DEEP DOWN THE OCEANS BLOSSOM AND OFFER A SEA PHARMACY

The PHARAMASEA project reveals blue treasures: globally collected marine bio-resources for new drugs, cosmetics and nutraceuticals

The project: Discoveries in the marine bio-pipeline

New antibiotics and new ingredients for food and cosmetics will soon come from the deep sea. In the PHARMASEA project scientists from the UK, Belgium, Norway, Spain, Ireland, Germany, Italy, Switzerland and Denmark are working together to collect and screen samples of mud and sediment from huge, previously untapped oceanic trenches. Once the samples are collected, the new fungi and bacteria are grown in labs, genetically screened and processed. The PHARMASEA project hopes to show the value of marine bio-resources to the discovery of new pharmaceuticals. In particular, the consortium investigates marine microorganisms that live in deep and cold oceans, for their potential to produce new antibiotics and pharmaceuticals for diseases of the central nervous system such as epilepsy or Alzheimer's disease.

The product: Drugs for neurological, inflammatory and other infectious diseases

The discovery of new pharmaceuticals is the main deliverable from the PHARMASEA project. It will generate a large amount of knowledge about microorganisms that dwell in extreme environments, as well as their potential to produce novel chemical entities. Bacterial diversity within sea sponges may also open a new universe of potential applications. Moreover, marine organisms that live more than 6,000 metres below the sea level are considered to be an interesting source of novel bio-active compounds as they survive under extreme conditions. Deep under water, the sea blooms, the researchers tell us.

One of the aims of PHARMASEA is to discover new marine bacteria that can produce novel antibiotics to fight the growing challenge of antibiotic resistance. There's a real lack of good antibiotics in development at the moment. There hasn't been a completely new antibiotic registered since 2003. If nothing's done to combat this problem we're going to be back to a "pre-antibiotic era" in around ten or twenty years, where bugs and infections that are currently quite simple to treat could be fatal,' says Marcel Jaspars, scientific leader of the project and Professor of Chemistry and Director of the Marine Biodiscovery Centre at the University of Aberdeen. PHARMASEA will also focus on drug discovery for neurological, inflammatory, and other infectious diseases. With this, chemistry with new activity will be established.

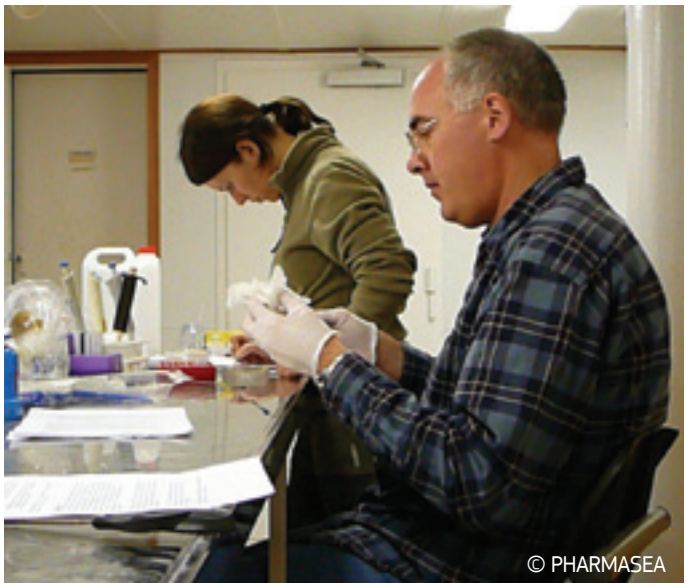
An extract library is being created during the project. This can offer new pathways to researchers and end-users.

To make the process of marine bio-discovery attractive to industry, the project will address the bottlenecks that are preventing greater industry uptake of marine bio-technology. The main challenges lie in purification and pharmaceutical testing of toxicity and bio-activity. PHARMASEA applies stringent filters to obtain only the highest quality marine resources and uses state-of-the-art methods to speed up the technical parts of the bio-discovery pipeline.

The end-users: The pharmaceutical industry, medical research, clinics, personal care, food producers, processors, consumers

The entire pharmaceutical and nutraceutical value chain from industry to consumers can be envisaged as potential clients. PHARMASEA's goal is to deliver one or two drug candidates in the near future with some pre-clinical evaluation carried out on them.

