32 屆 國際

天然藥物研討會

THE 32nd INTERNATIONAL SYMPOSIUM ON NATURAL PRODUCTS

THE 32nd INTERNATIONAL SYMPOSIUM ON NATURAL PRODUCTS PROGRAM BOOK

32 屆 國際

天然藥物研討會

THE 32nd INTERNATIONAL SYMPOSIUM ON NATURAL PRODUCTS

大會手冊 PROGRAM BOOK

2017.10/13-14

中國醫藥大學B1國際會議廳

科技部 Ministry of Science and Technology

明通製藥 CKF 順天堂

議程 Program

第 32 屆天然藥物國際研討會
The 32nd International Symposium on Natural Products

2017 年 10 月 13 日(星期五) | Friday, 13th Oct, 2017

時間 Time	內容 Content
08:00-09:00	報到 **Registration**
09:00-09:30	致詞 **Welcome Address** 李文華校長	*中國醫藥大學* President Wen-Hwa Lee	*China Medical University* 黃怡超司長	*衛生福利部中醫藥司* Dean Yi-Tsau Huang	*Ministry of Health and Welfare*
09:30-10:50 專題演講 **Keynote Speech**	主持人 **Moderator** 吳天賞 特聘教授	*國立成功大學藥學系* Prof. Tian-Shung Wu	*School of Pharmacy, National Cheng Kung University*
時間 Time	內容 Content
09:30-10:10	**Topic： Phytochemical genomics - A basis for the future research of plant natural products chemistry** Prof. Kazuki Saito	*College of Pharmacy Chiba University, Japan*
10:10-10:50	**Topic：Natural Product Synergy Analysis with a Virtual Human System CODA** Prof. Doheon Lee	*Department of Bio and Brain Engineering, Korea Advanced Institute of Science and Technology, Korea*
10:50-11:00	休息時間 **Coffee Break**
11:00-12:20 專題演講 **Keynote Speech**	主持人 **Moderator** 吳永昌 講座教授	*高雄醫學大學天然藥物暨新藥開發中心主任* Chair Prof. Yang-Chang Wu	*Director, Research Center for Natural Products and Drug Development*
時間 Time	內容 Content
11:00-11:40	**Topic： Continuous Processing: from natural products bioactivity to medicines** Prof. Svetlana Ignatova	*Advanced Bioprocessing Centre Brunel University London,UK*
11:40-12:20	**Topic： Exploration with Natural Products and Cancer: Metabolomics Approaches** Prof. Hyung-Kyoon Choi	*College of Pharmacy Chung-Ang University, Korea*
12:20-13:30	中餐 **Lunch** 中華天然藥物學會會員大會	(憑餐卷至 1 樓報到處領取便當) 地點：立夫教學大樓 6 樓第一會議室
13:30-14:00	科技部藥學暨中醫藥學門說明	地點：立夫教學大樓 6 樓第一會議室

時間 Time	內容 Content
14:00-15:30 專題演講 **Keynote Speech**	主持人 **Moderator** 張永勳 教授 | *中國醫藥大學 中國藥學暨中藥資源學系* Prof. Yuan-Shiun Chang | *Department of Chinese Pharmaceutical Sciences and Chinese Medicine Resources, CMU*
時間 Time	內容 Content
14:00-14:30	**Topic**：中藥複方的系統生物學應用：當歸補血湯的品質控制和機理研究 詹華強 教授 | *香港科技大學 生命科學部暨中藥研發中心主任*
14:30-15:00	**Topic**：天然小分子調控內源抗病毒細胞因數抗機體感染新藥研究 賀震旦 教授 | *深圳大學醫學院 藥學系*
15:00-15:30	**Topic**：**Discovery and development of anticancer agents on natural products – difficulties and opportunities** 顧記華 教授 | *國家中醫藥研究所所長* Prof. Jih-Hwa Guh | *Chief/Director – National Research Institute of Chinese Medicine, Ministry of Health and Welfare*
15:30-15:40	休息時間 **Coffee Break**
15:40-17:40 專題演講 **Keynote Speech**	主持人 **Moderator** 顧記華 教授 | *國家中醫藥研究所所長* Prof. Jih-Hwa Guh | *Chief/Director – National Research Institute of Chinese Medicine, Ministry of Health and Welfare*
15:40-16:10	**Topic**：**Adjuvant effects of a standardized Wedelia chinensis extract on the clinical therapeutic modalities for advanced prostate cancer** 蕭培文 博士 | *中央研究院農業生物科技研究中心* Dr.Pei-Wen Hsiao | *Agricultural Biotechnology Research Center, Academia Sinica, , Taiwan*
16:10-16:40	**Topic**：**Investigating the therapeutic potential of the derivatives of Salvinolic acid F and tournefolic acid A on Alzheimer's diseas** 蕭永基 博士 | *國家中醫藥研究所* Dr.Young-Ji Shiao | *National Research Institute of Chinese Medicine, Ministry of Health and Welfare*
16:40-17:10	**Topic**：**Natural Products R&D under Genetic Expression Modulation** 張芳榮 教授 | *高雄醫學大學 天然藥物研究所* Prof. Fang-Rong Chang | *Graduate Institute of Natural Products*
17:10-17:40	**Topic**：**Studies on the constituents and biological activities of *Artemisia morrisonensis* Hayata** 周聖杰 副教授 | *中國醫藥大學 藥學系* Prof. Shen-Chieh Chou | *School of Pharmacy, College of Pharmacy,CMU*
18:00-19:30	**Dinner Reception** 晚宴

2017 年 10 月 14 日(星期六) | Saturday, 14th Oct, 2017

時間 Time	內容 Content
08:00-09:00	壁報張貼
09:00-10:00 專題演講 **Keynote Speech**	主持人 **Moderator** 謝明村 講座教授 | *中國醫藥大學中國藥學暨中藥資源學系* Chair Prof. Ming-Tsuen Hsieh | *Department of Chinese Pharmaceutical Sciences and Chinese Medicine Resources, CMU*
時間 Time	內容 Content
09:00-10:00	**Topic**：許鴻源 **100** 週年專題演講 莊武璋 博士 | *順天堂藥廠股份有限公司 總經理* Dr. Chuang, Wu-Chang | *President, Sun Ten Pharmaceutical Co., Ltd.*
10:00-12:00	**Poster Flash (poster presentation)**
12:00-14:00	中餐 **Lunch** 壁報論文時間 **Poster session** 中醫藥食療與健康產業連結座談 **(**地點：立夫教學大樓 **1** 樓 **105** 講堂**)**
14:00-14:40 專題演講 **Keynote Speech**	主持人 **Moderator** 黃聰龍 教授 | *長庚大學中醫學系天然藥物研究所* Prof. Tsong-Long Hwang | *Graduate Institute of Natural Products, Chang Gung University*
時間 Time	內容 Content
14:00-14:40	**Topic**： **Impact of Artificial Intelligence and Robotization on Natural Products Researches** 李慶國 教授 | *臺北醫學大學 藥學系* Prof. Lee, Ching-Kuo | *School of Pharmacy, Taipei Medical University*
14:40-15:00	頒獎典禮與閉幕典禮 ***Awards ceremony and closing ceremony***

Keynote Speech 專題演講

時　間｜Time　09:30-10:50　Friday　13th Oct, 2017

主　持　人　｜　Moderator

吳天賞 特聘教授
Prof. Tian-Shung Wu
國立成功大學藥學系
School of Pharmacy,
National Cheng Kung University

09:20-10:00 Friday 13th Oct, 2017

Topic：

Phytochemical genomics - A basis for the future research of plant natural products chemistry

Prof. Kazuki Saito
College of Pharmacy Chiba University, Japan

Abstract

The recent advances of genomics and metabolomics in plants accelerate our understanding about the mechanism, regulation and evolution of biosynthesis and function of plant specialized products. The questions now can be addressed how the metabolomic diversity of plants is originated at the levels of genome and how we should apply this knowledge to medicine and industry. Such study called as 'Phytochemical Genomics' is regarded as the new sector in plant science and natural products chemistry, which elucidates the genomic basis of the biosynthesis and the function of plant metabolites [1-3]. In this presentation, I will report an overview of our recent studies on the phytochemical genomics in a model plant, Arabidopsis thaliana, and medicinal plants. The topics include:

- Strategy of phytochemical genomics for understanding the origins of the chemical diversity of plants as A. thaliana as the model.
- A couple of examples for identification of genes involved in the biosynthesis of specialized products in medicinal plants

Key references

1. Saito, K.: Phytochemical genomics - a new trend. Curr. Opin. Plant Biol. 16: 373–380 (2013)
2. Sumner, L.W., Lei, Z., Basil, N.J., Saito, K.: Modern plant metabolomics: advanced natural product gene discoveries, improved technologies, and future prospects. Nat. Prod. Rep., 32: 212-229 (2015)
3. Rai, A., Saito, K., Yamazaki, M.: Integrated omics analysis of specialized metabolism in medicinal plants. Plant J., 90: 764-787 (2017)

10:00-10:50 Friday 13th Oct, 2017

Topic：

Natural Product Synergy Analysis with a Virtual Human System CODA

Prof. Doheon Lee
Department of Bio and Brain Engineering, KAIST
Director, Bio-Synergy National Research Project, MSI

Abstract

Recently, there are growing interests in combinational bio-agents interacting with multiple targets to overcome the limitations of the current single target approaches. Many drug development efforts based on the Paul Ehrlich's magic bullet principle, where a single therapeutic agent with ideal selectively could successfully regulate a single target causing a particular disease, have been suffering critical hindrances including unwanted off-target effects and degraded efficacy. Synergistic regulation of multiple targets with multiple agents is expected to remedy those hindrances. Furthermore, recent trends of 4P healthcare require more comprehensive spectrum of bio-agents for disease prevention as well as treatment. Functional food and ingredients have drawing increasing attention especially for preventive medicine and life-time healthcare. As they are composed of multiple components inherently, their precise interactions with human physiology are thought to be synergistic regulation of multiple targets with multiple agents This talk introduces a national initiative where multiple-agent-multiple-target systems biology technology for natural product-based healthcare is being developed. Core components of the technology platform are virtual cell and human systems, which are computational models of molecular, cellular, and organ-level physiological mechanisms. The synergistic effects of multiple agents on multiple targets are simulated and predicted with those virtual systems, and validated in real systems including model cells and animals.

Keynote Speech 專題演講

時　間｜Time　11:00-12:20　Friday　13th Oct, 2017

主　持　人　｜　Moderator

吳永昌 講座教授

Chair Prof. Yang-Chang Wu

高雄醫學大學天然藥物暨新藥開發中心主任

Director, Research Center for Natural Products and Drug Development

11:00-11:40 Friday 13th Oct, 2017

Topic：

Continuous Processing: from natural products bioactivity to medicines

Prof. Svetlana Ignatova
Bioprocessing Centre,
Brunel University London, UK

Abstract

We reported that fibroblasts release soluble factors which control cyclooxygenase-2 (COX-2) overexpression in cancer and inflammatory cells. Analysis with HPLC and NMR revealed that the soluble factors are small molecules containing indole moiety which were named cytoguardins. Metabolomic analysis uncovered the chemical identity of one of the cytoguardins as 5-methoxytryptophan (5-MTP), a tryptophan metabolite synthesized via a novel pathway. Fibroblast derived 5-MTP inhibited cancer cell migration and epithelial mesenchymal transition (EMT) and blocked cancer growth and lung metastasis in a xenograft model. Our recent results indicate that endothelial cells (EC) are a major source of 5-MTP and contributes to a relatively high 5-MTP concentration in circulating blood. Pro-inflammatory cytokines and bacterial endotoxins suppress 5-MTP production which is correlated with overexpression of cytokines/chemokines and COX-2/iNOS by macrophages. Exogenous 5-MTP restores the control of expression of cytokines and COX-2 and abrogated cytokine and eicosanoid storms seen in systemic inflammatory syndromes such as sepsis. 5-MTP exerts its anti-inflammation and anti-cancer effects by a common mechanism. It blocks p38 MAPK activation in inflammatory and cancer cells and thereby inactivates p300 HAT and NF-kB. Our preliminary data suggest that 5-MTP inhibits p38 MAPK activation by disrupting the interaction of phospho-p38 with peroxiredoxin-1. These findings indicate that 5-MTP acts as a novel circulating molecule to maintain inflammation homeosis and control cancer cell metastasis and is a valuable lead compound for new drug development.

11:40-12:20 Friday 13th Oct, 2017

Topic：

Exploration with Ginseng and Melanoma: Metabolomics and Lipidomics Approaches

Prof. Hyung-Kyoon Choi

Natural Product Biotechnology and Metabolomics Laboratory
College of Pharmacy, Chung-Ang University, Seoul, Republic of Korea

Abstract

As one of the new areas of 'omics' technology, there is increasing interest in metabolomics, which involves the analysis of low-molecular-weight compounds in cells, tissues, and biofluids, and considering interactions within various organisms and reactions of external chemicals with those organisms. NMR and MS have been used widely as platforms for metabolic and lipidomic profiling of various natural products and human cells. In this presentation, it is presented that NMR and MS coupled with multivariate analysis technique can be used to discriminate and predict cultivation ages of *Panax ginseng* roots, and estimation of metastatic potential of human melanoma cells.

Keynote Speech 專題演講

時　間｜Time　14:00-15:30　Friday　13th Oct, 2017

主　持　人　｜　Moderator

張永勳 教授
中國醫藥大學中國藥學暨中藥資源學系
Prof. Yuan-Shiun Chang
Department of Chinese Pharmaceutical Sciences and Chinese Medicine Resources, CMU

14:00-14:30　　Friday　13th Oct, 2017

Topic：

中藥複方的系統生物學應用：當歸補血湯的品質控制和機理研究

The osteogenic properties of Danggui Buxue Tang, a Chinese herbal decoction containing Astragali Radix and Angelicae Sinensis Radix: genomics analysis of specific chemical knock-out herbal decoction

詹華強 教授

香港科技大學生命科學部暨中藥研發中心主任

Abstract

Danggui Buxue Tang (DBT), a Chinese herbal decoction, contains 2 herbs of Astragali Radix (AR) and Angelicae Sinensis Radix (ASR) at the ratio of 5:1. Clinically, DBT was utilized to mitigate menopausal osteoporosis; however, the signaling mechanism and the active compounds contributed in bone formation remained unclear. Calycosin and ferulic acid, being the most abundant distinct chemicals in AR and ASR, respectively, were depleted specifically from DBT by HPLC separation. Authentic DBT, a calycosin-depleted DBT ($DBT_{\Delta cal}$) and a ferulic acid-depleted DBT ($DBT_{\Delta fa}$) were applied onto cultured rat osteoblasts. Mineralization assay illustrated that both DBT and $DBT_{\Delta fa}$ significantly induced osteoblastic differentiation, while $DBT_{\Delta cal}$ exhibited a reduced activation in mineralization. The total RNA from herbal decoction-treated osteoblasts was isolated for transcriptome analysis by RNA-seq. The gene expressions of osteogenic markers during differentiation, including Alpl, Runx2, Sparc, Sp7 and Spp1, were significantly increased under the treatments of DBT and $DBT_{\Delta fa}$. Signaling pathway analysis by KEGG and GO-Elite revealed that 11 pathways were activated by DBT, including MAPK/ERK and Wnt/β-catenin signalings, as compared to the untreated control; these signaling pathways were the well-known cascades for osteoblast formation. In contrast, $DBT_{\Delta cal}$ was not able to trigger Wnt/β-catenin signaling. Thus, our findings indicated that calycosin could be an indispensable chemical in DBT to orchestrate multi-components of DBT as to achieve maximal osteogenic properties.

Acknowledgement: Supported by Hong Kong Research Grants Council GRF (662713, M-HKUST604/13), TUYF15SC01, Shenzhen Science and Technology Committee Research Grant (JCYJ20160229205726699, JCYJ20160229205812004, JCYJ20160229210027564, and 20170326).

14:30-15:00　　Friday　13th Oct, 2017

Topic：

天然小分子調控內源抗病毒細胞因數抗機體感染新藥研究

賀震旦 教授

深圳大學醫學院教授，藥學院院長

摘要

天然小分子是中藥、藥用植物和天然藥物的重要活性成分，是重要的藥用資源研究方向和內容。大多數抗病毒藥用植物，如夏枯草、黃芪和黃芩等，其活性成分均為天然小分子。抗病毒細胞因數為一類生物體中具有聯繫機體固有免疫和特異性免疫應答，捕殺或抑制體內病毒的小分子功能蛋白。近年來研究表明，植物中的多酚類、苷類以及寡糖等小分子化合物可調控機體內抗病毒細胞因數的表達水準，繼而作用於各類 DNA 或 RNA 病毒：一方面刺激機體產生抗病毒蛋白，直接捕殺病毒；另一方面聯動機體固有免疫和獲得性免疫應答，抑制病毒複製，抗病毒感染，清除被病毒感染的細胞。

本課題組定義抗病毒細胞因數。人類自身具有先天性的抗病毒感染能力，體內抗病毒細胞因數在這方面發揮重要的作用。藥用植物中的天然小分子結構複雜，資源豐富，成藥性強，然而目前有關天然小分子誘生抗病毒細胞因數的研究缺乏系統性，尚待進行深入研究。對抗病毒藥用植物進行分離提取以及進行體外細胞模型篩選，進行動物免疫學和動物病毒學研究，從而發現活性天然小分子，進而有望開發出誘生機體細胞因數的抗病毒藥物，我們預計此類相關的研究將成為抗病毒藥物研發的新途徑。目前，用於臨床的抗病毒藥物主要有化學藥物和疫苗兩類，而通過誘生抗病毒細胞因數途徑的藥物有望成為第三類新型抗病毒藥物。

關鍵字：抗病毒中藥、抗病毒細胞因數、天然小分子、作用機制

15:00-15:30　　Friday　13th Oct, 2017

Topic：

中草藥於癌症治療之研究 – 困境與挑戰

Discovery and development of anticancer agents on natural products – difficulties and opportunities

顧記華 教授

國家中醫藥研究所、臺大藥學專業學院

Abstract

Malignancy is the leading cause of death in a lot of countries. Our lab has been working on preclinical development of anticancer agents. We have established a screening system, sulforhodamine B assay (SRB assay), according to National Cancer Institute in USA and have been doing a large scale of screening tests to discover potential agents against cancers. In recent decade, we have screened more than 7000 samples from both chemically synthetic compounds and natural products. The mechanisms of anticancer abilities of the effective compounds were studied. Several natural products will be focused in this presentation. The first is cryptocaryone, a natural dihydrochalcone. Several pharmacological and biochemical assays were used to characterize the apoptotic signaling pathways of cryptocaryone in prostate cancer cells. The data suggest that cryptocaryone displays anticancer activity through the stimulation of death receptor and associated molecule clustering, leading to caspase-8 and 3 activation, and apoptosis. The next is reevesioside series of compounds, including Reevesioside A, Reevesioside F and *Epi*-reevesioside F provided by professor Ih-Sheng Chen (Kaohsiung Medical University). The data suggest that the reevesioside compound inhibits c-myc expression and down-regulates the expression of CDC25A, cyclin D1 and cyclin E, leading to a profound decrease of RB phosphorylation. G1 arrest is, therefore, induced through E2F1 suppression. Consequently, reevesioside A causes mitochondrial damage and an ultimate apoptosis in human hormone-refractory prostate cancer cells. Interestingly, these compounds induce anticancer activities through different signaling pathways in different types of cancer cells. They induce apoptosis through the down-regulation of survivin and Mcl-1, and the formation of pro-apoptotic fragments from Bcl-2 family members in leukemic cells. The loss of $\Delta\Psi m$ and mitochondrial damage are responsible for the activation of caspases. Moreover, the amplification of caspase-3-mediated signaling pathway contributes largely to the execution of apoptosis. After the identification of potential compound candidates, a variety of derivatives that may have better PKs, solubility and efficacies, and less toxicities can be obtained for further development.

Keynote Speech 專題演講

時　間｜Time　15:40-17:40　Friday　13th Oct, 2017

主　持　人　｜　Moderator

顧記華 教授

國家中醫藥研究所、臺大藥學專業學院

Prof. Jih-Hwa Guh

National Research Institute of Chinese Medicine and School of Pharmacy, National Taiwan University

15:40-16:10　　Friday　13th Oct, 2017

Topic：

黃花蜜菜標準化抽出物作為輔助臨床之前列腺癌療法加強療效/ Adjuvant effects of a standardized Wedelia chinensis extract on the clinical therapeutic modalities for advanced prostate cancer

蕭培文 博士

中央研究院農業生物科技研究中心

Abstract

The incidence of prostate cancers (PCa) is highly prevalent along with urbanization and population aging. However, the aggressive cancer cells may spread to distant tissues and become lethal, particularly the lymph nodes and bones. Although androgen deprivation therapy (ADT) is effective for most PCa, cancer eventually progresses from ADT, often associated with the upregulation of androgen receptor (AR) and HER2/3-AKT signaling pathway. However, single agent therapy targeting AR, HER2/3 or AKT usually has failed due to the reciprocal feedback loop. By targeting the AR signaling pathway in a castration-resistant PCa cell line, we identified that wedelolactone, apigenin, and luteolin are the active compounds in *Wedelia chinensis* herbal extract (WCE), acting synergistically to inhibit the AR activity in PCa. We combined the mechanism-based bioassay and chemical analysis to establish the standardized preparation and qualification criteria of WCE to treat PCa and benign prostatic hyperplasia. Recently, we demonstrated that WCE effectively disrupted the AR, HER2/3, and AKT signaling networks, therefore, enhanced the therapeutic efficacy of ADT. Interestingly, oral WCE also significantly inhibited the hormone-refractory PCa. Genome-wide transcriptome analysis of these tumors revealed that WCE suppressed the expression of IKKα/β phosphorylation and downstream cytokines/chemokines, e.g., IL6, CXCL1, and CXCL8. Through restraining the cytokines expression, WCE reduced tumor-elicited infiltration of myeloid-derived suppressor cells (MDSCs), tumor-associated macrophages (TAMs) and endothelial cells, therefore inhibited angiogenesis, tumor growth, and metastasis. In MDSCs, WCE also reduced STAT3 activation, downregulated S100A8 expression, and prevented their expansion. Use of WCE in combination with docetaxel effectively suppressed docetaxel-induced NFκB activation, boosted the therapeutic effect and reduced the systemic toxicity. This study demonstrates that WCE can intensify the therapeutic efficacy of not only hormonal therapy but also chemotherapy with docetaxel through immunomodulation. These data establish a solid basis for the adjuvant use of WCE with different therapeutic modalities for advanced prostate cancer.

Key words：IKKα/β, Immunomodulation, Prostate cancer, *Wedelia chinensis*

16:10-16:40　　Friday　13th Oct, 2017

Topic：

丹參酚酸 F 與紫草酸 A 之衍生物用於治療阿茲海默氏症之潛力研究

Investigating the therapeutic potential of the derivatives of Salvinolic acid F and tournefolic acid A on Alzheimer's disease

蕭永基　博士

國家中醫藥研究所

Abstract

Two classes of drugs are currently used to treat Alzheimer's disease (AD): acetylcholinesterase inhibitors and N-methyl-D-aspartate (NMDA) receptor antagonists. Unfortunately, the benefits of these drugs are limited, and no medication has been clearly proven to cure or delay the progression of AD. Most candidate AD drugs aim to reduce the accumulation, aggregation, and toxicity of amyloid (Ab). Hence, in the current study, we demonstrate the efficient synthesis of hydroxyl-functionalized stilbene and 2-arylbenzo[b]furan derivatives derive from salvinolic acid F and tournefolic acid A, respectively, and report on the therapeutic potential on AD of these phenolic compounds both in vitro and in an animal model. We found that part of the hydroxyl-functionalized stilbenes and 2-arylbenzo[b]furans likely (1) confer neuroprotective effects on neuron cells, (2) confer anti-neuroinflammatory effects on glial cells, and (3) ameliorate the nesting behavior of APP/PS1 transgenic mice. These compounds possess the therapeutic potential on AD.

