BIOACTIVE POLYETHER METABOLITES FROM DINOFLAGELLATES

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Over the last years our research group has been focused on the study of microalgal metabolites as a source of bioactive compounds. Marine dinoflagellates are a rich source of secondary metabolites, including a diversity of highly bioactive compounds, such as the phycotoxins associated with harmful algal blooms (HABs). These phycotoxins comprise a variety of structures including guanidine derivatives, cyclic imines as well as linear, polycyclic and macrocyclic polyether toxins. The pharmacological and toxicological properties of some of them are currently well described, as ion channel blockers or activators, phosphatase inhibitors, etc.

Among them, the most commonly found toxins in the Spanish shores belong to the DSP (Diarrhetic Shellfish Poisoning) and the PSP (Paralytic Shellfish Poisoning) types. DSP toxins have unique chemical features and after their isolation focused natural product chemist attention, not only because of their public health repercussion and economical impact on the shellfish industry, but also to establish the real origin of the poisoning. Moreover the isolation and the structure elucidation of minor new toxins is imperative for designing proper countermeasures such as their detection in contaminated samples and for the determination of their biosynthetic pathway. In addition, marine toxins are more than just tools of biological chemistry; they are also powerful molecular probes that shed light on the molecular details of important cellular events. In this way, for example, the remarkable selectivity of okadaic acid and derivatives to inhibit some serine-threonine protein phosphatases (PP1 and PP2A) lead directly to the discovery and characterization of some members of that family of soluble proteins.

However, despite serious advances in structure determination techniques relatively little is known about the biosynthetic pathways or structural/functional relationships of these secondary metabolites.

The structures of some compounds obtained from artificial cultures of the dinoflagellate *Prorocentrum belizeanum* will be discussed on the basis of their spectroscopical data, essentially obtained by NMR techniques, in combination with molecular modelling studies. In addition the utility of these new compounds to understand the structural requirements necessary to inhibit protein phosphatases will be commented.