There is a critical need for these compounds, recognised in the Infectious Disease Society of America's influential report 'Bad Bugs, No Drugs', which led to the proposal of the 10 x 20 initiative – ten new antibiotics by 2020. The current market model for antibiotics is broken and this can be fixed by new economics (much higher prices for antibiotics) or by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public–private partnerships involving, as in our case, a blend of universities, research institutes, not-for-profit organisations and SMEs.

In addition, diseases of the central nervous system are currently poorly served, which is why the sea pharmacists are searching for better treatments for epilepsy and neurodegenerative diseases.

The estimated market value of the sea pharmacy is estimated at several billion euros.

The inventors: Academics, research institutions, industries

The collaborative PHARMASEA project builds upon a highly interdisciplinary consortium of 24 partners from 13 countries from the fields of industry, academia and non-profit organisations. World-leading experts from Belgium, UK, Norway, Spain, Ireland, Germany, Italy and Denmark as well as partners from China, South Africa, Chile, Costa Rica and New Zealand are taking part in the PHARMASEA project. PHARMASEA brings together researchers from the areas of marine genomics, bio-synthesis and chemical-structure analysis, as well as legal experts. The international team of scientists is led by Professor Marcel Jaspars of the University of Aberdeen in Scotland, and coordinated by Dr Camila Esguerra of the University of Leuven in Belgium.

The project partners have broad expertise in almost every area of the pipeline. They offer SME/NFPs in antibiotic discovery academic, and SME, expertise in molecular genetics and heterologous expression, the capacity to produce at scale, and expertise in natural-product isolation and structural identification. One partner provides world-beating data-mining and chemical software capabilities.

Several members of the project are part of several consortia, most notably Macumba. They cooperate with the projects BLUEGENICS and SEABIOTECH on legal/policy aspects as well as dissemination. The PHARMASEA research is committed to the long-term maintenance of samples via OPENSCREEN and of data via ChemSpider.

Development stage: Proof of principles, up-scaling, optimisation of fermentation processes

The primary aims of the project's business focus, are to take forward bio-active compounds and to evaluate their potential as new drug leads or ingredients for nutritional/cosmetic applications, including up-scaling and optimisation of the fermentation process beyond 1L to 20L.

So far, the researchers have analysed the entire marine bio-discovery pipeline and identified the bottlenecks. State-of-the-art solutions for each of these will be provided. The goals are to deliver one or two drug candidates.

For instance, access to really deep water is restricted by lack of access to oceanography ships and deep-sea sampling equipment. The project's fix for this is to develop inexpensive and robust equipment based on that developed for the salvage industry. The researchers will use other scientific and technical fixes to optimise the discovery process of novel microorganisms and the mining of their genomes.

Policy impact: Improved bio-discovery processes

One of the main barriers to the greater uptake of marine bio-discovery is access to samples, as there are multiple legal regimes that apply to the collection of marine bio-resources. The project's work on access to marine genetic resources with legal certainty has been very successful. They have advised policy makers, convened a panel of experts from the EC, NGOs and academia, and have published an advisory article on legal regimes applied to the use of marine genetic resources. PHARMASEA will add to that an article explaining the marine bio-discovery process to policy makers and a user toolkit to allow marine bio-discovery researchers to navigate the legal regimes necessary to access marine genetic resources with legal certainty.

Next steps: To develop lead molecules and attract the pharma industry

The next step is to develop any lead molecules found for pre-clinical and then clinical evaluation. For this we will need to licence products, or co-develop them with industry.

Getting the pharmaceutical industry interested in the results of the project is complex, 'however, we have had discussions with major pharma and have invited them to the open part of the PHARMASEA general assembly in September this year to hear the latest results from the PHARMASEA project,' says Camila Esguerra, pharmacist at the University of Leuven and project coordinator. She continues, 'We have had positive responses to this, and by doing this we hope to have a dialogue with companies so that any successful products from PHARMASEA can be co-developed.' The project will also provide asset notes to explain important results which might interest industry. This will be a way to communicate with potential end-users. Potential end-users can get involved with PHARMASEA by contacting the scientific project leader, Marcel Jaspars.

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