Key words：Alzheimer's disease; salvinolic acid F; tournefolic acid A; stilbene; 2-arylbenzo[b]furan; neuroprotection; anti-neuroinflammation

16:40-17:10　　Friday　13th Oct, 2017

Topic：

基因表現調控應用於天然藥物研發
Natural Products R&D under Genetic Expression Modulation

張芳榮 教授

高雄醫學大學 天然藥物研究所

Abstract

In these two decades, a trend in combining molecular biotechnology and chemistry for natural products development is forming. We have investigated on several subjects involved epigenetic and genetic modulation on secondary metabolites production on natural products. For examples, genetic modified Arabidopsis plants, pER8-GFP & pER8-GUS with human estrogen receptor alpha was applied for detection of phytoestrogens or environmental hormones, and several undiscovered phytoestrogens were revealed.

Moreover, a new technology for epigenetic chemical modulating agents on two important gene expression enzymes HDAC and DNMT is also studied. Many new secondary metabolites were induced on the basis of this method. Some of them have a wonderful story behind. In this presentation, I will share the stories and update ideas in the new trend for natural products development in combining molecular biotechnology and chemistry.

Key words：Secondary metabolites, Epigenetic, Genetic, Natural Products

17:10-17:40　　Friday　13th Oct, 2017

Topic：

細葉山艾之成分與活性研究(Studies on the constituents and biological activities of Artemisia morrisonensis Hayata)

周聖杰 副教授

中國醫藥大學 藥學系

Abstract

Artemisia is one of the largest genera of family Compositae. *Artemisia* comprises hardy herbaceous plants and shrubs and attracts much attention for its highly economic values in particular for its medicinal uses. Artemisia morrisonensis Hayata is an endemic species in Taiwan. Traditionally, this plant is used for the treatment of rheumatoid arthritis, allergic rhinitis, headache and edema in aboriginals. However, the therapeutic potential and underlying mechanisms still remain elusive and the active components of this plant have not been systematically identified. Our study demonstrated that the ethanolic extract decreased writhing response for both the acetic acid assay and the licking time in formalin test and significantly decreased induced paw edema three to four hours after λ-carrageenan injection. The extract decreased the levels of NO, MDA, TNF-α and IL-6 levels in the edematous paw. We had identified p-hydroxyacetophenone (130 mg/g as major component), picein, friedelin, capillene, capillaridin C and capillaridin F from the whole plant. In the HBV inhibition, p-hydroxyacetophenone involved the regulation of viral surface gene expression and blocked virion secretion by interference with the ER stress signaling pathway. Besides, Western blot showed that the expression of cleaved-PARP, cleaved-caspase-9 and cleaved-caspase 3 were up-regulated with the increase of capillene concentration in cell apoptosis detected by Annexin V FITC staining. The protein expression in the BcL-2 family was observed and the expression of BcL-2 was decreased. These results suggest that capillene could cause apoptosis for A549 cell line. Our studies will provide with the evidence for the ethnobotanical uses of A. *morrisonensis* Hayta in the treatment of inflammation, HBV, and even lung cancer.

Key words：細葉山艾(*Artemisia morrisonensis* Hayata)、鎮痛(Analgesia)、抗發炎(Anti-inflammation)、B 型肝炎(Hepatitis B)、肺癌(Lung cancer)

Keynote Speech 專題演講

時　間｜Time　09:00-10:00　Saturday　14th Oct, 2017

主　持　人　｜　Moderator

謝明村 講座教授

中國醫藥大學中國藥學暨中藥資源學系

Chair Prof. Ming-Tsuen Hsieh

Department of Chinese Pharmaceutical Sciences and Chinese Medicine Resources, CMU

09:00-10:00　　Saturday　14th Oct, 2017

Topic：

許鴻源 100 週年專題演講

莊武璋 博士

順天堂藥廠股份有限公司 總經理

Keynote Speech 專題演講

時　間｜Time	14:00-14:40	Saturday	14th Oct, 2017

主　持　人　｜　**Moderator**

黃聰龍 教授

長庚大學中醫學系天然藥物研究所

Prof. Tsong-Long Hwang

Graduate Institute of Natural Products,

Chang Gung University

14:00-14:40　　Saturday　14th Oct, 2017

Topic：

人工智慧與自動化對天然物研究的衝擊

Impact of Artificial Intelligence and Robotization on Natural Products Researches

李慶國 教授

臺北醫學大學 藥學系

Abstract

「人工智慧」的技術可以提高人類生活的便利性、增加企業的競爭力，並且提高生產效率及準確度；而自動化是直接節省人力成本，並可保證製造品質的一致性與穩定性，並且利用流通資訊來降低生產的不確定性。然而，我們所知的天然物研究，從分離、到活性成分的純化與結構的鑑定是費時、費力，需要人力支援的科學。

如何將人工智慧與自動化觀念和技術應用於天然物的研究，是值得大家一起思考與探討。

The technology of "Artificial intelligence" is able to bring the convenience to human life, increase the competitiveness for enterprises, and improve the efficiency and accuracy on productions. Robotization is able to save the manpower costs directly, moreover, to keep the quality of manufacturing with consistent and stable conditions, and then, to reduce the production uncertainty using the circulated information. However, the science of natural product researches from separation to purification of active ingredients and determination of structures is a time-consuming and manpower-required work.

How to apply the concepts and techniques of artificial intelligence and robotization into natural products research is a special issue merited to discuss together.

關鍵字/Key words：Artificial Intelligence, Robotization, Natural products

壁報論文 | Poster Flash

時間 | Time

10:00-12:00 Saturday 14th Oct, 2017

天然物組 | Natural Products

PN-01

Chemical profile analysis and active components from the root of *Cynara scolymus*

Chien-Chih Chen[1#], Chia-Lin Lee[2, 3], Juan-Cheng Yang[3], Yang-Chang Wu[4, 5, 6, 7*]

[1]School of Pharmacy, Department of Pharmacy, China Medical University

[2]Associate Professor, Department of Cosmeceutics, China Medical University

[3]Assistant Researcher, Chinese Medicine Research and Development Center, China Medical University Hospital, Taichung 40447, Taiwan

[4]Chair Professor, Department of Pharmacy, China Medical University

[5] Graduate Institute of Natural Products, Kaohsiung Medical University, Kaohsiung 80708, Taiwan

[6] Research Center for Natural Products & Drug Development, Kaohsiung Medical University, Kaohsiung 80708, Taiwan

[7] Department of Medical Research, Chung-Ho Memorial Hospital,Kaohsiung Medical University, Kaohsiung 80708, Taiwan

Abstract:

Cynara scolymus (Asteraceae) is a famous and well known plant for its antioxidant property to improve human liver functions. However, previous studies only focused on the aerial part of *C. scolymus*; whereas, the phytochemical and biological studies of the root of this species has never been researched. During our bioassay screening, it was found that the EtOH crude extract prepared from the root has anti-allergy and antioxidant activities. Therefore, the purpose of this research was not only to isolate the active components from the aerial part of *C. scolymus*, but also to compare the chemical profiles between aerial and underground portions of this plant with high performance liquid chromatography (HPLC). The EtOH extracts of the dried roots of *C. scolymus* (CCR) were partitioned into EtOAc- (CCR-E), *n*-BuOH- (CCR-B), and aqueous- (CCR-W) soluble fractions. The chromatographic isolation of the CCR-E led to three sesquiterpenes, puliglutone (**1**), 1-oxo-bisabola-(2,10*E*)-diene-12-ol (**2**), ptilostemonol (**3**), one lignan (**4**), one 1, 5-dicaffeoyl quinic acid (**5**), and one benzenoid (**6**). Their structures were identified by nuclear magnetic resonance (NMR). The chemical fingerprintings of the leaves and roots were conducted by HPLC and discussed herein. Currently, the bioassays of the isolated compounds are still undergoing.

Keywords: *Cynara scolymus*, Nuclear magnetic resonance (NMR), High performance liquid chromatography (HPLC), Chromatography, Root

PN-02

Quality Control of the Root and Rhizome of Helminthostachys zeylanica (Daodi-Ugon) by HPLC Using Quercetin and Ugonins as Markers

吳坤璋 **Kun-Chang Wu#**[1] · 高駿彬 **Chun-Pin Kao2** · 何玉鈴 **Yu-Ling Ho3** · 張永勳 **Yuan-Shiun Chang**[*,1,4]

1 Department of Chinese Pharmaceutical Sciences and Chinese Medicine Resources, College of Chinese Medicine, China Medical University, Taichung 40402, Taiwan

2 Department of Nursing, Hsin Sheng Junior College of Medical Care and Management, Taoyuan 32544,Taiwan

3 Department of Nursing, Hungkuang University, Taichung 43302, Taiwan

4 Chinese Crude Drug Pharmacy, China Medical University Hospital, Taichung 40402, Taiwan

Daodi-Ugon is the dried root and rhizome of *Helminthostachys zeylanica* (L.) Hook. and has been used for centuries in the treatment of inflammation, fever, pneumonia, burns, and various disorders. However, the chromatographic methods to determine the phytochemical composition of *H. zeylanica* have never been reported. This study not only aims to develop a valid high-performance liquid chromatography (HPLC) method and to establish a chromatographic fingerprint for the quality control of *H. zeylanica*, it also establish the proposed content limits of Quercetin, Ugonin J, and Ugonin M. An HPLC method with a RP18 column (250 × 4.6 mm, 5 μm) was developed for the quantitative analysis of Quercetin, Ugonin J, and Ugonin M in *H. zeylanica*. A simple gradient of (A) methanol/(B) phosphoric acid in water (5–45 min, 70–80% A; 50–55 min, 80–70% A) was used and 360 nm was selected as the detection wavelength. The average contents and proposed content limits for *H. zeylanica* were calculated with a *t*-test and a measurement uncertainty test based on 20 batches of authentic *H. zeylanica* samples. Limits of detection (LOD), quantification (LOQ), linearity, precision, repeatability, stability, and recovery of the developed method were validated. All of the validation results of quantitative determination and fingerprinting methods were satisfactory. The developed method was then applied to assay the contents of Quercetin, Ugonin J, and Ugonin M and to acquire the fingerprints of all of the collected *H. zeylanica* samples. At the 99% confidence level, the calculated content limits were 56.45, 112.15, and 277.98 mg/kg for Quercetin, Ugonin J, and Ugonin M, respectively. Those validated HPLC quantitative method, fingerprinting profile, and the proposed content limits of three chemical markers that could be used in the quality control of *H. zeylanica* in the market.

Key words：quality control; *Helminthostachys zeylanica*; *Daodi-Ugon*; Quercetin; Ugonin J; Ugonin M

PN-03

Secondary Metabolites from the Soft Coral *Sarcophyton cinereum* Tixier-Durivault

陳怡儒 **Yi-Ju Chen**[1,#]，黃子胤 **Tzu-Zin Huang**[1]，黃瓊瑤 **Chiung-Yao Huang**[1]，
許志宏 **Jyh-Horng Sheu**[1,2,*]

[1]Department of Marine Biotechnology and Resources, National Sun Yat-sen University, Kaohsiung 804, Taiwan
[2]Frontier Center for Ocean Science and Technology, National Sun Yat-sen University, Kaohsiung 804, Taiwan

The Formosan soft coral *Sarcophyton cinereum* Tixier-Durivault, collected from the Liuqiu, Taiwan, in 2012, at a depth of 10–15 m, was stored in a freezer at the Department of Marine Biotechnology and Resources, National Sun Yet-Sen University. The frozen bodies of *S. cinereum* were sliced and extracted with ethyl acetate (EtOAc) repeatedly. Combined EtOAc extract was evaporated and the residue was fractioned over silica gel gravity column. The resolved fractions were further purified by reversed phase HPLC to yield a new natural product sarcinerolide A (**1**) and 11 known compounds (**2**–**12**), including sarsolenone(**2**),sartrolidesD(**3**),(4*Z*,8*S*,9*S*,12*Z*,14*E*)-9-hydroxy-1-isopropyl-8,12-dimethyloxabicyclo-[9.3.2]-hexadeca-4,12,14-trien-18-one(**4**),isosarcophine(**5**),isosarcophytonolide D (**6**), sarcrassin E (**7**), glaucumolide A (**8**), glaucumolide B (**9**), sartrolide C (**10**), sartrolide D (**11**) and sarcophytonolide J (**12**). The structures of all compounds were established by spectroscopic analyses, including 1D and 2D NMR and MS data.

Key words: Soft coral, *Sarcophyton cinereum*, secondary metabolites

PN-04

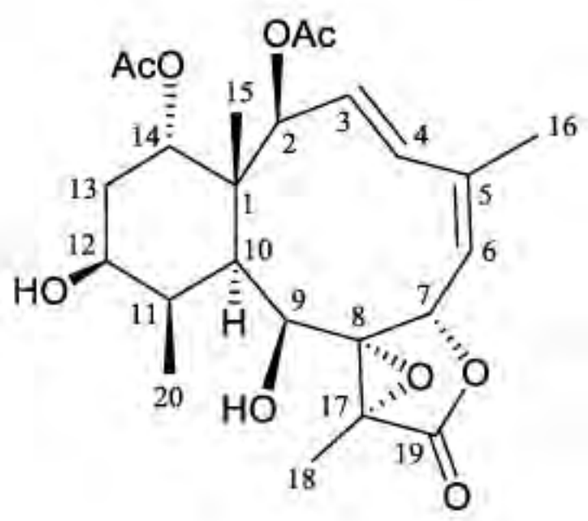
Briarenols B–E, new polyoxygenated briaranes from the octocoral *Briareum excavatum*

Yin-Di Su(蘇尹帝)[1,#], Tsong-Long Hwang(黃聰龍)[2], Zhi-Hong Wen(溫志宏)[3], Jyh-Horng Sheu(許志宏)[3], Ping-Jyun Sung(宋秉鈞)[1,4,*]

[1]National Museum of Marine Biology & Aquarium, Pingtung, Taiwan
[2]Graduate Institute of Natural Products, Chang Gung University, Taoyuan, Taiwan
[3]Department of Marine Biotechnology & Resources, National Sun Yat-sen University, Kaohsiung, Taiwan
[4]Graduate Institute of Marine Biology, National Dong Hwa University, Pingtung, Taiwan

Four new polyoxygenated briarane diterpenoids, briarenols B–E (**1–4**), were isolated from the octocoral *Briareum excavatum*. The structures of briaranes **1–4** were elucidated by interpretation of spectroscopic data, and the methylenecyclohexane ring in **2** was found to exist in a twisted boat conformation. Briarenols B (**1**) and D (**3**) displayed inhibitory effect on the release of elastase by human neutrophils with an IC_{50} value of 3.33 and 4.65 μM. Briarenol E (**4**) was found to inhibit the protein expression of pro-inflammatory inducible nitric oxide synthase (iNOS) in a murine macrophage-like cell line, RAW264.7, stimulated with lipopolysaccharide (LPS).

Key words：Briarenol, briarane, elastase, iNOS



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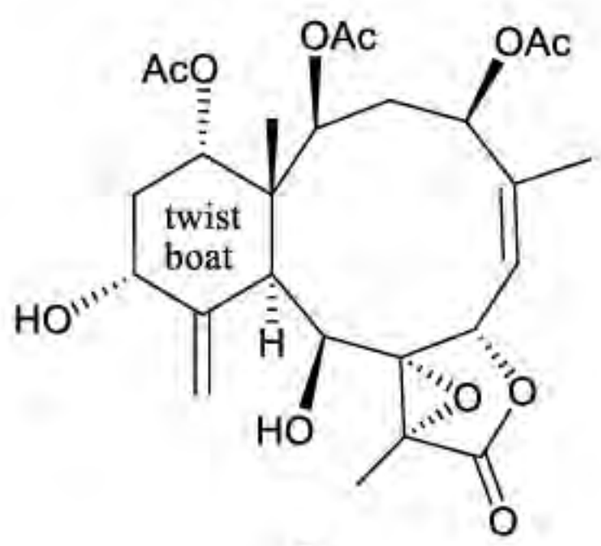

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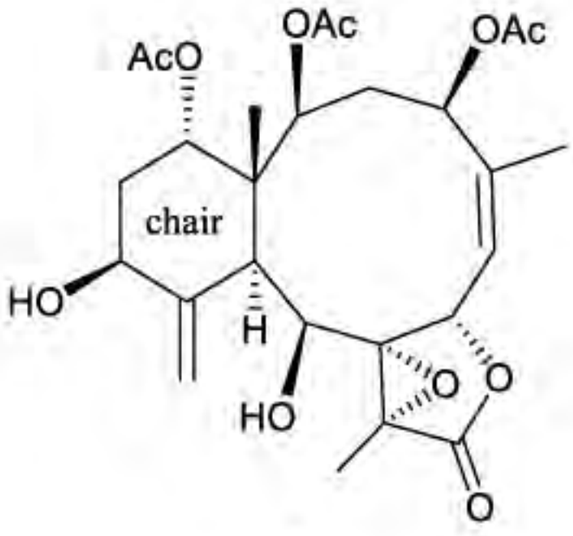

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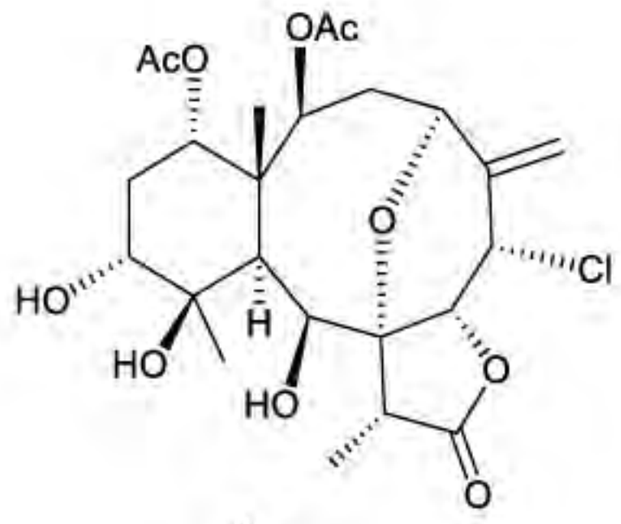


4

PN-05

Bafilomycins M–O, new cytotoxic bafilomycin analogues produced by *Streptomyces* sp. GIC10-1 isolated from a marine sponge *Theonella* sp.

Yu-Hsin Chen(陳毓昕)[1,2,#], Yin-Di Su(蘇尹帝)[1], Jia-Wen Yao(姚佳妏)[3], Mei-Chin Lu(呂美津)[2,3],Ching-Feng Weng (翁慶豐)[1,*], Jimmy Kuo (郭傑民)[2,3,*], Ping-Jyun Sung (宋秉鈞)[2,3,*]

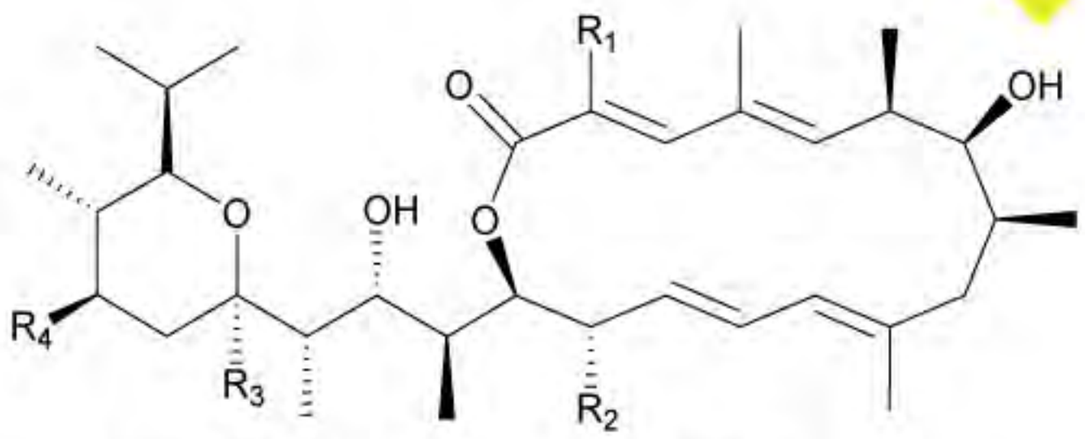
[1]Department of Life Science and Graduate Institute of Biotechnology, National Dong Hwa University, Hualien 974, Taiwan
[2]National Museum of Marine Biology and Aquarium, Pingtung 944, Taiwan.
[3]Graduate Institute of Marine Biology, National Dong Hwa University, Pingtung 944, Taiwan

Three new 16-membered diene macrolides, bafilomycins M–O (**1–3**), along with three known compounds JBIR-100 (**4**), bafilomycin K (**5**) and bafilomycin C1 (**6**) were produced from *Streptomyces* sp. GIC10-1. This bacterium was isolated from a marine sponge *Theonella* sp. The structures of **1–6** were established by spectroscopic methods and by comparison the spectral data with known analogues. These five compounds were found to exhibit significant cytotoxicity toward MOLT-4, K-562, SUPT-1 and LNCaP tumor cells.

Key words：*Theonella*, *Streptomyces*, bafilomycin, cytotoxicity

Theonella sp.

Streptomyces sp. GIC10-1



Bafilomycin M (**1**):R_1=CH_3, R_2=R_3=OCH_3, R_4=OH
Bafilomycin N (**2**):R_1=R_2=CH_3, R_3=OH, R_4=$OC(O)C(H)=C(H)COOH$
Bafilomycin O (**3**):R_1=R_2=CH_3, R_3=R_4=OH
JBIR-100 (**4**):R_1=CH_3, R_2=OCH_3, R_3=OH, R_4=$OC(O)C(H)=C(H)COOH$
Bafilomycin K (**5**):R_1=CH_3, R_2=OCH_3, R_3=R_4=OH
Bafilomycin C1 (**6**):R_1=R_2=OCH_3, R_3=OH, R_4=$OC(O)C(H)=C(H)COOH$

PN-06

Briaviodiol B, a new cembranolide from the cultured-type soft coral *Briareum violacea*

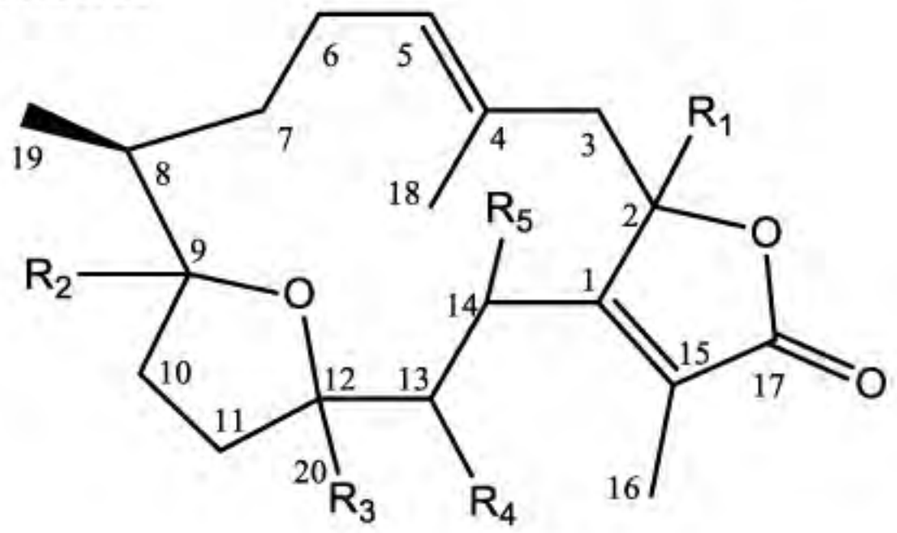
Pin-Chang Huang (黃品彰) [1,2,#], Ping-Jyun Sung (宋秉鈞) [1,2,*]

[1]Graduate Institute of Marine Biology, Nationl Dong Hwa University (NDHU), Pingtung 944, Taiwan

[2]National Museum of Marine Biology and Aquarium (NMMBA), Pingtung 944, Taiwan

Six cembranolies, including a new compound, briaviodiol B (**1**), as well as five known analogues, briaviodiol A (**2**), pachyclavulariolides E (**3**), G (**4**), H (**5**) and K (**6**), were isolated from an octocoral identified as *Briareum violacea* (Figure 1), which was cultured in the NMMBA, Taiwan, with a 0.6-ton tank equipped with a flow-through sea water system. The structure, including the relative configuration of cembranolide **1** was established by spectroscopic analyses. The biomedical activity of compounds **1**–**6** will be assayed in the future.

