平成２９年度　環境科学院　修士論文内容の要旨

Cytotoxic Secondary Metabolites from a Cultured Marine Cyanobacterium *Leptolyngbya* sp.
（海洋シアノバクテリア *Leptolyngbya* sp.の培養藻体から得られた細胞毒性物質）

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Introduction

Cyanobacteria have proven to be a prolific source of novel, structurally diverse secondary metabolites and these secondary metabolites are one of the most successful source of potential drug leads. However, one of the major reasons why drug candidates do not make it onto the world pharmaceutical market, is that many of the most promising natural lead compounds are available only in extremely small quantities from natural stocks. Therefore, laboratory culture became a key option for sourcing these drug candidates for preclinical and clinical research. This study aims to isolate cytotoxic secondary metabolites from a laboratory cultured cyanobacterium *Leptolyngbya* sp.

Methods

The cyanobacteria samples were collected from Sabah, Malaysia. Collected samples were identified using 16S rRNA gene sequencing analysis. Samples were homogenized and extracted 3 times with MeOH repetitively, and then further partitioned with EtOAc, BuOH and H_2O. The chemical profiles were observed by ESI-LC-MS analysis and the cytotoxicity was conducted by MTT assay.

Three live samples were cultured in SWBG11 medium at 27 ℃ with a 16 hour light - 8 hour dark cycle (~10 μmol photons s^{-1} m^{-2}). Cultured samples were identified and analyzed using the same methods as well. The EtOAc fraction of one cultured sample was subsequently fractionated by normal phase open column chromatography over silica gel eluting with a stepwise gradient. Fractions containing target compounds were further purified using RP HPLC column to obtain the compounds. The gross structure of compounds was investigated by NMR.

Results and Discussion

Two collected samples were identified as cyanobacteria *Moorea* sp. while two collected samples were identified as *Symploca* sp. ESI-LC-MS analysis showed the richness of secondary metabolites including known cytotoxic compounds such as apratoxin A and wewakazole. Most of the extracts gave cytotoxic activities against human MCF7 breast cancer cells.

One cultured sample which labeled as CM1611 was identified as *Leptolyngbya* sp. It was chosen as the case study for this research because of its cytotoxicity and the large amount of cultivation in lab. In addition, *Leptolyngbya* sp. is less common in this sampling field. Several fractions of CM1611 exhibited cytotoxicity. HR-ESI-MS analysis of these fractions revealed several compounds. The purification of these fractions by HPLC resulted in the isolation of compound **(1)**, compound **(2)** and others. Both **1** and **2** showed cytotoxicity against human H460 lung cancer cells.