

Abstract: Fungi usually contain gene clusters that are silent or cryptic under normal laboratory culture conditions. These cryptic genes could be expressed for a wide variety of bioactive compounds. One of the recent approaches to induce production of such cryptic fungal metabolites is to use histone deacetylases (HDACs) inhibitors. In the present study, the cultures of the marine-derived fungus *Penicillium brevicompactum* treated with nicotinamide and sodium butyrate were found to produce a lot of phenolic compounds. Nicotinamide treatment resulted in the isolation and identification of nine compounds 1–9. Sodium butyrate also enhanced the productivity of anthranilic acid (10) and ergosterol peroxide (11). The antioxidant as well as the antiproliferative activities of each metabolite were determined. Syringic acid (4), sinapic acid (5), and acetosyringone (6) exhibited potent in vitro free radical scavenging, (IC₅₀ 20 to 30 µg/mL) and antiproliferative activities (IC₅₀ 1.14 to 1.71 µM) against HepG2 cancer cell line. Furthermore, a pharmacophore model of the active compounds was generated to build up a structure-activity relationship