Key words : *Briareum violacea*, octocoral, cembranolide, briaviodiol, pachyclavulariolide



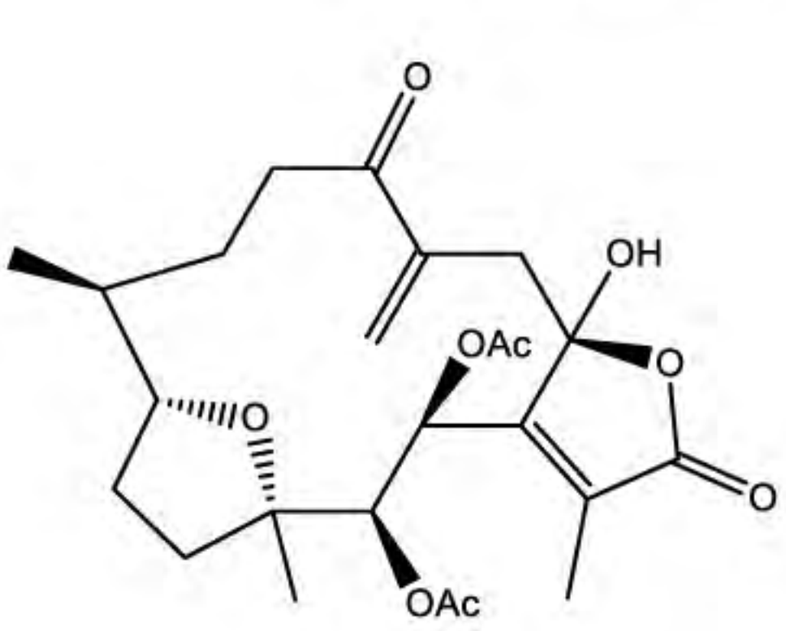
1: R_1=β-OCH_3, R_2=α-H, R_3=α-CH_3, R_4= R_5=β-OH

2: R_1=β-OCH_3, R_2=α-H, R_3=α-CH_3, R_4= R_5=α-OH

3: R_1=α-OH, R_2=β-H, R_3=β-CH_3, R_4=R_5=β-OAc

4: R_1=α-H, R_2=β-H, R_3=β-CH_3, R_4=R_5=β-OAc

5: R_1=R_2=β-H, R_3=β-CH_3, R_4=R_5=β-OAc



6

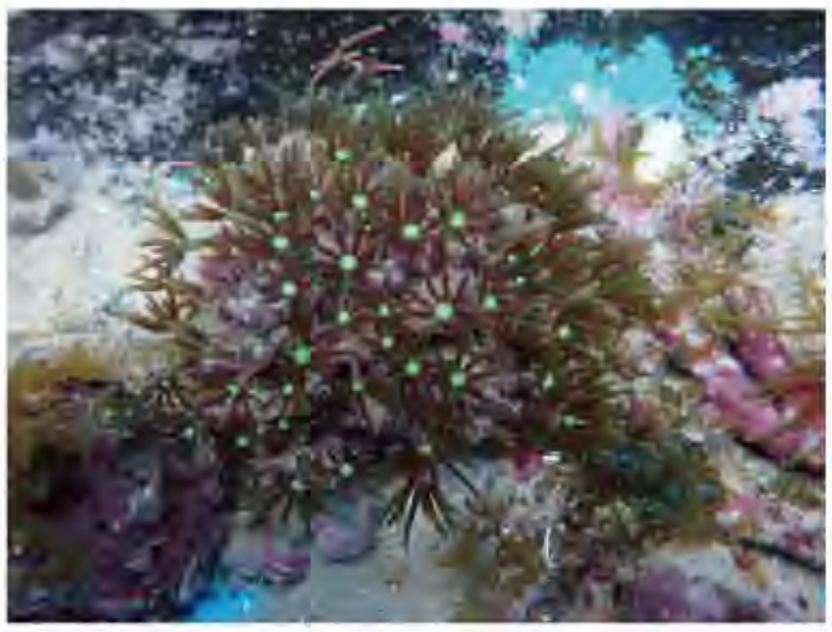


Figure 1. *Briareum violacea*

PN-07

Four new briarane-type diterpenoids from the cultured octocoral *Briareum violacea*

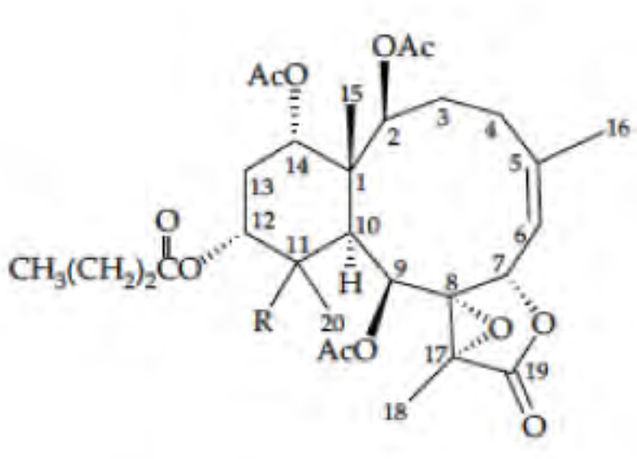
Jing-Hao Xu (許景皓) [1,2 #], Ping-Jyun Sung (宋秉鈞) [1,2,*], Yin-Di Su(蘇尹帝) [2]

[1] Graduate Institute of Marine Biology, National Dong Hwa University (NDHU), Pingtung 944, Taiwan

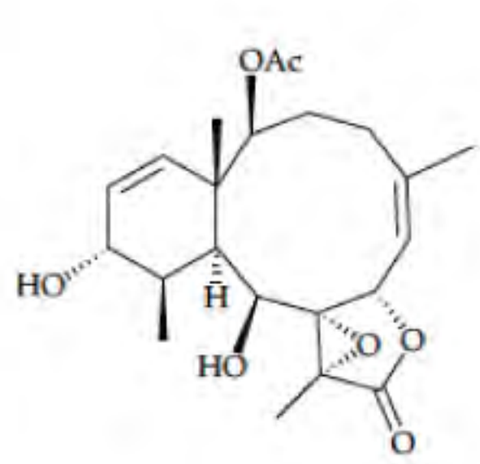
[2] National Museum of Marine Biology and Aquarium (NMMBA), Pingtung 944, Taiwan

Chemical investigation on the cultured soft coral *Briareum violacea* have afforded six briarane-type (3,8-cyclized cembranoid) natural products **1**–**6**. In above metabolites, briaranes **1**–**4** are new compounds. The structures of new metabolites **1**–**4** wwere elucidated on the basis of extensive spectroscopic methods, in particular with 1D and 2D NMR experiments. The anti-inflammatory activity of briaranes **1**–**6** will be assayed in the future.

Key words：*Briareum violacea*, octocoral, briarane



1 : R = β-OH, **2** : R = α-OH



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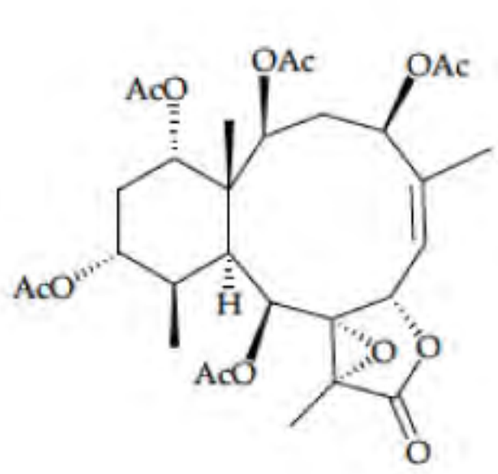

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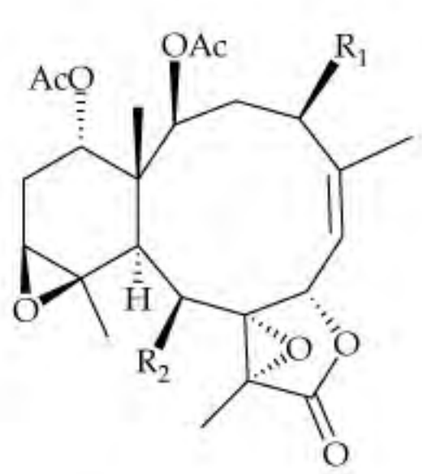
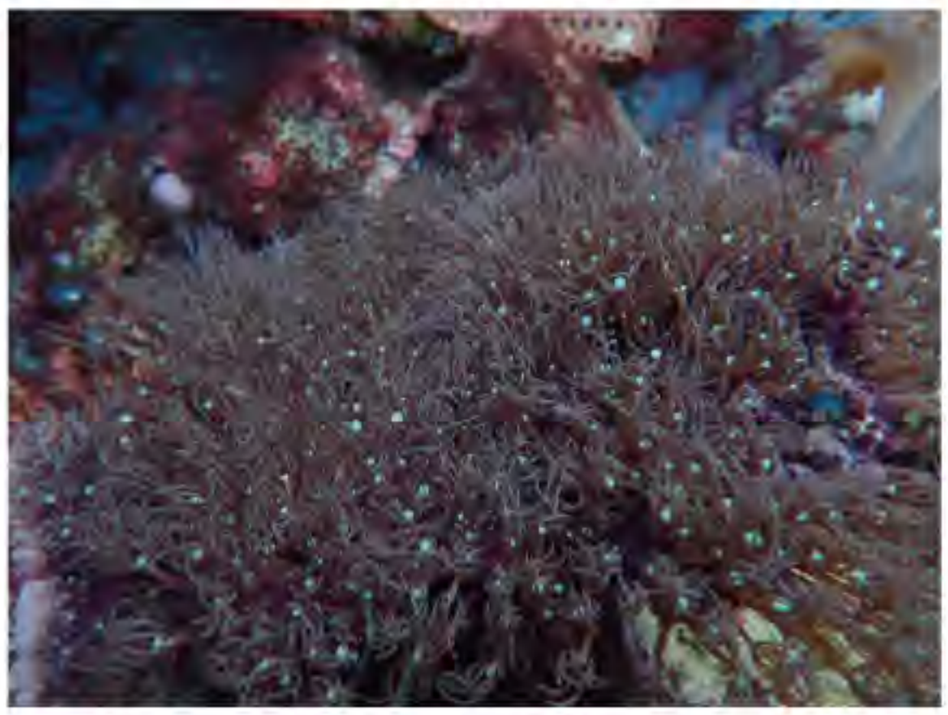


5 : R_1 = H, R_2 = OH

6 : R_1 = R_2 = OAc



Briareum violacea

Briareum violacea

PN-08

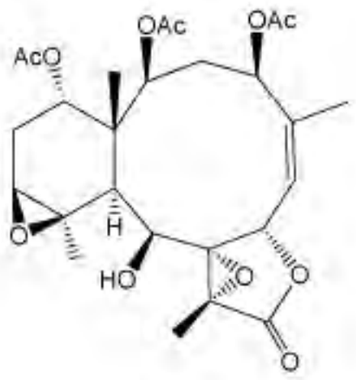
Briarane-type diterpenoids from the Sea Slugs *Phyllodesmium briareum*

Bo-Rong Peng (彭柏融)[1,2,3,#], Yin-Di Su(蘇尹帝)[3], Feng-Yu Lin (林鳳瑜)[4], Chang-Yih Duh (杜昌益)[1, 2, 5,*], Ping-jyun Sung (宋秉鈞)[3, 5, 6,*]

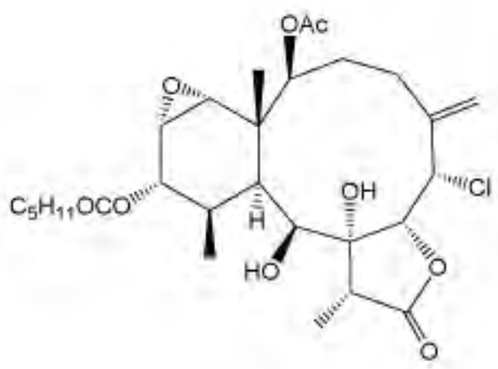
[1]Doctoral Degree Program in Marine Biotechnology, National Sun Yat-Sen University, Kaohsiung 804, Taiwan
[2]Doctoral Degree Program in Marine Biotechnology, Academia Sinica, Taipei 155, Taiwan
[3]National Museum of Marine Biology and Aquarium, Pingtung 944, Taiwan
[4]Department of Applied Chemistry, National Pingtung University, Pingtung 900, Taiwan
[5]Department of Marine Biotechnology and Resources, National Sun Yat-Sen University, Kaohsiung 804, Taiwan
[6] Graduate Institute of Marine Biology, National Dong Hwa University, Pingtung 944, Taiwan

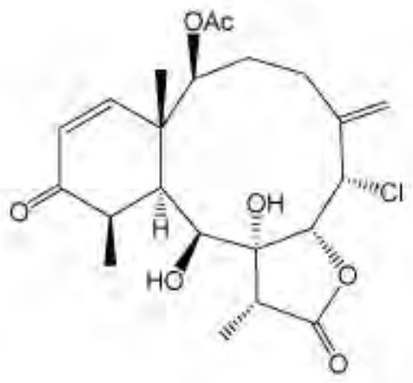
Six briarane-type diterpenoids, stecholide C (**1**), solenloides A (**2**), E (**3**), excavatolides B (**4**), Z (**5**) and briaexcavatolide P (**6**) were isolated from the sea slugs *Phyllodesmium briareum*. The structures of the isolates were elucidated using several spectroscopic techniques and by comparison of their spectroscopic data with those of the related metabolites. The intriguing feeding behavior of *P. briareum* on the octocoral *Briareum* sp. will be studied in the future.

Key words：Sea slugs, *Phyllodesmium briareum*, briarane-type

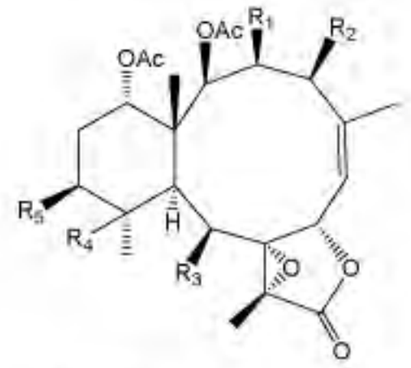


1





3



4 : R_1=OCOPr, R_2=H, R_3=OAc, R_4=H, R_5= OH

5 : R_1=H, R_2=H, R_3=OH, R_4=β-OH, R_5=OCOPr

6 : R_1=OH, R_2=OCOPr, R_3=OAc, R_4=H, R_5=OH

Phyllodesmium briareum

PN-09

台灣海綿 *Phyllospongia* sp.中的二倍半萜與混源二萜類抗血癌成分及其透過抑制第二型拓撲異構酶與熱休克蛋白90而促進癌細胞凋亡之功效

Anti-leukemic Scalarane Sesterterpenoids and Meroditerpenoid from *Phyllospongia* sp., Induce Apoptosis via Dual Inhibitory Effects on Topoisomerase II and Hsp90

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Two new scalarane sesterterpenoids, 12β-(3'β-hydroxybutanoyloxy)-20,24-dimethyl-24-oxo-scalara-16-en-25-al (**1**) and 12β-(3'β-hydroxypentanoyloxy)-20,24-dimethyl-24-oxo-scalara-16-en-25-al (**2**), along with one known tetraprenyltoluquinol-related metabolite (**3**), were isolated from the sponge *Phyllospongia* sp. In leukemia Molt 4 cells, **1** (125 nM) triggered mitochondrial membrane potential (MMP) disruption and apoptosis showing more potent effect than **2** and **3**. The isolates inhibited topoisomerase IIα expression. The apoptotic-inducing effect of **3** was supported by the *in vivo* experiment through suppressing the volume of xenograft tumor growth (47.58%) compared with the control. Compound **1** apoptotic mechanism of action in Molt 4 cells was further elucidated through inducing ROS generation, calcium release and ER stress. Using the molecular docking analysis, **1** exhibited more binding affinity to N-terminal ATP-binding pocket of Hsp90 protein than 17-AAG, a standard Hsp90 inhibitor. The expression of Hsp90 client proteins, Akt, p70S6k, NFκB, Raf-1, p-GSK3β, and XIAP, MDM 2 and Rb2, and CDK4 and Cyclin D3, HIF 1 and HSF1 were suppressed by the use of **1**. However, the expression of Hsp70, acetylated tubulin, and activated caspase 3 were induced after **1** treatment. Our results suggested that the anti-apoptotic effect of the isolates is mediated through the inhibition of Hsp90 and topoisomerase activities.

Key words: *Phyllospongia* sp., scalarane sesterterpenoids, apoptosis, topoisomerase II, heat shock protein 90

PN-10

Comparison of components and bioactivities of *Equisetum ramosissimum* ssp. *ramosissium*, *E. ramosissimum* ssp. *debile* and *E. hyemale*

節節草、台灣木賊和木賊的成分及活性分析

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Equisetum species are collectively known as horsetails. Extracts from horsetails are used as diuretic and a source of natural antioxidants. *E. hyemale* has been used as a traditional herbal medicine to treat various diseases such as hypertension, inflammatory diseases, acute stroke, bleeding and cancer. In this study, three *Equisetum* species, *E. hyemale*, *E. ramosissimum* ssp. *ramosissium and E. ramosissimum* ssp. *debile* were evaluated for their compound differences and antioxidant activity. Four compounds kaempferol 3-*O*-sophoroside (**1**), quercetin 3-*O*-sophoroside (**2**), kaempferol 3-*O*-sophoroside-7-*O*-glucopyranoside (**3**), and herbacetin 3-*O*-sophoroside-8-*O*-glucopyranoside (**4**) were isolated from three *Equisetum* speaes. The bioactivties of three extracts and four isolated compound were determined by DPPH, $ABTS^{\cdot+}$ radical scavenging and α-glucosidase inhibition assays. *E. ramosissimum* ssp. *ramosissium* extract showed the potential antioxidant activity. In HPLC analysis, we found three *Equisetum* species plants have different major compounds. *E. ramosissimum* ssp. *ramosissium* have best antioxidant activity among the three plants, but it main antioxidant activity source still unclear. *E. hyemale* have best α-glucosidase inhibit activity in three plants. Compound **3** has great α-glucosidase inhibit activity, it also plays an important role in the antioxidative activity of *E. hyemale*.

Key words : *Equisetum hyemale*, *Equisetum ramosissimum*, antioxidant, α-glucosidase inhibition

PN-11

Epigenetic Manipulation Induces the Production of the Coumarin-Type Secondary Metabolite from *Arthrobotrys foliicola*

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Abstract: Pursuing epigenetic manipulation approach in fungi led to the isolation of a coumarin metabolite. An addition of the histone deacetylase inhibitor, suberohydroxamic acid (SBHA), to the culture medium of *Arthrobotrys foliicola* induced a single intensive peak in the HPLC profile of the ethyl acetate extract. The compound which was identified as 4-ethyl-7-hydroxy-8-methyl-2H-chromen-2-one (**1**), was isolated from nature for the first time. Moreover, the investigation in the remaining part of the HPLC profile led to the isolation of 6-ethyl-2,4-dihydroxy-3-methylbenzaldehyde (**2**) and ten 2,5-diketopiperazine compounds (**3-12**). The structures of isolates were established by their mass and NMR spectroscopic data. The coumarin-type secondary metabolite (**1**) with peculiar smell induced by epigenetic stimulation is found for the first time in the *Arthrobotrys* species and the family Orbiliaceae, and this compound may be possibly related to nematode-trapping or nematicidal activities of the fungus.

Keywords: *Arthrobotrys foliicola*; suberohydroxamic acid; coumarin; 2,5-diketopiperazine

PN-12

Anti-inflammatory flavan-3-ol-dihydroretrochalcones from *Daemonorops draco*

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Four A-type flavan-3-ol-dihydroretrochalcone dimers, dragonins A-D (**1-4**), were characterized from the traditional Chinese medicine, Sanguis Draconis. The structures of **1-4** were elucidated by spectroscopic and spectrometric analyses. Compounds **1** and **2** exhibited significant inhibition of fMLP/CB-induced superoxide anion and elastase. The signaling pathways accounted for the inhibitory effects of compound **2** were also elucidated. These purified A-type flavan-3-ol-dihydroretrochalcones are new potential leads for the development of anti-inflammatory drugs.

Key words: Dragon's blood; deoxyproanthocyanidin; superoxide anion generation; elastase release

PN-13

台灣己及的萜類成分與抗發炎作用

Isolation and anti-inflammatory Effect of Terpenoids from *Chloranthus oldhami* Solms.

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Chloranthus oldhami Solms (Chloranthaceae) is a rare Chloranthus species endemic in Taiwan. It is an erect perennial herb about 30~50 cm height, generally growing in forests at an altitude of about 500-1000 m in northern mountain area of Taiwan. In folk medicine, the whole herb was used for promoting blood circulation, detoxification, and treatment swelling, amenorrhea, blood stasis pain, rheumatism, and traumatic injury. Our preliminary assay showed that the extract of the whole herb of *C. oldhami* had significantly inhibitory effects on NF-κB activity in LPS-stimulated RAW 264.7/Luc macrophage. In order to identify novel anti-inflammatory compounds of *C. oldhami,* a systemic examination of chemical constituents were carried out. 18 principles were isolated and identified from the EtOAc and *n*-BuOH extracts of *C. oldhami*. They are phenylpropenes, sesquiterpenes, diterpenes, dimer sesquiterpenes, coumarin, and phenylpropanoic acids. Among these isolated compounds, methyl rosmarinate, rosmarinic acid, curzerenone, 1(10)Z,4Z-furanodiene-6-one, and ent-7,13-abietadien-3b-ol showed concentration-dependent inhibition of NF-κB activation in LPS-induced macrophages.

關鍵字/Key words：*Chloranthus oldhami*; Chemical Constituent; Terpenoid; Anti-Inflammatory

PN-14

Total Synthesis of Naturally Occurring Morachalcones B and C

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游錫榕(Hsi-Jung Yu),[1] 靳宗玫(Tsung-Mei Chin),[1] 劉清揚(Ching-Yang Liu),[1]
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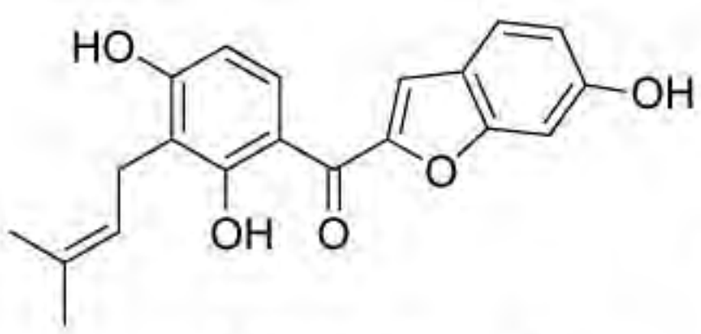
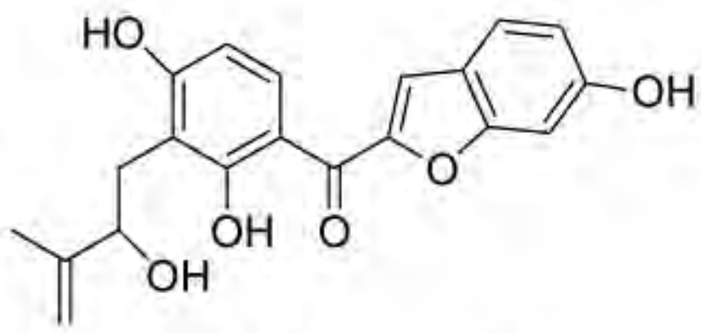
Morachalcones B and C (**1** and **2**), two novel chalcone derivatives, were isolated and characterized from leaves of *Mora alba* L., and showed moderate cytotoxic activity against HCT-8 and BGC823 human cancer cell lines. Naturally occurring chalcones and synthesized analogues have been reported to have various bioactivities, such as antioxidant, antimicrobial, anticancer, and vasorelaxant activities. Due to the variety of their beneficial effects, compounds related to chalcones have attracted attention as synthetic targets. To our knowledge, no work has been done on total synthesis of **1** and **2**. It seems to be important to develop synthetic routes of **1** and **2** for further biological activity study. Herein, an efficient method to synthesize morachalcones B and C (**1** and **2**) was described. Rap–Stoermer condensation and 1,3-prenyl rearrangement were used as two key synthetic methods. Morachalcone C was obtained by photooxygenation of morachalcone B.



