The Promise of the Sea

Oceans cover seventy per cent of the surface of the planet. Countless marine plants and animals contain biochemical secrets that, if unlocked, can provide new insights and understanding of human diseases and their treatment. Today, with the modern tools of molecular biology and advanced technology, the potential for marine environment to provide new drugs to treat human illnesses has never offered greater promise. Just as plants have provided numerous medical drugs, from aspirin to morphine, marine organisms are another vast reservoir of original molecules* that could prove to have therapeutic properties. Marine organisms are hugely diverse, and so are the chemical compounds extracted from them. For example, at ISOMER, an French Institute on Substances and Organismes, Professor Jean Michel Komprobst, studies squalimine, which comes from shark, an animal that never is affected by cancer. "This molecule strongly stops the growth of blood vessels of cancerous cells, provoking an asphyxiation of the cells. They are very effective on several types of cancers affecting the brain, the breasts, the prostate, the ovaries and the colon." Another product on the verge of being authorized for the markets is the KRN 7000 that comes from Japanese sponge. "On mice, the KRN 7000 proved itself to be particularly anti-tumular, especially for colon cancer. And the GST 21 is the only molecule originating from the sea that has been tested for Alzheimer's disease, and it comes from a worm, the nemerte." American and Europeen researchers are working on these very interesting molecules whose origins come from marine sources. It is probable that within the next two years at least one marine-derived novel agent will enter commerce as an anticancer or analgesia drug following governmental approval. The ocean is a vast frontier for new discoveries and we are at the beginning.

Professor William Fenical , Director of the Center for Marine Biotechnology and Biomedicine in San Diego (USA) is pioneering the discovery of new anti-cancerous molecules from the sea. (Pictures 01 to 13).
"I was enthusiastic about the ocean since I was 12 years old. The enormous untapped resources of the oceans strongly suggested it was a vast resource. The fact that drugs are almost all based on natural products provided strong societal reasons to explore this resource," says Professor William Fenical. Working at the SCRIPPS Institution of Oceanography at the University of California in San Diego (USA) which is one of the oldest, largest, and most important centers for global science research in the world, Professor William Fenical is well known in the scientific world for being one of its most effective researchers. W.Fenical : « Our group conducts research relevant to defining the roles and biomedical applications of the unique organic molecules produced by marine life. Programs are integrated to isolate and define chemical compounds which function as chemical defenses and molecules used for communication, and to assess the potential of these same compounds in the treatment of human and animal diseases. In drug discovery, a major focus is upon cancer, inflammatory diseases and in the discovery of new anti-infectives. Research support from the National Cancer Institute, the National Science Foundation, the National Sea Grant Program, the California BioStar Program and various pharmaceutical companies provide financial support for these studies. » Many of the compounds discovered in the ocean and developed in the laboratory were found effective in combating human diseases. One was "Eleutherobin", isolated from a rare soft coral discovered by W Fenical. Eleutherobin proved very promising as an alternative drug in the treatment of breast, ovarian, pancreatic, and colon cancer. The vastness of the ocean reverts researchers to study an infinitely small part of it. Professor W. Fenical recently discovered potential anti-cancerous or antibiotic microorganisms that measure one or two microns on grains of sand (picture 09).

Erin Gontang, a Graduate Researcher at the Scripps Institution of oceanography in San Diego, explains: “We test our strains using preliminary essays here in the lab and if the compounds present in our bacterial strains show any promise as anti-cancer, antibiotic or anti-fungal compounds, they go to our industry collaborators for further tests…The filamentous actinomycetes **, isolated from soils, have been exploited as a major resource of novel antibiotics.” Research in new antiviral drugs for the treatment of AIDS and other viral diseases is also an important activity within CMBB, the Centre for Marine Biotechnology and Biomedicine. “There is no doubt that the great chemical diversity of the ocean can contribu to the search for an AIDS cure,” says W. Fenical. **(**For example, AZT, come from marine sponge).

