synthesis, which was the first breakthrough in AIDS therapy.

Tethya crypta

CONCLUSIONS

✓ Commercializing a new marine drug involves a high investment of time and money but provides more profits.
✓ Marine drugs are a booming sector. Due to the long time that involves to develop a new drug, the most of marine drugs are still in clinical phases and we will have to wait to see the final results. Marine drugs that are currently in use are reporting efficient results for the treatment of many different pathologies, so it is expected to happen the same with the new ones.
✓ Despite being a relatively new science, marine drugs topic is becoming more and more popular and it is expected to increase its popularity for the new years.
✓ There are a lot of promising new marine drugs in experimental phases towards the main diseases affecting population of the 21st century and more of them expecting to be discovered. Thus, it makes sense to intensify the awareness programs for taking care of the oceans, because we could be contaminating the main source of drugs against our future pathologies.

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