1, Morachalcone B



2, Morachalcone C

關鍵字/Key words：Morachalcone B, Morachalcone C, *Mora alba*, Rap–Stoermer condensation, Photooxygenation

PN-15

Study on Chemical Constituents and Biological Activities of the Twigs of *Ficus pumila* var. *awkeotsang*

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Ficus pumila var. *awkeotsang* (Moracace family) is a scandent shrub growing in the mountainous areas of Taiwan, and southeast China. This genus is an endemic subspecies, and the fruit of *F. pumila* is widely used for beverage in Taiwan. Extracts from *F. pumila* have been used traditionally to treat rheumatism, sciatica, diarrhea, edema, amenorrhea, postpartum blood stasis abdominal pain, sore throat, orchitis, and lacquer. The chemical constituent of *F. pumila* var. *awkeotsang* has not previously been investigated; thus, it was research worth. Investigation of the methanolic extract of the twigs of *F. pumila* var. *awkeotsang* and purification by normal phase HPLC using a CN column yielded twenty-one compounds, contained eight simple type coumarins, five furano types coumarins, four pyrano linear type coumarins, a chromen, a triterpenoid, and two C_{13} nor-isoprenoids. The structures of all isolated compounds were determined by analyzing their Mass and NMR spectroscopic data. Antiviral activity of the isolated compounds was tested and evaluated. However, all pure compounds showed no bioactivity against influenza virus H7N9, even though the crude extract displayed a moderate antiviral activity.

Key words: *Ficus pumila* var. *awkeotsang*, coumarin, chromen, antiviral

PN-16

Analysis of (-)-Sarcophytoxide in Cultured Soft Coral *Sarcophyton tenuispiculatum* by MALDI-TOF MS

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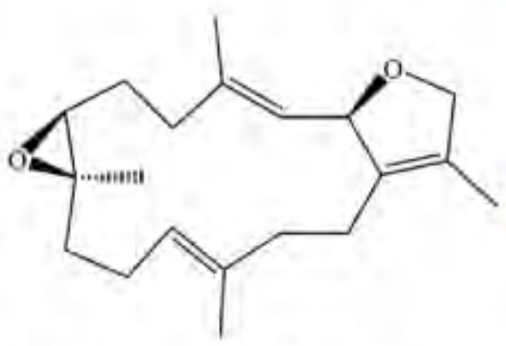
Abstract

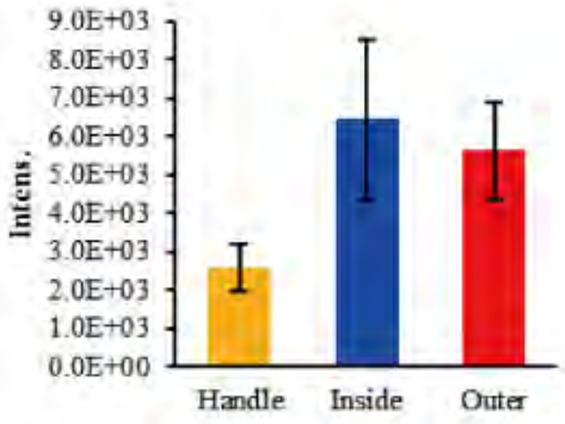
The current MALDI-TOF MS technology has been developed as a powerful tool in analytical chemistry due to their high accuracy and efficiency. However, there are some limitations and obstructions existing especially in marine application, such as molecular milieu and matrix selection.

(-)-Sarcophytoxide, a major secondary metabolite of *Sarcophyton tenuispiculatum*(*S. tenuispiculatum*), has been shown to display potent cytotoxic and anti-inflammatory activities. In this study, we focus on the identification of (-)-sarcophytoxide from the cultured *S. tenuispiculatum* using MALDI-TOF MS technique. The qualitative results demonstrated the content differences between various parts of cultured soft corals. The quantitative analyzing spectra also showed the linear dynamic ranging from 0.5 to 7.5 mM with a correlation coefficient (R^2) of 0.9992. Our data not only revealed the (-)-sarcophytoxide distribution patterns, but also advanced the analytic application of MALDI-TOF MS spectrometry in marine natural products.

Keywords: *Sarcophyton tenuispiculatum* , MALDI-TOF MS; (-)-Sarcophytoxide; Quantitative analysis



(-)-Sarcophytoxide



PN-17

Anti-inflammatory Polyoxygenated Steroids from the Soft Coral *Lobophytum michaelae*

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Three new polyoxygenated steroids, michosterols A–C (**1**–**3**), were isolated from the ethyl acetate (EtOAc) extract of the soft coral *Lobophytum michaelae*, collected off the coast of Taitung. The structures of the new compounds were elucidated on the basis of spectroscopic analyses and comparison of the nuclear magnetic resonance (NMR) data with the related steroids. The cytotoxicity of compounds **1**–**3** against the proliferation of a limited panel of cancer cell lines was assayed. Compound **1** was found to display potent anti-inflammatory activities of suppressing superoxide anion generation and elastase release in *N*-formyl-methionyl-leucyl-phenylalanine/cytochalasin B (fMLP/CB)-induced human neutrophils. Furthermore, **3** could effectively inhibit elastase release, too.

Key words：Soft coral; *Lobophytum michaelae*; cytotoxicity; anti-inflammatory activity

PN-18

Secondary Metabolites Isolated From the Fungal Strain *Monascus pilosus* (V)

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Monascus spp. have been used in oriental fermentation foods for thousands of years. Various secondary metabolites useful as food additives and/or pharmaceuticals have report being produced by *Monascus* spp. In this study, we investigated the bioactive compounds from the red yeast of *M. pilosus* BCRC 38072. One new benzopyran derivative, (–)-*rel*-5,7-dihydroxy-2-(4-methoxy-pentyl)-4,6-dimethyl-isochroman-8-one (**1**) was isolated from the red yeast rice of *Monascus pilosus*. The structure was determined by analyses of mass spectrometry and 1D- and 2D-NMR data. The relative configuration of the isolated compound was assigned on the basis of 2D-NOESY experiments. This experiment keeps on working and the biological activities of the isolates are currently under investigation.

Key words: *Monascus pilosus*, Eurotiaceae, secondary metabolites

PN-19

Daphglaucines A-C: anti-virus alkaloids from *Daphniphyllum glaucescens*

自奧氏虎皮楠分離出具抗病毒活性成分

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Three new alkaloids, daphglucenes A–C (**1**–**3**), and a known compound **4** were isolated from *Daphniphyllum glaucescens*. Their structures, including absolute configurations, were elucidated by spectroscopic analysis and theoretical calculation of electronic circular dichroism. The possible biogenetic relationship between the isolates was proposed. The isolates could reduce the MDCK cell death when infected with influenza virus (H1N1).

自奧氏虎皮楠的萃取物中分離出三個新的生物鹼 daphglucenes A–C (**1**–**3**)，以及一個已知化合物(**4**)。它們的結構及絕對立體藉由二維核磁共振光譜光譜分析以及理

論圓二色光譜計算來加以證實。這些化合物在生合成上可能的關係也在此提出。

此外化合物 **1-4** 具有降低宿主細胞在感染流感病毒後的死亡率。

Keywords: daphglucenes A–C; influenza virus; *Daphniphyllum glaucescens*

虎皮楠生物鹼，流感病毒，奧氏虎皮楠

PN-20

双黃 1 號(薑黃素葉黃素複方)之層析分析及抗氧化抗發炎活性研究

Chromatographic Analysis of YD01 (Curcumin-Lutein Complex) and Evaluation of Its Antioxidant and Anti-inflammatory Activities

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Combining multiple phytochemicals in nutraceuticals has gained momentum in the last decade resulting in improved therapeutic activity and lower side effects. YD01 was developed as a nutraceutical for eye disorders and inflammatory diseases. It was prepared by combining curcumin and lutein. Curcumin is a diferuloylmethane derivative isolated from the rhizomes of *Curcuma longa* (commonly known as turmeric). It has shown significant biological activity *in vitro* and *in vivo* models studying cancers, diabetes, cardiovascular, kidney, neurological, and ocular diseases. Lutein is a xanthophyll derivative which has also demonstrated potent antioxidant, anti-inflammatory, and immunomodulatory properties. Curcumin has been used in combination with other phytochemicals such as resveratrol, quercetin, sulforaphane, retinoic acid, and folates to target different types of cancers. However, the multifaceted therapeutic and pharmacologic effects of curcumin when given in combination with lutein are still in their infancy. In this study, we used several chromatographic techniques including TLC, HPLC, and TD-ESI/MS to analyze YD01 (curcumin-lutein complex). YD01 significantly decreased high-glucose induced oxidative stress and inflammation in human renal proximal tubular HK-2 cells. The antioxidant and anti-inflammatory activities were better than the curcumin extract (Y2), lutein extract (Y3), and commercial turmeric product (Y4).

Keywords: YD01, Curcumin, Lutein, Antioxidant Activity, Anti-inflammatory Activity

PN-21

蛹蟲草低極性萃取層化學圖資的抗發炎之活性關鍵

Chemical Characterization of *Cordyceps militaris* Hydrophobic Fraction: The Key to Unlocking the Mushroom Anti-inflammatory Activity

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Cordyceps militaris, a treasured edible mushroom, is native to China and has been used for millennia as a folk remedy against inflammatory disorders. Previous studies reported the isolation of several classes of bioactive compounds from *C. militaris* hydrophilic fractions including saccharides, nucleosides, and sterols. However, the chemical composition of *C. militaris* hydrophobic fractions remains elusive. In this study, the ethanolic extract of *C. militaris* was partitioned into *n*-hexane, 90% $MeOH_{(aq)}$, *n*-butanol and water. Among the four fractions, the *n*-hexane fraction showed the most potent inhibitory activity on superoxide anion, elastase release and calcium mobilization by human neutrophils in response to fMLP. To further investigate the composition of the *n*-hexane fraction, gas chromatography-mass spectrometry was used and the results indicated that the fraction was dominated by pentadecanoic, hexadecanoic, heptadecanoic, linoleic, oleic, and stearic acids. In the anti-inflammatory assays, linoleic and oleic acids significantly inhibited superoxide anion with IC_{50} values of 2.09 ± 0.36 and 1.59 ± 0.33 μM and elastase release with IC_{50} values of 3.43 ± 0.93 and 2.04 ± 0.14 μM, respectively. The $t_{1/2}$ values of Ca^{2+} mobilization of linoleic and oleic acids were 6.80 ± 0.76 and 7.33 ± 0.15 s, respectively in the fMLF-activated human neutrophils.

Our findings suggested that the linoleic acid and oleic acid might be responsible for the anti-inflammatory activity for *C. militaris*.

Keywords: *Cordyceps militaris*, Elastase release, Superoxide anion, Hydrophobic fractions, Ca^{2+} mobilization, Anti-inflammatory.

PN-22

Anti-inflammatory Constituents from Fruits of *Beilschmiedia tsangii*

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Plants of the genus *Beilschmiedia* (family Lauraceae) include more than 250 species and grow worldwide in tropical and subtropical areas, especially Africa and Asia. Some species of *Beilschmiedia* are used in folklore to treat uterine cancer, rubella, infection, malaria and rheumatisms. Literature surveys revealed that the endiandric acids isolated from this genus possessed anti-inflammatory activities. *Beilschmiedia tsangii* Merr., widely distributes in Southeast Asia, is an evergreen tree grows in the low altitudes of southern Taiwan especially in Hengchun Peninsula. Although there was no medical use in folklore, the constituents from the leaves of this plant were found to show potent anti-tubercular activities against *Mycobacterium tuberculosis*. Moreover, the bioassay-guided fractionations and characterization of bioactive natural products from the roots, and stem of *B. tsangi* revealed endiandric acid analogues, lignans, and sesquiterpenes. Because no prior investigation on the fruits of this species has been reported, the current work aimed towards discovering new bioactive metabolites from the fruits of *B. tsangii*.

A phytochemical investigation of the acetone extract of the fruits of *B. tsangii* has led to the isolation of three new endiandric acid analogues, which derived from polyketides. Besides, six known compounds, beilschmiedic acid E, erythrophlorins E–F, senkyunone, oligandrol, and dioxamin were also isolated. We report the structural elucidation of new metabolites on the basis of various spectroscopic analyses. The anti-inflammatory activities of them were also evaluated.

Key words：*Beilschmiedia tsangii,* endiandric acids, anti-inflammatory activities

PN-23

The biological activities of chemical constituents from the coast plant *Scaevola sericea* and marine-derived sulfur-containing compounds

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Six triterpenes (**1-6**), were isolated from the coast plant *Scaevola sericea*, and four marine-derived sulfur-containing compounds (**J4**, **J7**, **J14** and **SJH24**) were tested for their cytotoxic and anti-cancer cells dissemination abilities. We tested the cytotoxicity of these compounds, except **2-6**, against the growth of the human bile duct carcinoma cell line HuCCT-1, the results showed that all compounds are not cytotoxic toward the HuCCT-1 cancer cells. The *in vivo* anti-tumor cells dissemination effects of compounds **1**, **J4**, **J7**, **J14** and **SJH24** were also tested in zebrafish xenotransplantation model. These results revealed that compounds **1**, **J4** and **J7** could significantly inhibited the dissemination of HuCCT-1 cells at the concentrations of 20 μM and 50 μM (inhibited rates: 57.6%, 65.7%, 64.0%, 29.8 %, 40.0 % and 98.7 %, respectively) in zebrafish, in particular, **J7** could effectively reduce the 98.7 % of HuCCT-1 cells dissemination in zebrafish at 50 μM.

Key words：*Scaevola sericea*, triterpene, anti-cancer cells dissemination ability.

PN-24

Clovane-type derivatives from the gorgonian coral *Rumphella antipathies*

灌叢柳珊瑚中 clovane 類型二次代謝物研究

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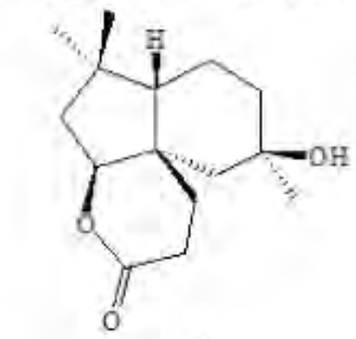
In the interest of identifying natural substances from marine invertebrates collected off the waters of Taiwan, we studied the gorgonian coral *Rumphella antipathies* for its organic extract showed interesting chemical constituents by NMR data analysis. In this presentation, including twelve compounds **1-12** were isolated from gorgonian coral *Rumphella antipathies*. The structures of these compounds and their derivatives were established primarily on the basis of NMR spectral analysis and chemical derivatization. The application of NMR techniques included ^{1}H NMR, ^{13}C NMR, DEPT, COSY, HMQC, HMBC, NOESY and so on.



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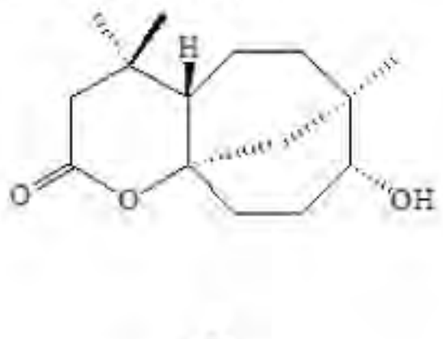

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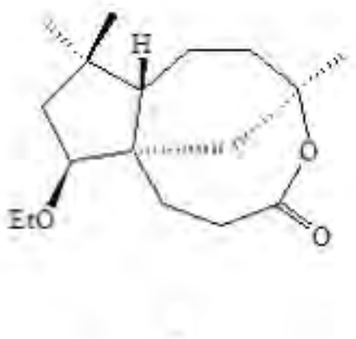

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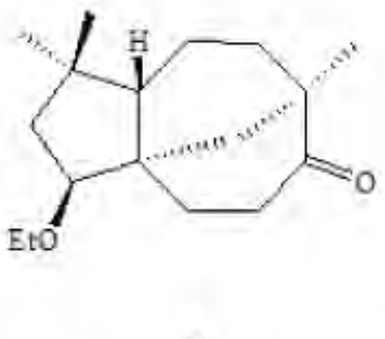

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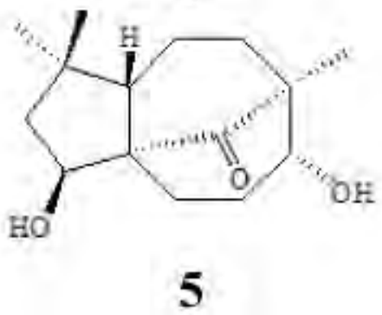

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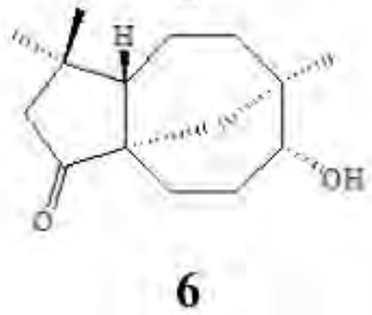

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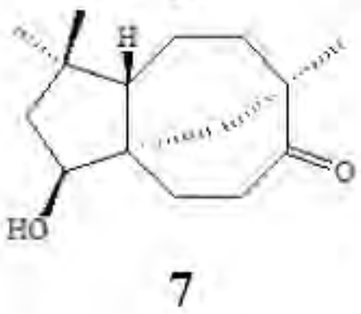

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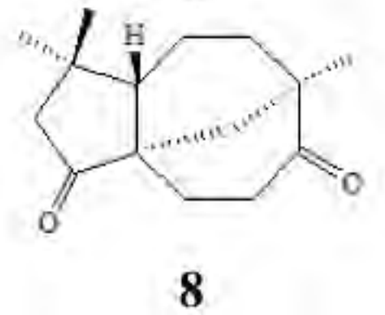

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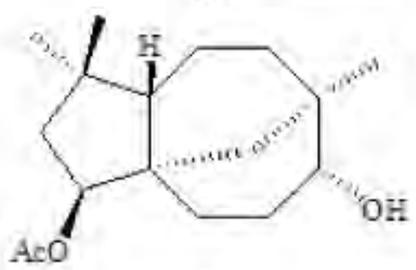

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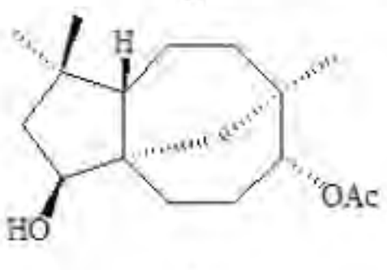

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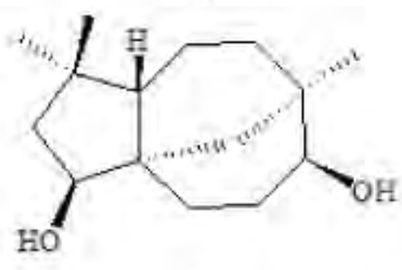

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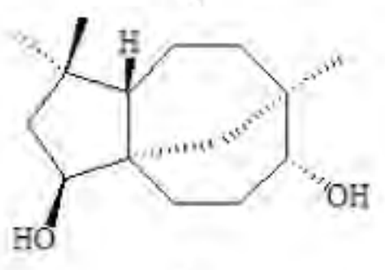

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Key words : Clovane, *Rumphella antipathies*, Anti-inflammatory, Superoxide anion, Elastase

PN-25

Anti-hepatitis C virus ingredients from the twigs and leaves of *Flueggea virosa*

自密花白飯樹枝葉部位分離出具抗丙型肝炎病毒活性成分

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[†]相同貢獻

In an attempt to study the chemical constituents from the twigs and leaves of *Flueggea virosa*, a new terpenoid, 9(10→20)-*abeo*-*ent*-podocarpane, 3β,10α-dihydroxy-12-methoxy-13-methyl-9(10→20)-abeo-ent-podocarpa-6,8,11,13-tetraene (**1**), as well as five known compounds were characterized. Their structures were elucidated on the basis of spectroscopic analysis. In addition, the structure of dehydrochebulic acid trimethyl ester was revised as (2*S*,3*R*)-4*E*-dehydrochebulic acid trimethyl ester based on a single-crystal X-ray diffraction study. The in vitro anti-hepatitis C virus (anti-HCV) activity and cytotoxicity against Huh7.5 cells for the isolated compounds were evaluated.

Keywords: *Flueggea virosa*; dehydrochebulic acid trimethyl ester; anti-HCV

密花白飯樹，丙型肝炎病毒，單晶繞射

PN-26

SPME/GC/MS 分析不同雜交品系蝴蝶蘭之香氣化合物研究

Analyses of aroma compounds in different hybrid *Phalaenopsis* using SPME/GC/MS

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Phalaeopsis is the most important economic fresh flower crops in Taiwan, and in recent years, the characteristics of the scent have become a concern for breeders.

In this experiment, *Phalaenopsis* Sogo Vivien is a cross between *P.* Sogo Alice and *P.* Zuma's Pixie. Second, *P.* Hsingying is a *P.* Sogo Twinkle and *P.* Taiwan Fancy hybrid. Last one, TYP08128 is a hybrid of *P.* Sogo Vivien and *P. modesta*. Extract the aroma of the samples by using solid-phase microextraction. Then, use gas chromatography and gas chromatography-mass spectrometry to analysis the difference of volatile compounds between three kinds of hybrid *Phalaenopsis*.

The result shows that *trans*-β-Ocimene is the main volatile compound of three kinds of hybrid phalaenopsis and the odor of *trans*-β-Ocimene smells like grass. Also, all of the samples are mainly composed of terpene and relative content is up to 50% or more. Finally, the aroma of TYP08128 is the richest. Peak area is up to 12614.5. However, the other two have lower aroma that their peak area don't even reach 2000.

關鍵字/Key words：蝴蝶蘭（phalaenopsis）、雜交（cross-breeding）、氣相層析質譜儀（GC-MS）、固相微量萃取法（SPME）

PN-27

Study on the antioxidant activities from the stems and leaves of *Clinacanthus nutans*

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Clinacanthus nutans Lindau (CN) belongs to the family Acanthaceae. It's a traditional herb in Thailand, and has been used to treat the insect and snake bite. The modern pharmacological researches were demonstrated that CN had anti-inflammatory, anti-HSV-2 and anti-1F activities, but their antioxidant study is not yet reported. This study used three antioxidant capacities determinations, including DPPH radicals scavenging capacity, Trolox equivalent antioxidant capacity and total phenol contents to evaluate antioxidant capacities from the H_2O and 95% EtOH extracts of stems and leaves of CN (H_2O and 95% EtOH extracts of stems were named CNSW and CNSE, the leaves extracts were named CNLW and CNLE, respectively). The results showed that DPPH radicals scavenging capacity of four extracts were lower than 50%, but $ABTS^{\cdot+}$ radicals scavenging capacity and total phenol contents of CNLW and CNLE had more effect than CNSW and CNSE. The results of this study are summarized at the antioxidant capacities of the CNLW and CNLE extracts are more effect than CNSW and CNSE.