However, the collection of sea organisms to the manufacturing of medication on the markets involves a long and difficult process. A number of tests, “in vivo” and in “vitro”*** are necessary, in order to know the toxicity of these molecules. A sufficient amount of these active substances are needed for these tests but researchers are concerned about how to collect it without destroying the natural milieu of the ocean. The solution may lie in finding recoverable resources in the oceans that scientists can take to the laboratory to manipulate in order to produce a drug for cultivation. It’s necessary to be able to synthesize the molecules. To gather orgnaisms from the depths of the ocean, scientists use several techniques. There are liveable submarines that are armed with robotic arms, that enables the collection of samples from the greatest depths (4000 meters). There are also scientists who are for the most part experienced divers who harvest themselves marine organisms. Somer researchers fabricate their own techniques such as the "Mud Snapper" which is a machine equipped with two large spoons. The Mud Snapper is manipulated from the surface and enables the collection of smaller quantities of mud.

Nature is sometimes generous enough to provide underwater organisms that are in sufficient quantities to assure an important production. For exemple, Dr. Gilles Gutierrez, Pharmacologist and President of ICP (Institute of Cellular Pharmacology) in Malta, works on the alga called ‘Padina pavonica’ . (Pictures 14 to 20) This seaweed grows in great quantity in the Mediterranean Sea and the annual harvest is more than 40 tons. The therapeutic interests of this seaweed are obvious. "The clinical results show that this newly discovered molecule has a huge potential for regenerating bone and skin loss associated with age, including osteoporosis and arthritis, " declares Dr Gutierrez.

The French National Centre for Scientific Research (CNRS) and the Institute for Research and Development (IRD) work on the promise of the sea. Cecile Debitus of IRD found a new active substance against malaria from a sponge found in New Caledonia named the “Oceanapia Fistulosa”. With more than a million deaths a year from malaria, the IRD French researcher has identified new molecules, which “in vitro” can stop the parasite. For the future, this is a veritable therapeutic potential, but more tests “in vivo” are still needed before a cure can be obtained.
The spiny starfish (Marthasterias Glacialis) living in the English Channel’s waters produces a surprising molecule against cancer. It was Dr. Laurent Meijer of CNRS of Roscof, France who discovered the “Roscovotine”. It’s a molecule used against breast and lung cancers. Therapeutic tests are underway. In blocking cancerous cells without affecting healthy ones, the “Roscovotine is a new potential chemical therapeutic weapon against cancer.

Dr Bernard Banaigs from INSERM (National Institute for Medical Research) works on fundamental research. (P ictures 34 to 37).He works with Dr. Susanna López-Legentil from Spain who dives to find marine organisms. The expertise of the laboratory is in the field of Marine Natural Products Chemistry, the study of compounds produced by marine plants and animals. Bernard Banaigs explains: " Our interest lies in two main areas. One is marine chemical ecology. The principal aim of this work is to understand why marine organisms produce such a wide array of interesting chemistry. We also study marine pharmacology because we are interested in the discovery of new pharmaceuticals from marine organisms".

Marine organisms are far less well known than their terrestrial counterparts. Scientists study marine life from surface waters to the deepest part of the ocean in search of new molecules from currently unknown bacteria. They search for bacteria that can thrive under the kind of pressure that would turn a man into a jelly! Researchers have opened fascinating new portals into the world of bacteria. For example, Dr Dominique Ribola created "Seadev" which is the first company of valorisation of marine public in Europe. (Pictures 21 to 27).Dominique Ribola is developing innovative molecules and production processes from the bacteria collected in the deepest parts of the ocean. Some bacteria are collected from more than 4000 meters deep with the help of habitable submarines such as the "Nautile."(picture 22). Surprising bacteria live in hypothermal sources where sulphurous gases spurt at 300 degrees. These sources are like mini underwater volcanoes where extreme pressure conditions, obscurity and temperature do not prevent the development of life. "It's probably because in order to survive in this inhospitable universe that these bacteria produce unknown molecules on the surface!" suggests Dr. Ribola. Working with IFREMER, a French research centre on marine life, the results are starting to fabricate entirely biodegradable plastic, effective oral hygiene ingredients, highly cosmetic products, and new substances of pharmacological interest. Dominique Ribola has opened fascinating new portals into the world of biotechnology and biomedicine**.**

***Molecule**: The smallest particle of a substance that retains the chemical and physical properties of the substance and is composed of two or more atoms; a group of like or different atoms held together by chemical forces.

** ***Actinomycete*** is a microorganism wich grows as long stands in the soil and resemble bacteria. It can only be seen under a microscope. Actinomycete are among the most common source of antibiotic.

***In vitro :** outside the living body and in an artificial environment growth of cells *in vitro*
In vivo :Within a living organism: *metabolic studies conducted in viv*

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