A Halogenated Secondary Metabolite from Marine Cyanobacteria Collected in Sabah, Malaysia

マレーシアサバ州由来の海洋シアノバクテリアから得られたハロゲン化２次代謝産物

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Introduction

The FDA-approved antibody-drug conjugate brentuximab vedotin, originated from the compound dolastatin 10 from cyanobacteria, lead to the exploration of new secondary metabolites from cyanobacteria, which are one of the natural marine organisms with highly evolved for secondary metabolites production. The high possibility of new secondary metabolites can be found in unexplored high biodiversity of marine environment, such as the coastal area of Sabah Malaysia in Borneo Island. This research aims to isolate a halogenated secondary metabolite and observe the cytotoxic activity on MCF-7.

Methods

Collected samples were identified using 16S rRNA gene sequencing analysis. The cyanobacteria samples were homogenized and extracted repetitively using methanol then further partitioned with ethyl acetate, butanol, and water fraction. The chemical profiles were observed by electrospray ionization liquid chromatography mass spectrometry (ESI-LC-MS) analysis. The crude ethyl acetate fraction was further fractioned using normal phase open column chromatography using a stepwise gradient solvent system of increasing polarity. The fraction containing target compound was further purified using reversed phase high performance liquid chromatography (HPLC) column to obtain the compound. The gross structure was determined by NMR and mass spectroscopy analysis whereas the cytotoxic test was conducted by *in vitro* MTT assay.

Results and Discussion

A total of 9 samples were identified as cyanobacteria genus *Moorea*. Two samples were identified as *M. producens* while 7 samples were *M. bouillonii*. The ESI-LC-MS analysis showed the richness of secondary metabolites including known cytotoxic compounds such as apratoxins and wewakazole and some halogenated compounds. Most of the crude extracts containing apratoxins gave cytotoxic activities on the MCF-7. A halogenated compound isolated from *M. bouillonii* possesses methylene chain, carbonyl functional group, and two chlorines, represent possible a dichlorinated columbamide type of compound. The HR-ESI-MS gave the $[M+H]^+$ peaks at *m/z* 494.2930. The yield of compound was 5.5 mg. Further analysis is needed to complete the absolute configuration. This compound exhibited 96% cytotoxic activity on MCF-7 cell line at concentration 100 µg/mL.