Key words : Clinacanthus nutans, DPPH radicals scavenging capacity, Trolox equivalent antioxidant capacity and total phenol contents

PN-28

Elicited production and analysis of phytoalexins in five peanut (*Arachis hypogaea* L.) cultivar seed

花生之植物防禦素誘導及其分析

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Peanut (*Arachis hypogaea* L.), a leguminous plant, is important in the economy. When peanuts are exposured to exogenous stimuli or mechanical damage, it can produce phytoalexins to protect itself against environment pathogens. Phytoalexins are a kind of plant secondary metabolites with some low-molecular-weight flavonoids, stilbenoids, and fatty acid-related compounds. In peanut, stilbenoids almost belong to resveratrol derivatives. Stilbenoids are important for human with antioxidant, antifungal, anti-inflammatory activities, and cytotoxic for tumor cells. In present, we optimize the induced condition for stilbenoids from peanut and compare the amount of stilbenoids in five kinds of peanut (included Tainan 11, Tainan 14, Tainan select 9, Black king kong and Hua ren peanut) . After germination, the peanut were separated into cotyledon, hypocotyls and plumule and then cut into slices, respectively. The peanut slices were put into an artificial aeration apparatus and aerated for 36h to induce phytoalexins. The slices were homogenized with methanol and then analyzed with HPLC. From the experiments, we found peanut cotyledon can produce highest stilbenoids than hypocotyls and plumule. The 4th day germinated cotyledon of peanut has the highest yields of stilbenoids. We also found Tainan 11 peanut can be induced more stilbenoids than other kinds of peanut in day4, day6 and day7.

Key words：peanut, stilbenoid, phytoalexin, cotyledon, HPLC

PN-29

The bioactivities of withanolides from the leaves of *Solanum capsicoides*

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Abstract

Eight new withanolides, name as D, E, F, G, H, I, J, and K (**1**–**8**), have been isolated from the EtOAc crude of the leaves of *Solanum capsicoides* along with four known metabolltes **9-12**. The relative structures of compounds **1-12** were elucidated by extensive spectroscopic analysis. These compounds were not shown to exhibit cytoxicity toward a limited panel of cancer cell lines. Meanwhile, the anti-inflammatory activity of compounds **1**–**6**, **9**, and **10** was studied by measuring their ability to suppress superoxide anion generation and elastase release in fMLP/CB-induced human neutrophils. Moreover, compound **2** was found to inhibit human intrahepatic cholangiocarcinoma cancer cell (HuCCT1) dissemination in the zebrafish human tumor xenograft model.

Key words: withanolides, *solanum capsicoides*, anti-inflammatory activity, and zebrafish human tumor xenograft model

PN-30

Anti-allergic Hydroxy Fatty Acids from *Typhonium blumei* explored Through ChemGPS-NP

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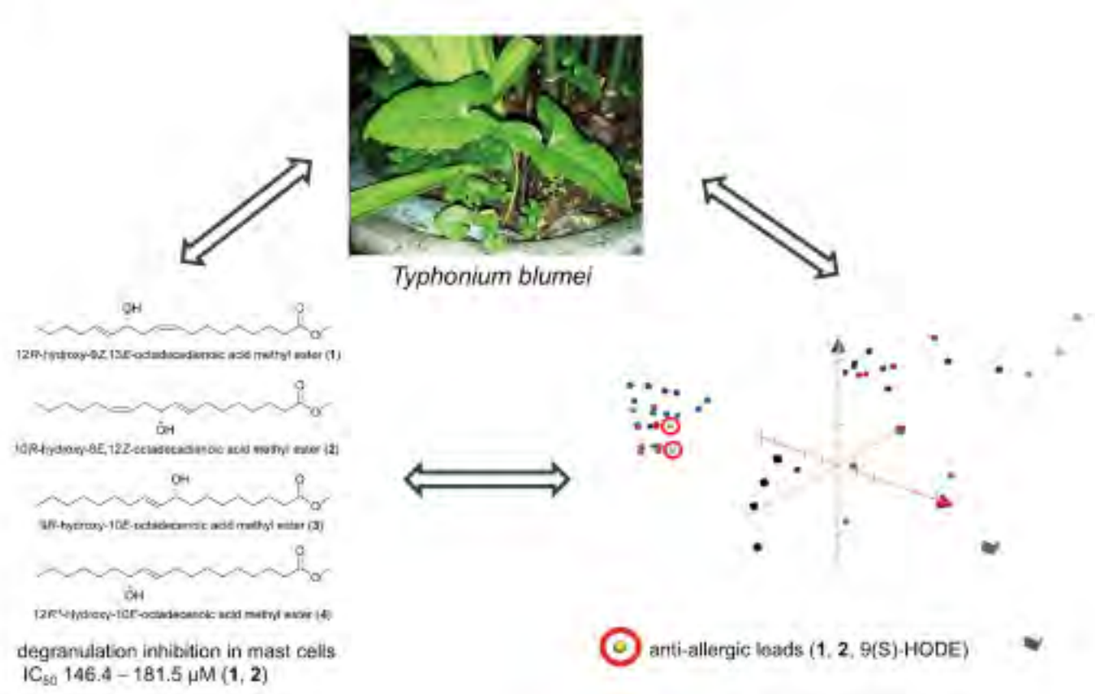
Phytochemical study on *Typhonium blumei* Nicolson & Sivadasan (Araceae), a folk anti-cancer and anti-inflammatory medicine, yielded four oxygenated fatty acids, 12R-hydroxyoctadec-9Z,13E-dienoic acid methyl ester (1) and 10R-hydroxyoctadec-8E,12Z-dienoic acid methyl ester (2), 9R-hydroxy-10E-octadecenoic acid methyl ester (3), and 12R*-hydroxy-10E-octadecenoic acid methyl ester (4). Isolated compounds were identified by spectroscopic methods along with GC-MS analysis. Isolated fatty acids together with a series of saturated, unsaturated and oxygenated fatty acids were evaluated for their anti-inflammatory and anti-allergic activities *in vitro.*

Unsaturated (including DHA and EPA) as well as hydroxylated unsaturated fatty acids exerted strong anti-inflammatory activity in superoxide anion generation (IC_{50} 2.14 – 3.73 μM) and elastase release (IC_{50} 1.26 – 4.57 μM) assays. On the other hand, in the anti-allergic assays, the unsaturated fatty acids were inactive, while hydroxylated fatty acids showed promising inhibitory activity in A23187- and antigen-induced degranulation assays (e.g. 9*S*-hydroxy-10*E*,12*Z*-octadecadienoic acid, IC_{50} 92.4 and 49.7 μM, respectively). According to our results, the presence of a hydroxy group in the long chain did not influence the potent anti-inflammatory activity of free unsaturated acids. Nevertheless, hydroxylation of fatty acids (or their methyl esters) seems to be a key factor for the anti-allergic activity observed in the current study.

Moreover, ChemGPS-NP chemical was explored to predict the structure-activity relationship of fatty acids. The anti-allergic fatty acids formed different cluster distant from clinically used drugs.

Keywords: hydroxy fatty acids, anti-allergic, anti-inflammatory, cytotoxic, *Typhonium blumei*, ChemGPS-NP



PN-31

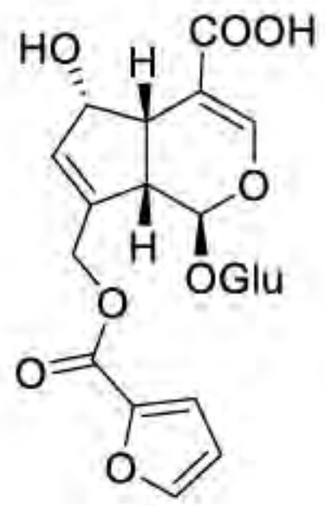
Phytochemical and Pharmacological Studies on *Psychotria serpens*

黃鈺玲 **Yu-Ling Huang#*** • 沈建昌 **Chien-Chang Shen** • 鄭靜枝 **Jing-Jy Cheng** • 潘巧柔 **Chiao-Jou Pan**

National Reaearch Institute of Chinese Medicine, Ministry of Health and Welfare

Psychotria serpens L. (Rubiaceae) has been used as folk medicine in Taiwan to treat carbuncles, rheumatoid arthritis, bone fracture and contusion. The EtOH extract of the roots with stems of *P. serpens* were treated using *n*-hexane, CH_2Cl_2-Me_2CO, and then MeOH to afford their own extracts. The MeOH extract was further treated with butanol and H_2O. Their extracts were individually repeatedly chromatographed to yield ten iridiod glucosides (**1-10**), including two new ones (**1** and **2**), along with 4-hydroxy-3,5-dimethoxyphenyl-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside and roseoside. The structures of the isolated compounds were established by spectroscopic analyses and comparison of their spectral data with those in the literature. Among the isolated compounds, iridiod glucosides were tested for anti-cancer activities on MCF-7 (breast), H460 (lung), HT-29 (colon), and CEM (leukemia) cancer cells. As a result, scandoside (**3**), desacetyl-asperuloside (**4**), 6-methoxygeniposidic acid (**5**), and daphylloside (**6**) showed significant activities on MCF-7 cells with IC_{50} values of 10.8, 8.4, 8.1, and 8.8 μM, respectively.

Key words : *Psychotria serpens*, Rubiaceae, iridiod glucoside, anti-cancer activity.



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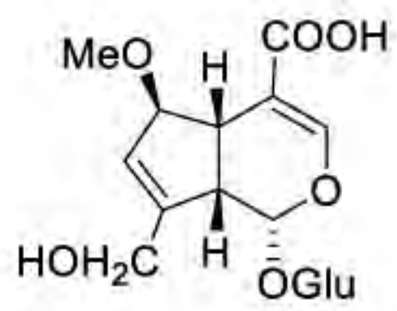

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PN-32

黑潮花群海葵新生物鹼/New alkaloids from *Zoanthus kuroshio*

陳姝蓉 **Shu-Rong Chen#**・張芳榮 **Fang-Rong Chang**・鄭源斌 **Yuan-Bin Cheng***

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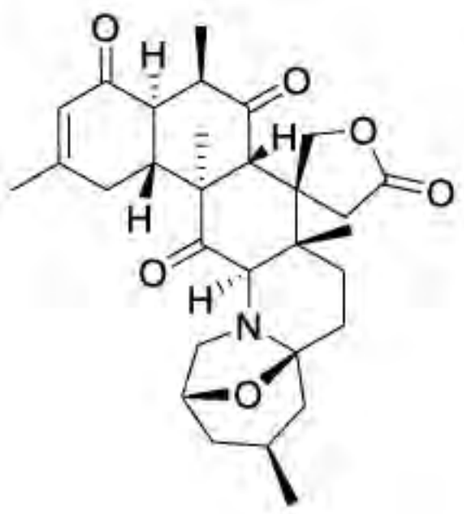
Zoanthid is a radial symmetry cnidarian with two rows of tentacles and is usually found on the rocky coast of subtropical and tropical areas. The various colors of zoanthids were due to the symbiotic relationships with single-celled zooxanthellae, such as dinoflagellates and green algae. Due to its fascinating colors, this sessile benthic organism often becomes ornamentals in aquariums. However, toxic substances produced by zoanthids sometimes cause cardiotoxicity, local itching, swelling, paralysis and necrosis to the keepers. Accordingly, zoanthids are also regarded as rich sources of novel secondary metabolites with diverse bioactivities. For example, ecdysones isolated from *Palythoa mutuki* suppress dengue virus production, while alkaloids purified from *Zoanthus kuroshio* inhibit superoxide anion generation and elastase release. Two new zoanthamine-type alkaloids, kuroshines H (**1**) and I (**2**) were isolated from the sea anemone, *Zoanthus kuroshio*. The species of research material was identified by its morphology and mt16S rDNA sequencing data. The structure of these compound were determined by spectroscopic methods, especially 2D NMR analyses (COSY, HSQC, HMBC, and NOESY). New compound **1** is a unique alkaloid with a hybrid frameworks between zoanthamine (**3**) and zoanthenamine (**4**). Compound **2** can be characterized as a new kuroshine A type alkaloid with a hemiacetal at C-28. The cytotoxic activities of compound **1** against MDA-MB-231, A549, HepG2 cancer cell lines were evaluated by MTT assays.



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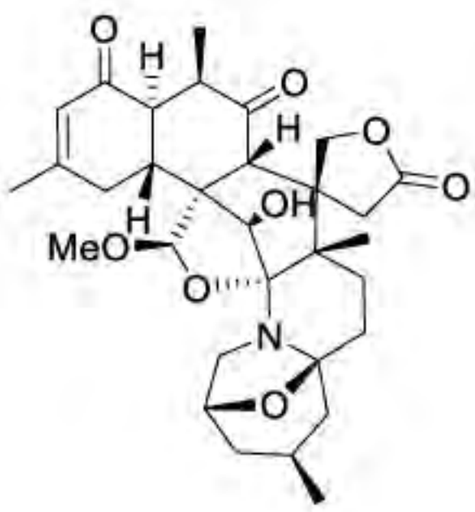

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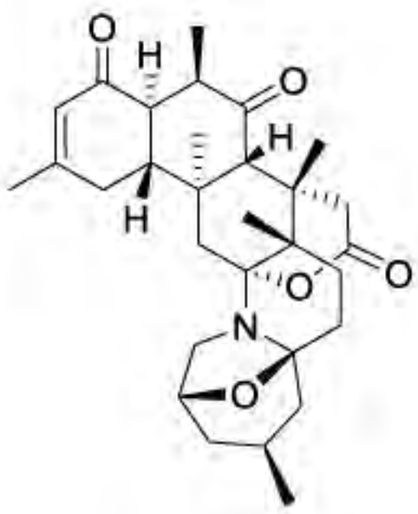

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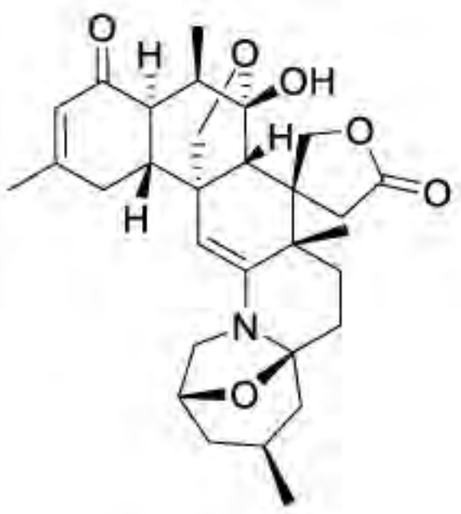

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關鍵字/Keywords: alkaloids; *Zoanthus kuroshio*; marine natural products

PN-33

Anti-hyperglycemic Constituents from the Leaves of *Cinnamomum macrostemon*

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Glucose transport and metabolism are tightly associated with diseases including diabetes. Sodium-coupled glucose co-transporters (SGLTs), SGLT1 and SGLT2, are important for in-testinal absorption and renal reabsorption of glucose, respectively. The previous study report-ed that dual SGLT1/SGLT2 inhibitor as an adjunct therapy to insulin in type 1 diabetes. This agent could improve glycemic control and overcome the side effects, such as hypoglycemia and weight loss.

Approximately 60 species of lauraceous plants have been screened for the SGLT inhibitory activity and *Cinnamomum macrostemon* Hayata (Lauraceae) was shown as the most active species. The methanolic extract of the leaves of this species was partitioned into water-soluble and ethyl acetate layers. Water-soluble layer showed the potent activity toward SGLT inhibition. Till now, the chemical constituents of water-soluble layer and bioactivity from C. *macrostemon* have never been investigated. Bioassay-guided fractionation of the active water-soluble layer from the leaves of this plant led to the isolation of one new megastigmane, cinnamacroside (1), along with 16 known compounds including two benzenoids, one coumarin, 11 flavonoid glycosides, and two lignans. Futhermore, three new lignans, macrostemonol A (2), macrostemonol B (3), and macrostemonol C (4), together with 29 known compounds, including one amide, eight benzenoids, four flavonoid glycosides, 12 lignans, three steroids and one quinone were isolated from the ethyl acetate layer of the leaves of C. *macrostemon*.

Among the isolates, kaempferol 3-O-(2"-β-D-glucopyranosyl)-α-L-rhamnopyranoside (11) and kaempferol 3-O-β-D-glucopyranosyl-(1→4)-α-L-rhamnopyranosyl-7-O-α-L-rhamno-pyr anoside (13) showed potent inhibitory activity toward SGLT, which IC50 values 475 ± 34.2 and

123 ± 11.6 nM for SGLT1, and 68.8 ± 14.2 and 12.5 ± 2.95 nM for SGLT, respectively.

Key words: Lauraceae, *Cinnamomum macrostemon*, SGLT, Lignan, Megastigmane, Flavonoids glycoside

PN-34

Secondary Metabolites from the Fungus, Ophiocordyceps sobolifera

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A fungus *Ophiocordyceps sobolifera* (Hill ex Watson) G.H.Sung, J.M.Sung, Hywel-Jones & Spatafora (Ophiocordycipitaceae), also called ChanHua in Chinese. It is a parasitic fungus growing on wing-less cicada nymphs and has been used as Traditional Chinese Medicine for improving the renal function. In previous pharmacological studies, the extract of *O. sobolifera* ameliorates nephrotoxicity-induced renal dysfunction in the rat and can improve the anti-tumor capacity of mice. However, the chemical costituents of this fungus have never been studies. In the current research, *O. sobolifera* was processed through liquid-state fermentation, and its liquid fermentate showed cholesterol inhibitory and hypoglycemic activities based on the preliminary screening.

The liquid fermentate was partitioned and afforded ethyl acetate, *n*-butanol and water soluble layers. Sixteen compounds have been isolated from the *n*-butanol soluble layer of the liquid fermentate of *O. sobolifera*, including 4-methoxybenzoic acid (**1**), indole-3-carboxylic acid (**2**), butyl-2-pyrrolidone-5-carboxylate (**3**), 5-(hydroxymethyl)-1*H*-pyrrole-2-carbaldehyde (**4**), β-carboline (**5**), cyclo-(Gly-Pro) (**6**), dihydrouracil (**7**), 3-propyl-hexahydro-pyrrolo[1,2-α]pyrazine-1,4-dione (**8**), cyclo-(Pro-Ser) (**9**), cyclo-(Gly-Val) (**10**), cyclo-(Ile-Gly) (**11**), cyclo-(Gly-Leu) (**12**), uracil (**13**), 2-deoxy-ribono-1,4-lactone (**14**), cyclo-(Ile-Ser) (**15**) and cordysinin B (**16**). Among them, compounds **8** and **15** were isolated from nature for the first time. The structures of these compounds were elucidated by spectral analysis. The isolation work is still in progress and the isolates are further evaluated with regard to cholesterol inhibitory and hypoglycemic activities.

Key words：*Ophiocordyceps sobolifera*, Fungus, Amino acid, Alkaloid

PN-35

Chemical Constituents and Cytotoxicity from the Stem of *Anodendron benthamianum*

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Anodendron (Apocynaceae) has eight species in tropical Asia and two species of *A. affine* Druce and *A. benthamianum* Hemsl. in Taiwan. *A. benthamianum* is a climbing shrub, endemic to Taiwan and distributed at low to medium altitudes forest throughout Taiwan. Prenylbenzoic acids and cardenolides had been isolated from the seeds and the leaves of *Anodendron* previously and many of these cardenolides exhibited cytotoxicity. The methanolic extract of the stem of this species showed potent cytotoxic activities against TOV-21G-RTx (paclitaxel-resistant ovarian cancer cells), SK-Hep-1 (hepatocellular carcinoma cells), and PC-3 (prostate cancer cells) cancer cell lines *in vitro* and further partitioned into ethyl acetate-soluble and water-soluble layers. However, the phytochemistry and biological activities of this plant have never been studied.

Bioassay-guided fractionation of active ethyl acetate-soluble layer from the stem of *A. benthamianum* led to the isolation of thirty-four compounds, including ten benzenoids, two coumarins, seven lignanoids, one quinol, one quinone, seven steroids, two terpenoid, one diterpenoid, two apocarotenoids, and one aliphatic compound. The structures of these isolates were elucidated by spectral analysis. The isolation of chemical constituents and their cytotoxicity assay are still in progress.

Key words: *Anodendron benthamianum*, Apocynaceae, Stem, Cytotoxicity, Benzenoid, Lignan

PN-36

Investigation of Potential Agents with Antimicrobial Activity and Anti-biofilm formation from Marine Extracts Database

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The high biodiversity of marine organisms make them generate a reservoir of potential bioactive secondary metabolites (high chemical diversity). Many of those marine secondary metabolites have already been successfully applied in day-to-day life, especially, in medicinal uses, such as anticancer drugs, pain releaser, and antibiotics. On the other hand, antibiotic abuse makes the serious problem of public health. More medicinal requirements are emergent to search new antimicrobial agents or compounds with anti-biofilm formation, which is regarded as one of the causes that pathogens could resist the effects of antibiotics. In our ongoing study to search new antimicrobial agents from marine resources by the established bioassays of antimicrobial activity and anti-biofilm formation, we have screened 65 crude extracts from our marine extracts database toward *Staphylococcus aureus*. Among them, 18 extracts showed positive effects against *S. aureus*. Furthermore, we tried to isolate the bioactive components from three crude extracts (03M, 010E and 07E) by the bioassay-guided fractionation isolation. In the poster, we will mention the isolates from these extracts and their bioactivities by the aforementioned process.

關鍵字/Key words：marine secondary metabolites, antimicrobial activity, anti-biofilm formation, *Staphylococcus aureus*

PN-37

Antimicrobial Marine Symbionts from Marine Organisms

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Marine microorganisms symbiotic with marine organisms are recognized as potential sources for isolating bioactive compounds as drug candidates to treat human diseases. Hitherto, there are more evidences to clarify the bioactive marine natural products generated by symbiotic microorganisms in marine life. To build the marine extract database for further bioactive marine natural products discovery, we tried to collect indigenous marine invertebrates, such as sponges, soft coral, Zoanthids, sea slugs, and barnacle, from Dongsha Atoll and intertidal zone of southern Taiwan and further isolated the microorganisms in those organisms. In this study, total 185 microbial strains were isolated from marine sponges and 26 microbial strains were isolated from barnacles. Besides, 4 fungi strains were isolated from mangrove seawater on Sicao, Tainan. The antimicrobial activities of these microbial strains were evaluated toward three bacterial indicators (*Staphylococcus aureus*, *S. epidermidis*, *Acinetobacter baumannii*) and a fungal indicator (*Candida albicans*). Among them, ten strains, bar-12, bar-13, bar-22, DSI-G-7, DSI-G-14, DSI-G-15, 12/7-1, 12/7-2, 12/7-3 and 12/7-4 showed inhibitory activity against all three indicates. 16S rRNA sequences phylogenetic analyses indicate that strains bar-12, 13, and 22 belong to *Pseudoalteromonas elyakovii* (with percentage similarity of 99.84%, 99.92%, 99.77%, respectively), and the strain DSI-G-7 belongs to *Ruegeria atlantica* (with percentage similarity of 99.25%). The species identification of others strains is under investigation.

關鍵字/Key words：anti-microbial activity, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Acinetobacter baumannii*, *Candida albicans*, *Pseudoalteromonas elyakovii*, *Ruegeria atlantica*

PN-38

The Study on Antimicrobial Components of Marine-Derived Fungus, *Fusarium solani* by Molecular Network Analysis.

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Department of Marine Biotechnology and Resources, National Sun Yat-Sen University, Kaohsiung (Taiwan)

Microorganisms provided a lot of novel scaffolds of natural products, which are regarded as potential resources of drug discovery. In our group, we plan to search the potential anti-microbial secondary metabolites from marine-derived fungus. *Fusarium solani* FS-01 is a symbiotic fungus isolated from a *Palythoa* sp., which was collected from Wanlitong, Pingtung County, Taiwan. The fungus strain FS-01 showed good inhibitory activities against several bacterial indicators, for example, *Acinetobacter baumannii* and a fungal indicator, *Candida albicans*. Based on molecular networking analysis of LC-MS/MS data and bioassay-guided fractionation isolation, we could target the molecular weights of potential bioactive compounds from the extract of *Fusarium solani* FS-01, as well as their analogues. By repeatedly column chromatography and HPLC isolation of the EtOAc extract of the strain FS-01, we isolated a series of bioactive components. The structures of these isolates were elucidated by NMR, MS and others spectroscopic analysis data and comparison with the literature data. In the poster, we would like to show the rapid process to discover bioactive natural products from microbial resources.

