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• 中文關鍵字	真菌代謝物；抗癌；細胞毒性
• 英文關鍵字	Fungal metabolite；Antitumor；Cytotoxicity；Myrocin
• 中文摘要	微生物的代謝產物富含多樣且複雜的新天然化合物，是「新藥開發」重要的資源和基礎之一。真菌屬雙形性真核高等微生物，其代謝產物較一般細菌豐富且種類繁多，在上一次計劃裡我們曾針對土壤真菌，進行其菌種分離培養及其生理及藥裡活性天然代謝產物之探索研究。在系列篩選的過程中曾發現有一株屬於不完全菌類（Imperfect fungi） Myrothcium 菌屬之土壤分離菌株，可分泌一系列 Myrocins 類似物之新型雙帖類（Diterpenes）代謝物。本年度爲延續此一研究工作並擬證實其 in vivo 對細胞之毒殺作用及抗腫瘤動物實驗效果，以提供後續新藥開發時之必要參考，乃重新進行這類型菌屬之大量發酵及其代謝成分分析。並根據過去的篩選經驗，從本地土壤中篩選得到一疑似能分泌 Myrocins 類似物之絲狀型真菌菌株，並發現其發酵培養液中溶存有別於 Mycroins 之新類似代謝物，特命名爲 SYH-5501HC。該代謝物經 Amberlite XAD-2 多孔吸附性樹脂、Silica gel 順相矽膠及 Sephadex LH-20 膠體過濾等過程進行分離純化後，並以 EI-MS、CI-MS 等質譜分析，以及 1D /sup 1/H， /sup 13/C-NMR 和 2D /sup 1/H-/sup 1/H COSY NMR 等核磁共振光譜分析所得之結果證實，此代謝物爲分子量 324，分子式 C/sub 22/H/sub 22/O/sub 4/，含 γ-lactone 環，分子結構上類似 Mycroins 之新衍生物；此一物質再進一步針對肝癌細胞 HepG/sub 2/偵測其影響發現，此代謝物可有效抑制其增殖並可誘發其產生凋零化死亡。
• 英文摘要	As a part of our screening program in search of antitumor actives from microbial sources, we have reported the myrocins, a new structural class of antitumor agents produced by a strain of Myrothecium sp., a genus of imperfect fungi. The two major components of myrocins were previously characterized to be pentacyclic diterpenes with a cyclopropyl ring and a γ-lactone ring in their molecules. In connection with our work on the fungal metabolites, we further investigated the classically related strain of Myrothecium from domestic soils. This has resulted in the discovery of a

strain of myrocins producing fungus that was capable of secreting another novel metabolite, compound NO. SYH-5501HC. The new compound was elucidated to be a tetracyclic one and was revealed to comprise an α,β-unsaturated ketone and a remarkable γ-lactol ring in its molecule. The analytical results of its EI- and CI-MS spectra in combining with the NMR data revealed that its molecule formula is C/sub 22/H/sub 22/O/sub 4/(MW=324). The structure of this microbial product was finally proposed to be structurally related to the myrocins through various NMR(1D /sup 1/H, /sup 13/C-NMR as well as 2D /sup 1/H-/sup 1/H COSY NMR) analyses, nevertheless, it showed slightly inhibitory activity against tumor cell lines being tested including HepG2 in vitro resulting in cell apoptosis. In this fiscal year, we attempt to further confirm the molecular structure of this new natural product together with its stereo configuratoin. Moreover, we have noticed that this particular entity also show cytotoxicity to leukemia HL-60 cell and human lung cancer cell lines. Further study is necessary to confirm the activity of both of the cell lines mentioned above as well as the detail mode of action of the new metabolite. These finding might provide a clue for study of the structure-activity correction to such types of microbial products.