IN VITRO GROWTH INHIBITORY ACTIVITIES OF NATURAL PRODUCTS FROM IRCINIIDAE SPONGES AGAINST CANCER CELLS: A COMPARATIVE STUDY

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Abstract

Blue biotechnology includes the natural chemical diversity's exploration to develop new pharmaceuticals drugs. Among marine sponges, which have provided a rich supply of interesting bioactive substances, sponges belonging to the family Irciniidae contain bioactive furanosesterterpene tetronic acids (FTAs) and prenylated hydroquinones (PHCs), which are known to be toxic against human tumor cell lines. In the present study, a chemical investigation of Irciniidae sponges collected along Tunisian coasts led to the purification of both three different FTAs, and three PHCs, the activity of which has been evaluated under the same conditions against a panel of cancer cell lines and displayed various levels of sensitivity to pro-apoptotic stimuli.

Keywords: Porifera, Biotechnologies, Cell, South-Central Mediterranean

Sponges belonging to the genera *Ircinia* and *Sarcotragus* (Porifera: Dictyoceratida: Irciniidae) provided a variety of bioactive natural products which have attracted attention as promising drug candidates. Two major classes of compounds from irciniidae sponges have especially attracted the attention of chemists and pharmacologists: (a) linear terpenes containing both a furan ring and the tetronic acid moiety (FTAs), and (b) hydroquinones with a terpenoid portion (PHCs). Although it is not always clear whether the compounds are of dietary origin, produced by symbionts, or de novo biosynthesized by the sponges themselves, a panel of bioactivities with pharmaceutical potential, including cytotoxic, anti-inflammatory, antioxidant, and antimicrobial properties, have been attributed to both classes of compounds [1]. It is worth mentioning, however, that compounds belonging to the two different groups of compounds have not yet been compared in the same study using the same procedures, thus preventing to establish reliable differences in their efficacy against the same *in vitro* cellular models.

In the course of our investigation on secondary metabolites from irciniidae sponges from Tunisian coasts, we have isolated the known FTAs ircinin 1 (1), sarcotin A (2), and variabilin (3), along with the known PHCs 4-6. The isolated compounds were identified by comparison with NMR and mass spectral data available in the literature [2-4].

Subsequently, the in vitro growth inhibitory activity of compounds 1-6 has been investigated on the MCF7 mammary adenocarcinoma and the Hs683 oligodendroglioma, both displaying actual sensitivity to pro-apoptotic stimuli, the A549 non-small-cell lung cancer (NSCLC), the SKMEL-28 melanoma , and the U373 glioblastoma cell lines, the latter three lines showing various levels of resistance to pro-apoptotic stimuli. The compounds were also tested on murine B16F10 cells, a well-established tumor model for melanoma growth. Surprisingly, FTAs and PHCs exhibited very different inhibitory activities, with potencies varying by one to two orders of magnitude in favor of the PHCs in all cell lines (manuscript in preparation). The obtained comparative results are discussed in the light of a better selection of drug candidates from natural sources.

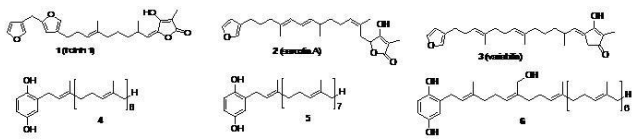

Fig. 1. Structures of compounds 1-6 extracted and purified from sponges samples.

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