關鍵字/Key words：*Fusarium solani*, *Acinetobacter baumannii*, *Candida albicans*, molecular network analysis

PN-39

The Investigation on Siderophore-like Components from Marine Symbiotic Microorganisms

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Marine biological resources are well known for producing a variety of novel secondary metabolites. Especially, microorganisms (such as bacteria, fungi, and microalgae) symbiotic with marine invertebrates are considered as a new source for discovery of novel scaffolds of marine natural products. Siderophores are the special groups of microbial secondary metabolites, which are generated by microorganisms, including bacteria and phytoplankton, and secreted out of cells to scavenge irons from the environments because iron is an essential element for key biological processes, such as respiration and DNA biosynthesis. Interestingly, literature survey indicated that the association between iron accumulation and oxidative cell damage in specific regions of the brain has raised the possibility of using iron chelation as a therapeutic strategy in neurodegenerative disorders. To search new sources of marine natural products, we found several marine-derived bacteria with iron-chelating activity by chrome azurol S (CAS) assay. In this study, we tried to isolate different types of marine siderophores from those marine-derived microbes. And we will further evaluate their possibility of medicinal application.

關鍵字/Key words: marine biological resources, marine-derived bacteria, chrome azurol S (CAS) assay, siderophores, and iron-chelating activity

PN-40

Chemical Constituents and Cytotoxic Activities from the Root of *Cryptocarya concinna*

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Cryptocarya concinna Hance (Lauraceae) is a medium-sized evergreen tree and distributed in altitude 500-1,500 m broad-leaved forests in Taiwan and southern China. In our cytotoxic screening, the methanolic extract from the root of *C. concinna* exhibited cytotoxic activities against human cervical cancer SiHa cells, human ovarian cancer SKOV-3 cells, and human osteosarcoma U2OS cells. Here we report the chemical constituents and their cytotoxic activities from the root of this plant.

The methanolic extract of the root of *C. concinna* was partitioned into the ethyl acetate soluble and water soluble layers. The ethyl acetate soluble layer showed potent cytotoxic activities against SiHa, SKOV-3, and U2OS cell lines. Bioassay-guided fractionation of the active ethyl acetate soluble layer led to the isolation of 22 compounds, including three new chalcones, concichalcones A-C (**1-3**), two new flavonoids, cryptoflavanones E-F (**20-21**) together with 17 known compounds, including 14 flavonoids, two chalcones, and a steroid. The structures of these new compounds were elucidated by NMR, UV, IR, ESIMS, and HRESIMS analyses. Most importantly, three pairs of flavonoid stereoisomers, cryptoflavanones A & B (**8**, **9**), cryptoflavanones C & D (**14**, **15**), and cryptoflavanones E & F (**20**, **21**) were separated for the first time by chiralpak® IA column. Among these isolates, cryptocaryone (**4**), infectocaryone (**5**), and a mixture of cryptocaryanones A & B (**11**, **12**) exhibited potent cytotoxic activities against U2OS and SiHa cancer cell lines, with IC_{50} values are between 2-5 μM. A mixture of cryptoflavanones A & B (**8**, **9**) showed cytotoxic activity on SiHa cells with IC_{50} values 15.76 μM, but it didn't exhibit cytotoxic activity on U2OS cells.

Key words: *Cryptocarya concinna*, Cytotoxicity, Chalcone, Flavonoid, Stereoisomer

PN-41

以固相微量萃取法與直接注射法分析辛夷精油之揮發性成分

Analysis of the Volatile Components in *Magnolia liliiflora* by Solid-Phase Microextraction and Direct Injection

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Abstract

Magnolia liliiflora is a commonly used Chinese herbal medicine. Its volatile oil is an important medicinal ingredient with anti-inflammatory, anti-allergy and other functions. In addition, the special smell of the essential oil also makes *M. liliiflora* an important spice. In this study, volatile oil was extracted by steam distillation (SD), and its volatile components were extracted by direct injection and solid-phase microextraction (SPME), coupled with gas chromatography (GC) and gas chromatography-mass spectrometer (GC-MS), reporting the analysis and content of volatile compounds of *M. liliiflora.*

The results determined that the essential oil yield of *M. officinalis* was 14.08 ± 1.01 mL/ kg by steam distillation. 105 volatile compounds were identified by direct injection, and 63 volatile components were identified by SPME. The major compounds analyzed by both methods were 1,8-cineole, *dl*-camphor and camphene. References revealed that 1,8-cineole has a cool herbal odor and has functions of analgesic and anti-inflammatory. The compounds identified by SPME were roughly overlapped with direct injection, but some trace compounds such as *trans*-piperitol and methylcarvacrol were not identified in direct injection. The volatile compounds could be identified more completely by direct injection, which can also identify more sesquiterpene compounds and terpene alcohol compounds.

Key words: *Magnolia liliiflora*, Steam distillation (SD), Direct injection, Solid-phase microextracton (SPME), GC, GC-MS

PN-42

Solubility Improvement of Rhein by Solid Dispersion with Hydroxypropyl - β - Cyclodextrin

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Rhein, a major constituent of *Rheum palmatum*, was reported to possess various beneficial bioactivities including anti-diabetic, anti-oxidation, anti-inflammatory, and anticancer effects. However, the low water solubility of rhein may limit its oral bioavailability. The preparation of solid dispersions with hydroxypropyl - β - cyclodextrin (HP-β-CD) to enhance the solubility of rhein was investigated in this study. The solid dispersions were prepared by solvent method. The crystallinity property of the powders was characterized by differential scanning calorimetry (DSC) and powder X-ray diffractometry (XRD). Solubility test was used to verify the performance of the practices. The result showed that solid dispersion with HP-β-CD improved the solubility of rhein, which would be a better formulation to enhance its oral bioavailability.

Key word : Rhein, hydroxypropyl-β cyclodextrin, solid dispersion, solubility.

PN-43

Studies of chemical constituents from the Formosan soft coral *Paralemnalia thyrsoides*

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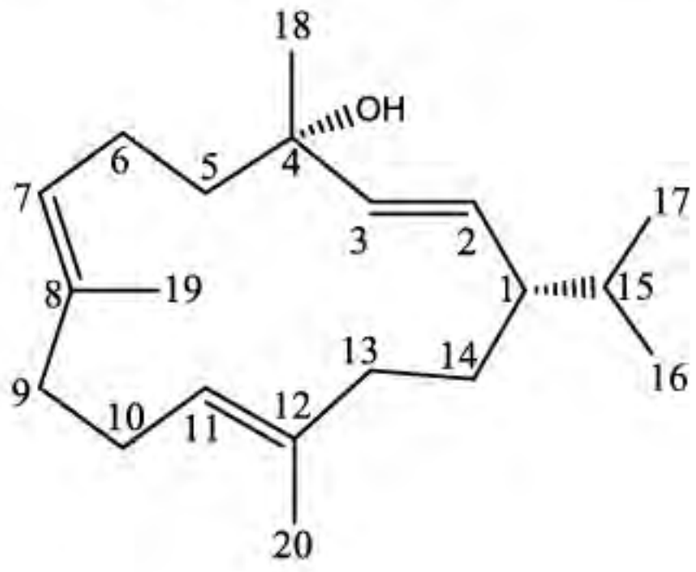
In the study of natural products from the cultured octocoral *Paralemnalia thyrsoides*, have afforded four compounds, thunbergol (**1**), laevinone A (**2**), napalilactone (**3**) and pathylactone A (**4**). The structures of metabolites were elucidated by spectroscopic methods and by comparison of their spectroscopic data with those reported analogues. This is the first time to isolate pathylactone A (**4**) from a natural source.
It is intriguing to note that compound **1** in cultured *P. thyrsoides* is more abundant than wild-type *P. thyrsoides*. Based on this finding, controlling the aquaculture conditions of the corals could be a way to produce specific compounds.

Key words : *Paralemnalia thyrsoides*, octocoral, thunbergol, laevinone, napalilactone, pathylactone



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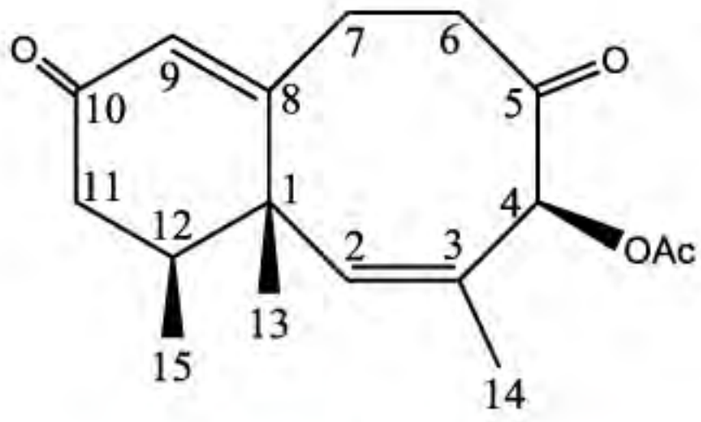

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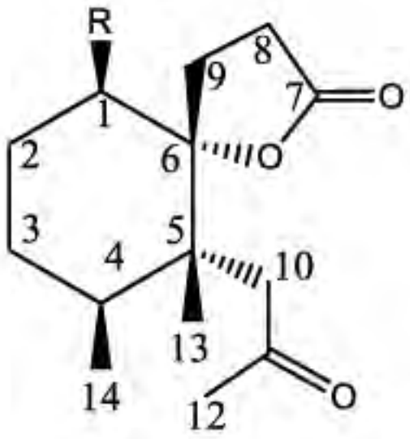

3: R= Cl
4: R= OH

Paralemnalia thyrsoides

PN-44

Hirsutinolide-type sesquiterpene lactones from *Vernonia cinerea* L.

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Vernonia cinerea L. is an annual herb which is used medicinally for a variety of purposes, including reducing fever, and promoting digestion. Previous investigations have shown that crude extracts of *V. cinerea* L. possess anti-oxidant, anti-inflammatory and anti-microbial activities. By a series of chromatography and bioassay-directed fractionation, twelve hirsutinolide-type sesquiterpene lactones (**1-12**) including four new compounds, 8*R*-tigloyloxyhirsutinolide-13-*O*- acetate and vernolide-K~M, eight known hirsutinolide compounds, along with the known (+)-dehydrovomifoliol, loliolide, 3β-hydroxy-5,6-epoxy-7-megastigmen-9-one, and 3α-hydroxy- 5,6- epoxy-7-megastigmen-9-one were isolated from *V. cinerea* L. The anti-NO production assay by LPS induced RAW264.7 macrophages showed that **1**, **4**, **5**, **6**, **8** and **9** had potent anti- NO activities (IC_{50} <1 μM). The results indicated that these isolated hirsutinolide compounds could be potential as a lead compound for the further development of anti-inflammatory drug.

Keywords: *Vernonia cinerea* L., hirsutinolide-type sesquiterpene lactones

PN-45

Antimicrobial polypeptides from the Marine-derived fungus, *Trichoderma reesei*

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Marine organisms are regarded as one of the most notable source for the drugs discovery. In recent years, microorganisms symbiotic with marine invertebrates, such as sponges and soft corals, have been found as real producers of important and unique bioactive metabolites from such resources. In our lab, one of our goals is to search the bioactive natural products from the symbionts of marine invertebrates. We isolated a fungus *Trichoderma reesei* (MR13-TR01) from a sponge *Niphates* sp. collected in Wan-Li Tong, Pingtung County. This fungal strain MR13-TR01 showed an interesting inhibitory activity against *Acinetobactor baumannii*, an opportunistic pathogen that could be a major cause of nosocomial infections in patients and increase the mortality in hospital. In the poster, we will mention four peptaibols from the EtOAc extract of the strain MR13-TR01. The structures and 3D conformation of these isolates will be elucidated on the basis of their spectroscopic analysis (CD, NMR, MS). The bioactivities of these constituents are under investigation.

關鍵字/Key words：symbionts of marine invertebrates, *Trichoderma reesei*, antimicrobial activity, *Acinetobactor baumannii*, polypeptides, peptaibols

藥理組 | Pharmacology

PP-01

臺灣筋骨草水萃取物抑制人類大腸癌細胞株生長之研究

Study on the antiproliferative activity of *Ajuga taiwanensis* Nakai ex Murata aqueous extract in human colon cancer cells.

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Colorectal cancer (CRC) is the second and the third in total incidence of cancer and mortality in Taiwan. Although there are many drugs developed for the treatment of colorectal cancer, there is no drug can effectively treat colorectal cancer. *Ajuga taiwanensis* Nakai ex Murata is used for treatment of colds, bronchitis, tonsillitis, mump and traumatic bleeding. The previous studies have been shown that *Ajuga* plants have anti-hypertensive, anti-bacterial, anti-malarial, hypoglycemic activities; however the pharmacological study of *Ajuga taiwanensis* Nakai ex Murata of the anti-cancer activity is rare. The aim this study is to investigate the anti-cancer activity of *Ajuga taiwanensis* Nakai ex Murata aqueous extract (ATAE). The MTT result showed that ATAE had a significant inhibitory effect on HT-29, but had no obvious inhibitory effect on SW620. In follow-up study, we take HT-29 as the research object. The data indicated that ATAE induced reactive oxygen species (ROS) production in colon cancer lines, HT-29. HT-29 was treated with N-acetylcysteine(NAC) and ATAE that would reversed ATAE induced ROS production. Furthermore, we will use the flow cytometry to prove that ATAE induced the HT29 apoptosis in the future.

Key words：*Ajuga taiwanensis*, ROS , NAC, Antiproliferative activity.

PP-02

Inhibitory Effect of Magnoliae Flos Essential Oil on LPS-Induced Dendritic Cell Activation and Contact Hypersensitivity Responses

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Abstract:

Magnoliae Flos is commonly used as a medicinal material in Asia which is flower buds of *Magnolia biondii*, *M. denudate*, and *M. sprengeri*. Magnolia Flos has been used to treating nasal congestion, sinusitis and hypersensitive skin in traditional Chinese medicine. Recent research found that essential oil from the flower buds of *M. biondii* showed anti-inflammatory function on rat. However, the mechanism of the immunomodulation of Magnoliae Flos essential oil (MFEO) still remains unclear. Dendritic cells (DCs) plays a critical role in adaptive immune response which are regarded as a major target of immunomodulator to control immune responses. The present study was to explore the immunomodulatory effect of MFEO on DCs *in vitro* and C57BL/6 mice *in vivo*. Immunosuppressive activity of MFEO was explored with bone marrow-derived DCs. Cytokines and surface markers productions were quantified by enzyme-linked immunosorbent assay (ELISA) and flow cytometer analysis. In addition, the inhibitory effect of MFEO on immune response was elucidated by investigating the contact hypersensitivity (CHS) responses in mice. Our results showed that MFEO decreases the cytokines production of TNF-α, IL-6 and IL-12p70 in lipopolysaccharide (LPS) -stimulated DCs. Furthermore, MFEO suppressed surface marker MHC II, CD80 and CD86 in LPS-stimulated DCs. Animal model showed that CHS response was inhibited by examining the swelling ears in mice treated with MFEO. We demonstrated that the MFEO exhibits an immunosuppressive effect both *in vivo and in vitro*, indicating that MFEO have potential to develop as a new drug for excessive immune diseases.

Keywords: Magnoliae Flos, essential oil, Dendritic Cell, Contact Hypersensitivity Responses

PP-03

澤瀉萃取物作用於 ATF-3 的保護機制探討

Protecting Activity Targeting ATF3 of Alisma canaliculatum.

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Shennong Bencaojing (神農本草經) is an ancient Chinese medical book composed of three volumes (君、臣、佐使) containing 365 entries on medicaments and their description. The first volume of the treatise included 120 drugs harmless to humans. These herbs are described as "noble" or "upper herbs" (君藥、上品藥，多服、久服不傷人，輕身益氣，不老延年)。After entering an aging society, although life span extends, it becomes major risk factor and triggers a variety of chronic diseases. It becomes a big issue to maintain a healthy body condition. In this study, we used a 3T3-L1 mouse fibroblast cell line, stably transfected with pGL4-ATF3 (ATF3-3T3 cells) to elucidate 60 kinds of Chinese Upper Herbs extracts (780 fractions). ATF3, a member of the ATF/CREB family, is an adaptive-response gene that could be targeted and induced therapeutically to help combat excessive inflammatory responses or regulate immunity. After screening, the extract of *Alisma canaliculatum* (澤瀉，YL1-63-2) with potential ATF3 induction activity was selected for further study. Dose-dependent increase of ATF-3 protein expression was observed and without significant cytotoxicity above 500 μg/ml in macrophages. Pretreatment of YL1-63-2 dose-dependently suppressed LPS-induced TNF-α and IL-6 secretions in macrophages. Further, anti-ATF3 siRNA transfection inhibited the induction of ATF3 expression by the ATF3 inducer tBHQ. Under the condition, after ATF3 siRNA transfection, the inhibition effect of these extracts on TNF-α and IL-6 secretion was abolished. These indicated that the enhancement of ATF3 expression of these extract including *Alisma canaliculatum* extract may imply in their regulation of inflammation. Utilize the ancient wisdom, standardized identification and preparation of Chinese Upper Herbs extracts will make the ancient medicine more scientific and recognizable for further development as preventive therapeutics.

關鍵字/Key words：*Alisma canaliculatum*, ATF3, IL-6, TNF-α

PP-04

Identification of plant extracts with potential PPARgamma agonists

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Peroxisome proliferator-activated receptorγ (PPARγ), one of the transcription factors that regulate energy use and lipid metabolism in tumor cells, is a viable target for cancer therapy. In our search for potential PPARγ agonist, extracts from five Formosan plants including *Cornus officinalis*, *Eriobotrya japonica*, *Litsea glutinosa*, *Myoporum bontioides,* and Momordica charantia were tested. Among them, M. charantia showed the highest ability to activate PPARγ, which led us to identify its potential constituents. Among the compounds isolated from M. charantia, Compound **1**, was identified as a PPARγ agonist with an IC_{50} of 10 μM in MCF-7 breast cancer cells. Flow cytometric analysis indicated that compound **1** concentration-dependently arrested cells in the G1 phase of the cell cycle. In addition, compound **1** modulated the phosphorylation/expression of cyclin D1, CDK6, and p53. Taken together, these findings suggest that compound **1** may have therapeutic applications in cancer treatment through PPARγ activation.

關鍵字/Key words：PPAR; Momordica charantia; *Breast cancer*

PP-05

Antcin M Prevents Hyperglycemia-Accelerated Pre-Mature Senescence in Dermal Fibroblasts by Direct Activation of Nrf2 and SIRT-1 Genes

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Abstract

Antcins, steroid-like compounds are rich in Antrodia species such as *Antrodia cinnamomea* and *Antrodia salmonea*. Initially, we screened an anti-aging agent from a group of antcins including antcin A, antcin B, antcin C, antcin H, antcin K and antcin M. Result shows that out of the antcin group, antcin M (ANM) is a potent anti-aging component. Further analysis revealed the anti-aging properties of antcin M (ANM) and elucidated the molecular mechanism underlying the effects. We found that exposure of human normal dermal fibroblasts (HNDFs) to high-glucose (HG, 30 mM) for 3 days, accelerated G_0/G_1 phase arrest and senescence. Indeed, co-treatment with ANM (10 μM) significantly attenuated HG-induced growth arrest and promoted cell proliferation. Further molecular analysis revealed that ANM blocked the HG-induced reduction in G_1-S transition regulatory proteins such as cyclin D, cyclin E, CDK4, CDK6, CDK2 and protein retinoblastoma (pRb). In addition, treatment with ANM eliminated HG-induced reactive oxygen species (ROS) through the induction of anti-oxidant genes, HO-1 and NQO-1 *via* transcriptional activation of Nrf2. Moreover, treatment with ANM abolished HG-induced SIPS as evidenced by reduced senescence-associated β-galactosidase (SA-β-gal) activity. This effect was further confirmed by reduction in senescence-associated marker proteins including, $p21^{CIP1}$, $p16^{INK4A}$, and p53/FoxO1 acetylation. Also, the HG-induced decline in aging-related marker protein SMP30 was rescued by ANM. Furthermore, treatment with ANM increased SIRT-1 expression, and prevented SIRT-1 depletion. This protection was consistent with inhibition of SIRT-1 phosphorylation at Ser47 followed by blocking its upstream kinases, p38 MAPK and JNK/SAPK. Further analysis revealed that ANM partially protected HG-induced senescence in SIRT-1 silenced cells. A similar effect was also observed in Nrf2 silenced cells. However, a complete loss of protection was observed in both Nrf2 and SIRT-1 knockdown cells suggesting that both induction of Nrf2-mediated anti-oxidant defense and SIRT-1-mediated deacetylation activity contribute to the anti-aging properties of

ANM *in vitro*. Result of *in vivo* studies shows that ANM-treated *C. elegens* exhibits an increased survival rate during HG-induced oxidative stress insult. Furthermore, ANM significantly extended the life span of *C. elegans*. Taken together, our results suggest the potential application of ANM in age-related diseases or as a preventive reagent against aging process.

Keywords: Antcin M, *Antrodia salmonea*, hyperglycemia, stress-induced premature senescence, SIRT-1, Gerotarget

PP-06

Plant Galactolipid dLGG Suppresses Lung Metastasis of Melanoma Through Deregulating TNF-α–mediated Pulmonary Vascular Permeability and Circulating Oxylipin Dynamics in Mice

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This study demonstrates the bioefficacy and gives mechanistic insights into a plant galactolipid 1,2-di-*O*-linolenoyl-3-*O*-β-galactopyranosyl-*sn*-glycerol (dLGG) against metastatic melanoma using a syngeneic mouse model implanted with $B16^{COX\text{-}2/Luc}$ melanoma. dLGG-20 (*p.o.* dLGG 20 mg/kg) and anti-cancer drug CP-2 (*i.p.* cisplatin 2 mg/kg) treatment significantly inhibited lung metastasis of melanoma in mice for 91% and 57%, respectively, as determined by bioluminescence intensity. Moreover, dLGG-20 and CP-2 treatment prolonged mouse mean survival time. dLGG-20 treatment significantly inhibited the expression levels of several protein markers, *i.e.*, PCNA, MMP2, COX-2, VEGF, vimentin, snail, TGF-ß, ß-catenin, TNF-α, PD-1 and PD-L1 in mouse lung tissues compared to tumor control mice. Significant inhibition of macrophage and neutrophil infiltration and promotion of CD8+ Tc cell recruitment in the lung microenvironment was observed in dLGG-20-treated mice. A LC/MS–based comparative oxylipin metabolomics study showed that dLGG-20 treatment significantly induced (5.0- to 12.8-fold) the 12/15-LOX catalyzed oxylipin products in mouse serum, including 17-HDHA from DHA, 15-HEPE from EPA, 8- and 12-HETEs from AA, and CYP450 derived 20-HETE from AA. CP-2 treatment increased 12/15-LOX derived 8-, 11- and 12-HETEs from AA, and CYP450 derived 11(12)-EET from AA and 9,10-DHOME from LA by 5.3- to 8.1-fold. Of note, dLGG and 17-HDHA were more effective than CP in preventing B16 melanoma cell-induced pulmonary vascular permeability in mice through inhibiting TNF-α production, up-regulating tight junction

proteins claudin1 and ZO-2, and deregulating Src activation. In conclusion, this study shows the novel therapeutic effect of phytoagent dLGG and suggests its potential as a therapeutic agent for metastatic melanoma.

Keywords: Metastatic melanoma, galactolipid, oxylipin metabolome, 17-HDHA, lung vascular permeability

PP-07

Develop **Scopoletin Derivatives** for Neurodegenerative Disease

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Common neurodegenerative diseases include Alzheimer's disease, Parkinson's disease that are mainly caused by oxidative stress, neuroinflammation and neuronal dysfunction. Compounds possessing multifunctional effects such as MAO inhibition, AchE inhibition, ion chelating and neuroprotection are developed as potent therapeutic drugs for curing neurodegenerative diseases. Scopoletin is a natural coumarin found in a variety of plants, including some species from the Scopolia and *Fraxinus* Genus Plants. In a preliminary study, we found the scopoletin ameliorated motor dysfunction caused by MPTP, and also reversed the impairment of passive avoidance performance in mice. Encourage by this results, the scopoletin derivatives were synthesis and evaluated for their MAO and AchE inhibitory activity. Some of them showed significant activity and may serve as a valuable compound in the development of neurodegenerative diseases therapy.

