

PLENARY PRESENTATIONS

TERRESTRIAL AND MARINE-DERIVED FUNGI AS SOURCES OF INTERESTING MOLECULES FOR DRUG DISCOVERY

Anake Kijjoa

*School of Medicine and Biomedical Sciences Abel Salazar (ICBAS) and CIIMAR, Rua
de Jorge Viterbo Ferreira, 228, Porto, Portugal, E-mail: ankijjoa@icbas.up.pt*

Fungi are prolific producers of biologically active secondary metabolites. Driven by millions of years of co-evolution, these organisms have developed intricate chemical defenses and symbiotic interactions to compete and survive alongside other microorganisms in complex ecosystems. These complex biological networks lead to the production of essential medicinal compounds, including antibiotics such as penicillin, cephalosporins and fusidic acid that revolutionized bacterial therapy, immunosuppressant drugs such as cyclosporine that have transformed the field of organ transplantation, and cardiovascular agents such as statins, which are widely used for lowering cholesterol.

Since the marine environment presents different physical and chemical conditions from the land, it can be an extraordinary reservoir of bioactive compounds, many of which possess unique structural features and novel modes of action. For this reason, researchers have been focusing more of their attention on marine-derived fungi as a source of interesting bioactive compounds since many consider them as one of the still untapped resources for new and biologically relevant chemical entities.

Since we have studied numerous fungal species of different habitats, only some examples of our studies of bioactive secondary metabolites from both terrestrial and marine-derived fungi as well as their relevant biological activities will be discussed. Eurochevalierine, isolated from the culture of a soil fungus, *Neosartorya pseudofischeri*, was found to display an *in vitro* anticancer activity in the range of etoposide and carboplatin. Computer-assisted phase-contrast microscopy revealed that it was not cytotoxic to human U373 glioblastoma and A549 non-small cell lung cancer cells but cytostatic effects involving marked inhibition of mitotic rates in these cells. Thus, it appears that eurochevalierine represents a novel chemical scaffold for the development of anticancer agents, effective against cancers unresponsive to traditional therapy with pro-apoptotic agent.

On the other hands, six diastereomeric fiscalins, four of which were characterized for the first time by us, were isolated together with five tryptoquivalines from both soil and marine-derived *N. siamensis* KUFC 6349. Moreover, several meroditerpenes have been isolated from various marine derived-*Neosartorya* species. However, only the meroditerpene, azonapyrone A, and the unreported diastereomer of fiscalins, neofiscalin A, exhibited significant antibacterial activity against multidrug resistant *Staphylococcus aureus* (MRSA) and *Enterococcus faecalis* (VRE) as well as inhibition of a biofilm formation. Additionally, verruculosic acid, an unreported bicyclic sesquiterpene acid, was isolated together with the labdane-type diterpenes, (+)-agathic acid and hypoxyterpenoid A, as well as a 3-nor-2,3-seco-labdane, penioxalacin, from the culture of the marine fungus *Penicillium verruculosum*. (+)-Agathic acid exhibited stronger inhibitory activity than the positive control, diclofenac sodium, against LPS-induced nitric oxide (NO) production in RAW264.7 macrophages, while hypoxyterpenoid A and penioxalacin were slightly less active than the positive control.