Key words：neurodegenerative diseases, scopoletin

PP-08

倒地蜈蚣萃取物藉由抑制緩激肽誘發腦部星狀細胞第九型基質金屬蛋白酶表現致使抗神經發炎作用

Anti-Neuroinflammatory Effects of *Helminthostachys zeylanica* Extracts via Inhibiting Bradykinin-Induced MMP-9 Expression in Brain Astrocytes

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Phytochemicals present in vegetables, fruits, and herbs are believed to reduce the risk of several major diseases including cardiovascular diseases, cancers as well as neurodegenerative disorders. Department of Nursing, Division of Basic Medical Sciences, Hook. (Ophioglossaceae) have been used for centuries in the treatment of inflammation and various disorders. This medicinal fern *H. zeylanica* is also used as a folk medicine in Taiwan. The plant has been shown to possess an array of medicinal properties, including antioxidants and anti-inflammatory activities. Moreover, bradykinin (BK) has been shown to be involved in several inflammatory diseases including the central nervous system (CNS) inflammation. A possible explanation for these findings is due to the secretion of several inflammatory proteins like matrix metalloproteinases (MMPs) by neuroglial cells triggered by various mediators. Moreover, a rising level of MMP-9 has been found in blood fluid of these patients suffering from brain inflammatory diseases, which may be considered an inflammatory biomarker in several inflammatory diseases, CNS inflammation especially. Previously, we have demonstrated the signaling mechanisms of BK-induced MMP-9 expression in brain astrocytes. Herein, we evaluate whether *H. zeylanica* extracts possess anti-inflammatory effects on BK-induecd MMP-9 expression in brain astrocytes and its inhibitory mechanism. The results showed that *H. zeylanica* extracts, including E0, E1, and E2 significantly reduce MMP-9 induced by BK in brain astrocytes (RBA-1 cells). These *H. zeylanica* extracts can inhibit BK-stimulated phosphorylation of c-Src, Pyk2, and PKC(α/δ). Moreover, BK-stimulated Nox-derived ROS generation also been attenuated by pretreatment with these extracts, suggesting that the *H. zeylanica* extracts have anti-oxidative activity. We further demonstrated that the *H. zeylanica* extracts blocked activation of MAPKs (*e.g.* ERK1/2 and p38 MAPK) by BK. These data indicated that the *H. zeylanica* extracts may be has anti-inflammatory activity by reducing BK-induced MMP-9 expression via these related pathways in brain astrocytes.

關鍵字/Key words：

Helminthostachys zeylanica，Anti-neuroinflammation，Bradykinin，MMP-9，Brain astrocytes

PP-09

Trichodermin 選擇性抑制人類胰臟癌細胞生長之研究

Trichodermin Exhibits the Potent and Selective Antitumor Activity against Pancreatic Cancer Cells

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Pancreatic cancer is an aggressive malignancy, which generally responds poorly to chemotherapy. In this study, trichodermin, an endophytic fungal metabolite from Nalanthamala psidii, was identified as a potent and selective antitumor agent in human pancreatic cancer. Trichodermin exhibited antiproliferative effects against pancreatic cancer cells, especially p53-mutated cells (MIA PaCa-2 and BxPC-3) rather than normal pancreatic epithelial cells. We found that trichodermin induced caspase-dependent and mitochondrial intrinsic apoptosis. Trichodermin also increased apoptosis through mitotic arrest by activating Cdc2/cyclin B1 complex activity. Moreover, trichodermin promoted the activation of c-Jun N-terminal kinase (JNK), and inhibition of JNK by its inhibitor, shRNA, or siRNA significantly reversed trichodermin-mediated caspase-dependent apoptosis. Trichodermin triggered DNA damage stress to activate p53 function for executing apoptosis in p53-mutated cells. Importantly, we demonstrated that trichodermin with efficacy similar to gemcitabine, profoundly suppressed tumor growth through inducing intratumoral DNA damage and JNK activation in orthotopic pancreatic cancer model. Based on these findings, trichodermin is a potential therapeutic agent worthy of further development into a clinical trial candidate for treating cancer, especially the mutant p53 pancreatic cancer

Key words : Trichodermin, JNK activation, Mitotic arrest, DNA damage, Pancreatic cancer.

PP-10

13-Acetoxysarcocrassolide, a Cytotoxic Cembranolide Derivative, Exhibited Apoptotic Activity on Oral Cancer Cells through the Inhibition of Heat Shock Protein 90

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Heat shock protein 90 (HSP90) plays a significant role in cellular proliferation, differentiation, and carcinogenesis. HSP90 has been recognized as a promising therapeutic target in the war on cancer because it affects various oncoproteins, and the inhibition of HSP90 leads to the suppression of multiple oncogenic pathways as well as client proteins. In this study, we found that the marine cytotoxic product 13-acetoxysarcocrassolide (13-AC), recently isolated from the alcyonacean coral *Lobophytum crassum*, exhibited potent inhibitory activity on HSP90. 13-AC induced apoptosis in oral cancer cells Ca9-22 through the disruption of mitochondrial membrane potential (MMP) and the stimulation of reactive oxygen species (ROS) generation. However, the pretreatment of Ca9-22 cells with N-acetylcysteine (NAC), an antioxidant, inhibited ROS production resulting in the attenuation of the cytotoxic activity of 13-AC. Under stressful conditions, Ca9-22 cells treated with 13-AC showed a rapid induction of Keap1-Nrf2 pathway and an increase in the expression of p62/SQSTM1, but a suppression in antioxidative function of Nrf2 with immunoprecipitation, immunocytofluorecent and western blotting analysis. Inhibition of p62 expression by siRNA considerably attenuated the growth-inhibited by 13-AC treatment. Moreover, 13-AC exerted antitumor effect against oral cancer cells as demonstrated by the *in vivo* xenograft animal model. It significantly reduced tumor volume (55.29%) and tumor weight (90.33%). The molecular docking analysis demonstrated that 13-AC binds to N-terminal domain of HSP90 protein showing binding affinity more than 17-allylaminogeldanamycin (17-AAG), a HSP90 inhibitor of N-terminal ATP binding site and suppressed HSP90 client proteins including p-Akt, CDK4, HIF-1a, and MMP-2. On the proteins level, 13-AC increased the expression of apoptosis related proteins such

as cleaved caspases-3 and -9 as well as cleaved PARP in a dose- and time-dependent manner. Moreover, the results suggested that 13-AC exerted its cytotoxic activity through the promotion of ROS generation and the suppression of antioxidant enzyme activities. Altogether, the apoptotic effect of 13-AC was found to be mediated through the inhibition of HSP90 suggesting its potential future application as an anticancer agent.

Keywords : Apoptosis, Anticancer, 13-Acetoxysarcocrassolide, HSP90 inhibitor, Oxidative stress, Keap1-Nrf2 pathway, p62/SQSTM1

PP-11

Derivatization of honokiol by integrated acetylation and methoxylation for improved cutaneous delivery and anti-inflammatory potency

和厚朴酚經乙醯化與甲氧基化促進其經皮吸收能力及抗發炎活性

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A set of honokiol derivatives was synthesized to evaluate skin permeation and bioactivity. The reaction for derivatization included acetylation and methoxylation. The anti-inflammatory activity against neutrophils and macrophages was examined. The experimental setup for the assessment of cutaneous absorption was the in vitro Franz diffusion assembly. Honokiol and its derivatives significantly downregulated superoxide anion and elastase production in neutrophils, with honokiol showing the greatest inhibition. All derivatives could be completely hydrolyzed to the parent compounds after passing into the skin. The skin deposition of honokiol at an infinite dose (3 mM) was 0.33 nmol/mg. 4'-*O*-acetylhonokiol (AH), and 2,4'-diacetylhonokiol (DAH) exhibited comparable or less absorption than honokiol. The integrated acetylation and methoxylation (2-*O*-methyl-4'-*O*-acetylhonokiol, MAH) led to a 10.5-fold improvement of absorption compared to honokiol. MAH was advantageous for the targeted cutaneous treatment due to the high skin deposition and minimal penetration across the skin (8.40 nmol/cm^2 compared to 93.49 nmol/cm^2 for honokiol). The predicted therapeutic index for superoxide and interleukin (IL)-6 inhibition was much higher for topically applied MAH than for the other penetrants tested. The total polarity surface and hydrogen bond acceptor number calculated by molecular modeling were the parameters used to anticipate the cutaneous absorption. Our data suggest that MAH is a potent and safe candidate for cutaneous inflammation therapy.

Keywords: honokiol; acetylation; methoxylation; cutaneous absorption; anti-inflammatory activity

PP-12

Anti-inflammation and anti-neuronal death of valproate in rat chronic constriction injury model

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Background: The effect of valproate, a classical antiepileptic drug, on neuropathic pain remains unclear. In this study we used chronic constriction injury (CCI) model to delineate the role and to clarify if valproate has anti-neuropathic pain effect and its possible molecular mechanism.

Methods: CCI model was used to induce neuropathic pain in rats treated with or without valproate. Rats were intraperitoneally injected with valproate (300 mg/kg) from post-surgery day 1 to day 14. The thermal paw withdrawal latency (PWL) and mechanical paw withdrawal threshold (PWT) were measured 1 day before surgery and 1, 3, 7, 14 days after CCI. The sciatic nerves (SN) was obtained on post-surgery at day 3, 7, and 14. Western blotting, immunofluorescence, and enzyme-linked immunosorbent assay (ELISA) were used to detect inflammatory proteins (pAKT/AKT, pGSK-3b/GSK-3b, NFκB, iNOS and COX-2) and proinflammatory cytokines (TNF-α and IL-1b).

Results: There were significant decreases in PWL and PWT after CCI. Valproate-treated group resulted in significant increases in PWL and PWT on day 7 and 14 post-surgery, compared with untreated group. Valproate attenuated CCI-induced inflammatory mediators (pAKT/AKT, pGSK-3b/GSK-3b, iNOS and COX-2) and reduced proinflammatory cytokines (TNF-α and IL-1b) levels in SN. Valproate also inhibited nuclear NFkB activation. Double immunofluorescent staining further demonstrated that COX-2 and pGSK-3 proteins were decreased by valproate in Schwann cells.

Conclusion: Valproate attenuated the thermal hyperalgesia and mechanical allodynia in CCI rats, which correlated with its anti-neuroinflammation by reduction of NF-κB/iNOS/COX-2 activation and inhibition of pAKT/pGSK-3b-mediated neuronal death in the peripheral nerve injury.

Key words: Valproate, chronic constriction injury, neuroinflammation, neuronal death

PP-13

子寶草甲醇萃取物誘導人類血癌 HL-60 細胞進行凋亡和細胞自噬

Kalanchoe crenatodaigremontiana Methanol Extract Induces Apoptosis and Autophagy in Human Leukemia HL-60 Cells

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Kalanchoe crenatodaigremontiana, a plant from the family of *Crassulaceae*, is a hybrid of *K. crenatum* and *K. daigremontianu*. Various species of *Kalanchoe* are commonly used in traditional medicine worldwide. Many studies reported that other plants from this genus have anticancer activities. However, the effect of *K. crenatodaigremontiana* for cancer treatment is still unknown. The study was to investigate the effect of *K. crenatodaigremontiana* methanol extract (KCM) on human leukemia HL-60 cells and its underlying mechanism. Our results showed that KCM dramatically decreases HL-60 cell viability in a dose-dependent manner (IC50: 0.4 μg/ml). Annexin V/PI assay showed apoptosis induced by KCM in a time-dependent manner. PI staining showed that KCM induces cell cycle arrest at G0/G1 phase. The results of western blot analyses elucidated that the apoptosis is triggered by both intrinsic and extrinsic pathways. In addition, autophagy induction was elucidated by examining the increase in the expressions of autophagy marker proteins, such as ATG5, ATG7, Beclin-1, and LC3II. In summary, we revealed that the major action of KCM to HL-60 cells was inducing cell death by apoptosis, autophagy and cell cycle arrest at G0/G1 phase. This study showed that KCM induced cytotoxic effects in human leukemia HL-60 cells dramatically. Thus, the *K. crenatodaigremontiana* seems to be a promising anti-leukemia cancer botanicals. Hopefully, the results from the further animal study will demonstrate the efficacy of anti-leukemia cancer.

Key words：*Kalanchoe crenatodaigremontiana,* HL-60, Apoptosis, Autophagy, G0/G1 phase

PP-14

Targeting redox regulatory site of protein kinase B impedes neutrophilic inflammation

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Dysregulation of neutrophils elicits acute or chronic inflammatory diseases. Protein kinase B (PKB)/Akt is significant in the inflammatory responses of neutrophils, despite fewer Akt inhibitors being used to cure neutrophil-dominant inflammation. Additionally, the biological significance of redox-controlled Akt activity in neutrophilic inflammation is still elusive. Here, we identified 5,7-dimethoxy-1,4-phenanthrenequinone (CLLV-1) to restrain neutrophilic inflammation via redox modification of Akt. CLLV-1 dose-dependently inhibited respiratory burst, degranulation and chemotaxis in activated human neutrophils and/or neutrophil-like differentiated HL-60 (dHL-60) cells. CLLV-1 selectively inhibited Akt phosphorylation in activated human neutrophils and dHL-60. Significantly, CLLV-1 blocked Akt kinase activity and covalently reacted with Akt Cys310 *in vitro*. The level of alkylation agent-conjugated Akt was inhibited by CLLV-1, suggesting that CLLV-1 abates the reduced/inactive form of Akt. CLLV-1 also assisted Akt in associating with protein phosphatase 2A which binds to oxidized Akt to dephosphorylate Akt. Additionally, CLLV-1 administration ameliorated lipopolysaccharide-induced acute lung injury and Complete Freund's Adjuvant-caused paw inflammation in mice. CLLV-1 repressed the neutrophil infiltration and Akt phosphorylation in the inflammatory regions. Together, CLLV-1 acts as covalent-allosteric Akt inhibitor via targeting Cys310 to retrain inflammatory responses in human neutrophils and *in vivo*. Our findings provide a mechanistic framework for redox modification of Akt that may be a novel pharmacological target to alleviate neutrophilic inflammation.

Key words： Akt inhibitor, inflammation, neutrophils, lung injury

PP-15

Protective effect of superfine particles of herbal medicine against CCL_4-induced liver damage in rats

超細顆粒草藥對大鼠 CCL4 誘導的肝損傷的保護作用

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Abstract

Background: *Antrodia camphorate* (AC) is a medicinal mushroom that grows on the inner heartwood wall of *Cinnamomum kanehirai Hay* (*Lauraceae*), an endemic species that is used in Chinese medicine for its anti-tumor and immunomodulatory properties. This study aims to investigate the hepatoprotective effect of extract of AC in animals.

Methods: Effects of AC were investigated from 250 to 1250 mg/kg on CCl_4-induced liver damages in rats. The treated groups were orally given AC one week after the induction of liver injury (W1) for successive 9 weeks. Liver damage was induced by intraperitoneally injected with 400 ml/l CCl_4 at 0.75 ml/kg body weight, once weekly, for 7 weeks. The control group was similar injected with olive oil.

Results: The oral intake of AC significantly reduced the levels of glutamic oxaloacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT) compared with the vehicle control group (CCl_4 alone). Content of hepatic malondialdehyde (MDA), which was oxidative stress marker, was decreased after treated with AC in CCl_4-induced rats. Histological finding also confirmed the hepatotoxic characterization in rats. Furthermore, liver fibrosis in CCl_4-induced rats was inhibited by oral intake of AC through down-regulation of the expression of hydroxyproline and STAT3/CTGF signaling.

Conclusion: AC significantly attenuated the increased GOT or GPT level and reduced MDA level to show significant amelioration in the liver fibrosis induced by CC l_4. Thus, AC has marked protective effect against liver damage induced by CCl_4 in rats.

Key words: Hepatic fibrosis, carbon tetrachloride, Antrodia camphorate, CTGF, hydroxyproline

PP-16

The apoptotic mechanisms of Cucurbitacin E, a triterpene obtained from the *Aquilaria hull extract*, in human non-small cell lung cancer cells

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Non-small cell lung cancer (NSCLC) is a frequent cause of cancer-related death worldwide. Although there have been numerous therapeutic strategies for the treatment of NSCLC, a great deal of interest in identifying novel compounds is currently ongoing in order to provide effectiveness and safety and exhibit improved pharmacological profiles. Here, we report that Cucurbitacin E (CuE), a triterpene compound obtained from the *Aquilariae* hull extract, could represent a potential compound for the treatment of NSCLC. We examined the action mechanism of CuE in the NSCLC A549 cell line, and revealed that treatment of cells with CuE caused cells to accumulate in G2 phase, with a concomitant reduction of MPM2 and cyclin B1. After 48 h of CuE treatment, cells underwent apoptotic cell death via caspase-3 activation and poly(ADP ribose) polymerase (PARP) cleavage. Upon CuE treatment, ROS generation and ATM activation were induced. Combination of CuE and ROS scavenger NAC partially prevented CuE-induced ROS production and CuE-induced cell viability suppression. In addition, blockade of ATM using an ATM-targeting shRNA reduced CuE-induced cytotoxicity. Our current findings suggest CuE is a potent anticancer agent with significant tumor suppressive effect via ROS generation and ATM activation that could be can be further investigated for NSCLC therapy in the future.

Key words: apoptosis, ATM, Non-small cell lung cancer

PP-17

Aqueous extracts of *Paeonia suffruticosa* modulates mitochondrial proteostasis by reactive oxygen species-induced endoplasmic reticulum stress in pancreatic cancer cells

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Abstract

Pancreatic cancer (PC) remains the leading cause of cancer mortality, with limited therapeutic targets, and alterations in endoplasmic reticulum (ER)-related proteostasis may be a potential target for therapy. The root bark of *Paeonia suffruticosa* has been shown to inhibit cancer growth and metastasis, although its impact on PC is unknown. This study is to ascertain the anti-cancer effects of *P. suffruticosa* on oncogenic functions of PC and determine the detailed molecular mechanisms. Results showed that PS stimulated ER stress and affected mitochondrial membrane potential to increase autophagosome numbers and block their degradation, followed by autophagy induction and finally cell apoptosis. Additionally, PS-mediated proteostasis impairment resulted in altered dynamics of the actin cytoskeleton, cell motility impairment, and cell cycle progression inhibition. Conversely, a ROS scavenger partially reversed PS-mediated degradation of peptidyl-prolyl cis-trans isomerase B (PPIB), an ER protein important for protein folding, suggesting that ROS generation by PS may be the upstream of PS-triggering of mitophagy and final cell apoptosis. Nevertheless, oral administration of PS, alone or in combination with gemcitabine, delayed tumor growth in a xenograft model without affecting body weight. These findings indicate that PS may constitute a potential new alternative or complementary medicine for PC.

Keywords: Chinese herbal medicine; *Paeonia suffruticosa*; pancreatic cancer; proteostasis; autophagy; apoptosis.

PP-18

The antiphotodamage effects of FT on hairless mice skin

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Abstract

Skin is the outermost organ of the human body and easily exposed to ultraviolet (UV) radiation. Chronic UV exposure may cause skin photoaging and photodamage, which are characterized by thickening epidermis and disrupting skin barrier function. In literature, UV irradiation upregulated matrix metalloproteinases (MMPs) in dermal fibroblasts, leading to type I, II and III collagen degradation in connective tissues. In addition, nuclear factor E2-related factor 2 (Nrf2), a transcription factor, is the master regulator of antioxidant enzymes. UVB irradiation inhibits Nrf-2 translocated into the cell nucleus, and then downregulates the expression of heme oxygenase (HO)-1, resulting in the accumulation of oxidative stress and causing skin photoaging and photodamage.

FT exhibited potent antioxidant activity. In this study, *in vivo* experiments were designed to investigate the antiphotodamage activity of FT in hairless mice. In the experiment, hairless mice were exposed to UVB irradiation, and FT was applied topically for 10 weeks, the results of this study found that FT alleviated transepidermal water loss (TEWL) induced by UVB exposure. In addition, the results of immunohistological staining indicated that FT inhibited the UVB-induced protein expression of MMP-1 and MMP-2 in hairless mice. Moreover, in immunohistological staining, the expression of Nrf2 and HO-1 are upregulated after applied FT on mice skin. Our experiment results strongly indicate that FT has significant beneficial effects on the activity of antiphotodamage and antiphotoaging, and suggest that FT can be developed as an antiaging agent.

Key words: FT, antioxidant, heme oxygenase-1, nuclear factor erythroid 2-related factor

PP-19

Hepatoprotective effect of extractive combination of *Curcuma longa*, *Crataegus pinnatifida* and *Schizandra chinensis* on carbon tetrachlorede-induced liver fibrosis in rats

薑黃、山楂、五味子萃取組合物對四氯化碳誘發大鼠肝纖維化之護肝功能研究

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ABSTRACT :

Chronic hepatitis that develops into liver fibrosis has been a serious medical issue for generations in Taiwan. According to the data from the Ministry of Health and Welfare, liver inflammation disease is among the top ten causes that result in human death. This study was investigated the hepatoprotective effect of extractive combination of *Curcuma longa, Crataegus pinnatifida* and *Schizandra chinensis* (abbrev. ECCS) on carbon tetrachlorede (CCl_4)-induced liver fibrosis in rats, and also detected the biochemical parameters of the liver fibrosis.

Effects of ECCS were investigated from 0.05 to 0.1 g/kg on CCl_4-induced liver fibrosis in rats. The treated groups were given ECCS after the induction of liver injury. Liver desease was induced by intraperitoneally injection with CCl4 (0.2%, v/v in olive oil, 10ml/kg), once per week, for 8 weeks. The control group was similarly injected with olive oil.

The oral intake of ECCS decreased obviously in the levels of Aspartate Aminotransferase (AST/GOT) and Alanine Aminotransferase (ALT/GPT) that compared with the CCl_4 group. Content of Glutathione Peroxidase (GPx) and glutathione reductase (GRd), which was oxidative stress marker, was increased after the treatment with ECCS in CCl_4-induced rats. The Histological result also confirmed the

effect of ECCS in liver disease on rats.
ECCS significantly attenuated the increase in activities of AST or ALT and showed significant amelioration in the liver fibrosis induced by CC l_4. Thus, ECCS has marked protective effect on CCl_4 –induced liver fibrosis in rats.

Key words：Liver fibrosis, ECCS, *Curcuma longa, Crataegus pinnatifida, Schizandra chinensis*

PP-20

探討 T8 銀耳多醣組成與改善高脂飲食小鼠體脂肪堆積之評估

The study of T8 *Tremella fuciformis* polysaccharides structure characterization and the body-fat lowering effects in high fat-diet-fed mice

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Abstract

T8 *Tremella fuciformis* is a local species of edible mushroom and be developed as an agricultural biotech product with completeness of vision. T8 *Tremella fuciformis* has high polysaccharides content property. In this study, we purified and analyzed the structural characteristics of the polysaccharides derived from *Tremella fuciformis* (TFPS) in chromatography elution, viscosity, molecular weight, monosaccharides composition, uronic acids and NMR analyses. Moreover, the TFPS was orally supplied (1 and 2 g/kg b.w.day) to C57BL/6 mice feed with high fat diet or normal diet for 8 weeks (n=10, per group). At the end of this experiment, we observed the effects of TFPS in mice body weight, food intake, adipose tissue weight, and serum triglyceride and cholesterols. The results showed that TFPS has high viscosity and molecular weight (1359 kDa) properties. Moreover, DEAE chromatography showed that TFPS was almost comprised by acidic polysaccharides with highly uronic acids content. Monosaccharides composition of TFPS was mannose, fucose, xylose, fructose, glucose, and galactose in the ratio of 55.4:22.8:13.8:7.5:4.9:0.8. The results also showed that the body weight of high fat diet fed mice was significantly increased than that of normal diet fed mice and the administration of TFPS could decline the weight gain in mice. Moreover the retroperitoneal and gonadal fat was significant decrease in both TFPS treated group. Serum cholesterol was also decreased after TFPS treatment. In conclusion, this study demonstrated the structural characterizations of T8 *Tremella fuciformis* polysaccharide and its bioactive function in the body-fat lowering effects.

Keywords：*Tremella fuciformis*, polysaccharides, mice, the body-fat lowering effects

PP-21

丹皮酚增加海馬迴神經傳遞:Kv2.1 鉀電流的角色

Paeonol promotes hippocampal synaptic transmission: the role of the Kv2.1 potassium channel

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ABSTRACT

Paeonol is a major constituent of the Chinese herb *Moutan cortex radicis* that has previously improved impaired learning and memory processes in animal models of Alzheimer's disease. However, its underlying mechanisms remain unclear. This investigation into the neuroprotective effects of paeonol found that paeonol protected against amyloid-beta ($A\beta_{25-35}$)-induced impairment of long-term potentiation (LTP) in hippocampal CA1 slices and also increased the frequency, but not the amplitude, of miniature excitatory postsynaptic currents (mEPSCs) in hippocampal CA1 neurons. Similarly, the frequency, but not the amplitude, of mEPSCs in hippocampal CA1 neurons were also increased by the acetylcholinesterase inhibitor rivastigmine and a Kv2.1 blocker. These results suggest that paeonol may contribute to neural protection of Aβ-induced impairment of LTP by enhancing presynaptic spontaneous transmitter release, and that these effects may be associated with inhibitory effects upon the Kv2.1 current.

Keywords: Paeonol; Rivastigmine; Patch-clamp; Long-Term Potentiation (LTP); miniature Excitatory Postsynaptic Currents (mEPSCs); Kv2.1 potassium channel

PP-22

Effect of *Cissus repens* in carbon tetrachloride-induced acute liver injury mice

粉藤對四氯化碳誘導小鼠急性肝損傷之作用

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Cissus repens Lam. belongs to the genus *Cissus* of the family *Vitaceae*. In Taiwanese folk medicine, the root of *C. repens* could decrease body-heat, cooling-blood, detoxification, and reduce-swelling. Some foreign species in the same genus *Cissus* have liver-protective efficacy. Nevertheless, the hepatoprotective bioactivity of *C. repens* remains to be identified in order to prove its importance to clinical use. In this study, the hepatoprotective effect of *C. repens* methanol extract (CR_{MeOH}) was evaluated with carbon tetrachloride (CCl_4)-induced acute liver injury in mice. Histopathological examination showed that CR_{MeOH} reduced the extent of liver lesions induced by CCl_4. Moreover, CR_{MeOH} decreased the MDA level, elevated the content of GSH and enhanced the activities of antioxidant enzymes, including SOD, GSH-Px and GSH-Rd in the liver. Therefore, CR_{MeOH} could alleviate CCl_4-induced acute liver injury in mice. Its hepatoprotective mechanism may be associated with the prevention of the activity reduction of SOD, GSH-Px and GSH-Rd to inhibit the damages form lipid peroxidation caused by CCl_4.

Key words：*Cissus repens*, Carbon tetrachloride, Hepatoprotective bioactivity.

PP-23

Antcin M Prevents Hyperglycemia-Accelerated Pre-Mature Senescence in Dermal Fibroblasts by Direct Activation of Nrf2 and SIRT-1 Genes

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Abstract

Antcins, steroid-like compounds are rich in Antrodia species such as *Antrodia cinnamomea* and *Antrodia salmonea*. Initially, we screened an anti-aging agent from a group of antcins including antcin A, antcin B, antcin C, antcin H, antcin K and antcin M. Result shows that out of the antcin group, antcin M (ANM) is a potent anti-aging component. Further analysis revealed the anti-aging properties of antcin M (ANM) and elucidated the molecular mechanism underlying the effects. We found that exposure of human normal dermal fibroblasts (HNDFs) to high-glucose (HG, 30 mM) for 3 days, accelerated G_0/G_1 phase arrest and senescence. Indeed, co-treatment with ANM (10 μM) significantly attenuated HG-induced growth arrest and promoted cell proliferation. Further molecular analysis revealed that ANM blocked the HG-induced reduction in G_1-S transition regulatory proteins such as cyclin D, cyclin E, CDK4, CDK6, CDK2 and protein retinoblastoma (pRb). In addition, treatment with ANM eliminated HG-induced reactive oxygen species (ROS) through the induction of anti-oxidant genes, HO-1 and NQO-1 *via* transcriptional activation of Nrf2. Moreover, treatment with ANM abolished HG-induced SIPS as evidenced by reduced senescence-associated β-galactosidase (SA-β-gal) activity. This effect was further confirmed by reduction in senescence-associated marker proteins including, $p21^{CIP1}$, $p16^{INK4A}$, and p53/FoxO1 acetylation. Also, the HG-induced decline in aging-related marker protein SMP30 was rescued by ANM. Furthermore, treatment with ANM increased SIRT-1 expression, and prevented SIRT-1 depletion. This protection was consistent with inhibition of SIRT-1 phosphorylation at Ser47 followed by blocking its upstream kinases, p38 MAPK and JNK/SAPK. Further analysis revealed that ANM partially protected HG-induced senescence in SIRT-1 silenced cells. A similar effect was also observed in Nrf2 silenced cells. However, a complete loss of protection was observed in both Nrf2 and SIRT-1 knockdown cells suggesting that both induction of Nrf2-mediated anti-oxidant defense

and SIRT-1-mediated deacetylation activity contribute to the anti-aging properties of ANM *in vitro*. Result of *in vivo* studies shows that ANM-treated *C. elegens* exhibits an increased survival rate during HG-induced oxidative stress insult. Furthermore, ANM significantly extended the life span of *C. elegans*. Taken together, our results suggest the potential application of ANM in age-related diseases or as a preventive reagent against aging process.

Keywords: Antcin M, *Antrodia salmonea*, hyperglycemia, stress-induced premature senescence, SIRT-1, Gerotarget

PP-24

2D Sepbox System Separation and Molecular Networking Relationship for Traditional Chinese Medicine

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Because of the various bioactivities of natural products, many researchers and chemists have highly interested in Traditional Chinese Medicine. Traditional Chinese Medicine has been used as clinical drugs for thousands of years and a large number of natural products have been purified as medicinal synthesis templates for new drug development. However, the purification of active compounds always spends a lot of time and manpower, and produced many wastes as well. Therefore, good separation models with suitable tools can faster the timeline of this kind of research. In this research, we demonstrated the speedy purification from the crude extract to pure compounds by 2D Sepbox System in one week.

Besides, to avoid the reduplicative work, molecular networking by LC-MS/MS was developed as a new research strategy to identify secondary metabolites in Traditional Chinese Medicine. In this method, we can fine the active or novel compounds rapidly by calculating the MS/MS data of tandem mass spectra and database comparison.

關鍵字/Key words： LC-MS/MS, Molecular Networking, 2D Sepbox System

PP-25

研究白藜蘆醇對抗細懸浮微粒誘發人類滑液膜中纖維母細胞發炎之保護機轉

The protective mechanisms of resveratrol on particulate matter-induced COX-2 expression in human fibroblast-like synoviocytes

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Abstract

Human fibroblast-like synoviocytes (FLSs) play a role in joint synovial inflammation in rheumatoid arthritis (RA). Some evidence indicates that particulate matter (PM) in air pollution could contribute to the progression of RA. However, more research is needed to clarify this relationship. Up-regulation of cyclooxygenase (COX)-2 and its metabolite prostaglandin E_2 (PGE_2) are implicated in various inflammatory diseases. Resveratrol, a polyphenol found mainly in grapes and red wine, has antioxidant and anti-inflammatory activities. In the present study, we demonstrated that resveratrol reduced PM-induced COX-2/PGE_2 expression in human FLSs, and attenuated PM-enhanced NADPH oxidase activity and ROS generation. In addition, PM induced Akt, ERK1/2, or p38 MAPK activation, which was inhibited by resveratrol. Finally, we demonstrated that PM enhanced NF-κB p65 phosphorylation and the NF-κB promoter activity, which were reduced by pretreatment with a ROS inhibitor or resveratrol. Thus, we concluded that resveratrol functions as a suppressor of PM-induced inflammatory signaling pathways by inhibiting COX-2/PGE_2 expression.

Keywords: Rheumatoid arthritis; Inflammation; Particulate matter; Cyclooxygenase-2; Prostaglandin E_2

PP-26

麵包樹活性成分 artocarpin 經由活性氧化物質誘發粒線體相關之神經膠質瘤細胞凋亡

Artocarpin induces mitochondria-associated cell death through reactive oxygen species signaling in human glioblastoma cells

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ABSTRACT

Glioblastoma multiforme (GBM) is one of the most aggressive and malignant intracranial tumors. Currently, GBM patients have a poor prognosis despite the continuous progress in various therapeutic strategies. Recent studies have revealed that Artocarpin, a natural prenylated flavonoid, has various anti-inflammatory and anti-tumor properties. Data also showed that artocarpin is associated with cell death of primary glioma samples, but the exact effects on human glioblastoma cells and underlying molecular mechanism remained largely unknown. In this study, we found that treatment of U87 or U118 cells (a human glioblastoma cell line) with artocarpin decreased the viability of U87 or U118 cells by induction of apoptosis. Artocarpin-induced apoptosis was associated with caspase activation and PARP cleavage and was mediated by the mitochondrial pathway, as exemplified by mitochondrial depolarization, mitochondrial-derived ROS production, cytochrome c release, up-regulation of Bad and Bax, and down-regulation of Bcl-2. Artocarpin induced NADPH oxidase/reactive oxidative species (ROS) generation, which appeared essential for the activation of the mitochondrial pathway. Artocarpin-induced mitochondrial-derived ROS production was associated with Akt and ERK1/2 activation. After treatment with artocarpin, ROS caused PI3K/Akt/ERK1/2-induced cell death of these cells. Taken together, our findings suggest that artocarpin induces mitochondria associated apoptosis of glioma cells, and artocarpine may be is a potential chemotherapeutic agent for future GBM treatment.

Keywords: Apoptosis; Artocarpin; Caspase; Glioblastoma multiforme; ROS

PP-27

白藜蘆醇抑制金黃色葡萄球菌誘發人類肺泡上皮細胞產生 TLR2/MyD88/NF-κB 依賴型 血管黏附分子-1

Resveratrol inhibits *Staphylococcus aureus*-induced TLR2/MyD88/NF-κB-dependent VCAM-1 expression in human lung epithelial cells

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ABSTRACT

Staphylococcus aureus is the most commonly found Gram-positive bacterium in patients admitted to intensive-care units, causing septicaemia or pneumonia. S. aureus is considered to play an important role in the induction of cell adhesion molecules. Resveratrol, a compound found in the skins of red fruits, may inhibit the inflammatory signalling pathways involved in lung diseases. In the present paper, we have shown that resveratrol reduced S. aureus-mediated VCAM-1 (vascular cell adhesion molecule-1) expression in HPAEpiCs (human lung epithelial cells) and lungs of mice. In an in vivo study, we have shown that resveratrol inhibited S. aureus-induced pulmonary haematoma and leucocyte count in BAL (bronchoalveolar lavage) fluid in mice. In an in vitro study, we observed that resveratrol attenuated S. aureus-induced TLR2 (Toll-like receptor 2), MyD88 (myeloid differentiation factor 88) and PI3K (phosphoinositide 3-kinase) complex formation. S. aureus stimulated Akt, JNK1/2 (c-Jun N-terminal kinase 1/2) and p42/p44 MAPK (mitogen-activated protein kinase) phosphorylation, which were inhibited by resveratrol. In addition, S. aureus induced IκB (inhibitor of nuclear factor κB) α and NF-κB (nuclear factor κB) p65 phosphorylation and NF-κB p65 translocation, which were reduced by resveratrol. Finally, we found that S. aureus induced NF-κB and p300 complex formation and p300 phosphorylation, which were inhibited by resveratrol. Thus resveratrol functions as a suppressor of S. aureus-induced inflammatory signalling not only by inhibiting VCAM-1 expression, but also by reducing TLR2-MyD88-PI3K complex formation and Akt, JNK1/2, p42/p44 MAPK, p300 and NF-κB activation in HPAEpiCs.

Keywords: lung inflammation; nuclear factor Bκ (NF-κB); resveratrol; Staphylococcus aureus; Toll-like receptor

PP-28

Study of the immunomodulatory polysaccharides from *Cuscuta japonica*

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Abstract:

Cuscuta japonica (日本菟絲子) is a parasitic plant, also named as Jin-Den-Teng (金燈藤). Its growth is easy and fast. The literature does not have pharmacological research report, especially in immunomodulation. Dendritic cells (DCs), professional antigen-presenting cells, play a critical role in the immune response. Monitoring the function of dendritic cells can be an indicator of the immune response. In this study, we found that the crude polysaccharides extracted from the whole plant grown on *Callicarpa formosana* Rolfe (白粗糠) have a strongly stimulatory activity to DCs. Also, the active polysaccharides were found to be present in the molecular weight greater than 100 kDa part. In addition, we separated polysaccharides by using anion exchange chromatography, and found that acid polysaccharides have the ability to activate DCs. Next, the components of the active polysaccharides, the activation through which receptor and intracellular signal regulation mechanism will be further elucidated. It is expected to be able to discover the active polysaccharides that promote the immune response, to analyze its detailed mechanism of action, and to develop an agonist that enhance DC function to apply in anti-cancer immunotherapy.

Keywords: *Cuscuta japonica*, Dendritic Cell, Polysaccharide, Immunomodulation

PP-29

Protodioscin Induces Apoptosis Through ROS-Mediated Endoplasmic Reticulum Stress via The JNK/p38 Activation Pathways in Human Cervical Cancer Cells

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Protodioscin (PD), the main steroidal saponin purified from various plants and foods, has various biologic functions, including anti-cancer effects. This study investigated the anti-tumor effects and mechanism of action of PD on human cervical cancer cells. First, we demonstrated that PD inhibits cell viability, causes a loss of mitochondrial function, and induces apoptosis, as evidenced by up-regulation of caspase-8, -3, and -9, PARP, and Bax activation and down-regulation of Bcl-2 expression. PD was shown to induce reactive oxygen species (ROS) and the endoplasmic reticulum (ER) stress pathway, including Grp78 (BiP), p-eIF-2α, ATF4, and CHOP. Scavenging of the intracellular ROS with N-acetyl cysteine (NAC) could block the PD induces ROS levels, and inhibited ER stress and apoptosis-related proteins. Transfection of Grp78/CHOP-siRNA effectively inhibited PD-induced ER stress-dependent apoptosis. Moreover, treatment with PD significantly increased p38MAPK and JNK activation. Co-administration of a JNK (SP600125) or p38MAPK inhibitor (SB203580) abolished cell death and ER stress effects during PD treatment. In addition, PD induced the expression of nuclear ATF4 and CHOP, as well as the binding ability of ATF4 to the CHOP promoter. Taken together, these findings suggest that ROS regulates JNK/p38 activation, which is dependent on Grp78/p-eIF2α/ATF4/CHOP pathways, and plays an important role in PD-induced apoptosis in human cervical cancer cells.

Key word: protodioscin; reactive oxygen species; endoplasmic reticulum stress; apoptosis; MAPK; cervical cancer

PP-30

Fisetin inhibits Epidermal Growth Factor-induced migration of ARPE-19 cells by suppression of AKT activation and Sp1-dependent MMP-9 expression

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Purpose: Proliferative vitreoretinopathy (PVR) can result in abnormal migration of retinal pigment epithelium (RPE) cells. Fisetin is a naturally occurring compound that has been reported to have antitumor effects, but its effects on epidermal growth factor (EGF)-induced cell migration and the underlying mechanisms remain unclear.

Methods: Effects of fisetin on EGF-induced cell viability and migration were examined by MTT and in vitro migration assays. Reverse transcription–polymerase chain reaction (RT-PCR) and immunoblot were performed to evaluate matrix metallopeptidase-9 (MMP-9) expression and activation of specificity protein-1 (Sp1) and AKT in ARPE-19 cells treated with EGF and with or without fisetin. Luciferase and ChIP assays were performed to examine Sp1 transcription activity and MMP-9 binding activity.

Results: Fisetin did not affect ARPE-19 cell viability and significantly inhibited the EGF-induced migration capacity of ARPE-19 cells. Furthermore, fisetin exerted an antimigratory effect and suppressed MMP-9 mRNA and protein expression. Treatment with EGF induced phosphorylation of AKT, and expression of MMP-9 and Sp1. Fisetin combined with LY294002 (an inhibitor of AKT) prevented the EGF-induced migration involved in downregulation of Sp1 and MMP-9 expression. Luciferase and ChIP assays suggested that fisetin remarkably decreased the EGF-induced transcription activity of MMP-9 and Sp1 and inhibited EGF-mediated Sp1 from directly binding to MMP-9 promoter in ARPE-19 cells.

Conclusions: Fisetin inhibited EGF-induced cell migration via modulation of AKT/Sp1–dependent MMP-9 transcriptional activity. Therefore, fisetin may be a potential agent in the treatment of migratory PVR diseases.

Key words：ARPE-19 cells, EGF, fisetin, Sp1, MMP-9, migration

PP-31

Taiwanese Native Plant on Protection against Osteoporosis: *In Vitro* and *In Vivo*

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Osteoporosis, a bone metabolic disorder, is a major health issue in the world. Menopausal hormone decline and aging contributes to increased risk of osteoporosis. Osteoblast promotes bone formation to balance the bone remodeling. DMM, one of the Taiwanese native plants, has been used as folk medicine for bone fracture healing. In this study, extraction of DMM was performed using different solvents, aqueous (DMMH) and 50% ethanol (DMME), for osteogenic activity evaluation. Cell viability was determined using the MTT assay. Osteogenic activity was analyzed using alkaline phosphatase (ALP) activity assay and Alizarin red S staining for mineralization in primary human osteoblasts (HOb). The results exhibited that DMMH has better osteogenic activity than DMME in *in vitro* model. Hence, we used *in vivo* model to evaluate DMMH in ovariectomized C57BL/6JNarl mice. Sham and ovariectomized mice were administered with water (SHAM and OVX) for control. DMMH low-dose group and high-dose group were further administered by oral gavage to ovariectomized mice. Positive control (PC) was administered with subcutaneous injection. Each group contained eight mice which were treated for 12 weeks. The results exhibited that groups treated with DMMH low-dose and high-dose did not increase the uterus index (uterus weight/body weight) in ovariectomized mice. Group treated with DMMH high-dose significantly increased bone mineral densities (BMD) of vertebrae and femur as well as reduced femur trabecular separation in ovariectomized mice. Based on these results, DMM seems to be a potential natural product to be developed into anti-osteoporosis drug, and its properties can provide a platform for anti-osteoporosis drug development.

關鍵字/Key words：osteoporosis, Taiwanese native plant, osteogenic activity, primary human osteoblasts, ovariectomized

PP-32

Total synthesis of hispidulin and the structural basis for its inhibition of proto-oncogene kinase Pim‑1

Hispidulin 之全合成及其對原致癌基因 Pim-1 抑制之結構基礎

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A new method is applied to synthesize hispidulin, a natural flavone with a broad spectrum of biological activities. Hispidulin exhibits inhibitory activity against the oncogenic protein kinase Pim-1. Crystallographic analysis of Pim-1 bound to hispidulin reveals a binding mode distinct from that of quercetin, suggesting that the binding potency of flavonoids is determined by their hydrogen-bonding interactions with the hinge region of the kinase. Overall, this work may facilitate construction of a library of hispidulin-derived compounds for investigating the structure–activity relationship of flavone-based Pim-1 inhibitors.

Key words: Hispidulin, Proto-oncogene Kinase, Pim-1

PP-33

Pterostilbene inhibit the proliferation of human hepatocellular carcinoma cells via induction of endoplasmic reticulum stress and autophagy

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Hepatocellular carcinoma (HCC) is the most frequent type of primary liver cancer and is the third leading cause of cancer related mortality worldwide. Current treatment for HCC suffer from poor response rate and severe side effects, therefore a more effective therapy with less side effects is urgently needed. Pterostilbene (PT), a natural analog of resveratrol with higher bioavailability, have been shown to possess several pharmacologic activities including anti-inflammation and anti-proliferation. However, the underlying mechanism of PT as an anticancer agent in HCC is poorly understood. Our results showed that PT inhibited the proliferation of two HCC cell lines Huh 7 and SK-Hep 1, while inducing autophagy and enhancing endoplasmic reticulum (ER) stress signaling. Anti-proliferation activity were attenuated by inhibition of autophagy through 3-MA and LC3 siRNA treatment, indicating that PT exerted anticancer activity via autophagic cell death in HCC cells. Moreover, reduction of ER-stress by ATF4 siRNA not only decreased the expression level of LC3-II but also increased cell viability of HCC cells. Taken together, our results showed that PT inhibit the proliferation of HCC cells via ER-stress enhanced antophagic flux.

關鍵字/Key words：pterostilbene, ER-stress, autophagy, ATF4, LC3

PP-34

7-Acetylsinumaximol B induces apoptosis and autophagy in human gastric carcinoma cells through mitochondria dysfunction and activation of the PERK/eIF2α/CHOP signaling pathway

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Abstract

7-Acetylsinumaximol B is an active compound of cembranoids, and was originally isolated from cultured soft coral *Simularia sandensis*. This study investigated the cytotoxicity of 7-acetylsinumaximol B towards the NCI-N87 human gastric cancer cell line. An MTT assay was used to measure cell survival after treatment, and immunofluorescence staining and western blotting were employed to analyze the effects of 7-acetylsinumaximol B on autophagy and apoptosis. Our results showed that 7-acetylsinumaximol B exerted a dose-dependent cytotoxic effect on NCI-N87 cells, and fluorescence staining indicated that the effect was due to the compound having induced apoptosis in the cells. In addition, the 7-acetylsinumaximol B-induced cytotoxicity towards NCI-N87 cells was associated with the release of cytochrome *c* from mitochondria, activation of pro-apoptotic proteins (such as caspase-3/-9, Bax and Bad), and inhibition of anti-apoptotic proteins (Bcl-2, Bcl-XL and Mcl-1). 7-acetylsinumaximol B treatment also triggered endoplasmic reticulum stress, leading to activation of the *p*-PERK/*p*-eIF2α/ATF4/CHOP apoptotic pathway. Furthermore, 7-acetylsinumaximol B initiated autophagy in NCI-N87 cells and induced the expression of autophagy-related proteins, including Atg3, Atg5, Atg7, Atg12, LC3-I and LC3-II. Our findings suggested that 7-acetylsinumaximol B has the potential to be developed as new anticancer drug for the treatment of human gastric cancer.

Keyword：7-Acetylsinumaximol B; apoptosis; autophagy; mitochondria dysfunction; ER stress

PP-35

6-Hydroxy-5,7-dimethoxy-flavone suppresses the neutrophil respiratory burst via selective PDE4 inhibition to ameliorate acute lung injury

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Over-activated neutrophils produce enormous oxidative stress and play a key role in the development of acute and chronic inflammatory diseases. 6-Hydroxy-5,7-dimethoxy-flavone (UFM24), a flavone isolated from the Annonaceae *Uvaria flexuosa*, showed inhibitory effects on human neutrophil activation and salutary effects on lipopolysaccharide (LPS)-induced acute lung injury in mice. UFM24 potently inhibited superoxide anion ($O_2^{\bullet-}$) generation, reactive oxidants, and CD11b expression, but not elastase release, in *N*-formyl-L-methionyl-L-leucyl-L-phenylalanine (fMLF)-activated neutrophils. However, UFM24 failed to scavenge $O_2^{\bullet-}$ and inhibit the activity of subcellular NADPH oxidase. fMLF-induced phosphorylation of protein kinase B (Akt) was inhibited by UFM24. Noticeably, UFM24 increased cyclic adenosine monophosphate (cAMP) concentration and protein kinase (PK) A activity in activated human neutrophils. PKA inhibitors significantly reversed the inhibitory effects of UFM24, suggesting that the effects of UFM24 were through cAMP/PKA-dependent inhibition of Akt activation. Furthermore, activity of cAMP-related phosphodiesterase (PDE) 4, but not PDE3 or PDE7, was significantly reduced by UFM24. UFM24 attenuated neutrophil infiltration, myeloperoxidase activity, and pulmonary edema in LPS-induced lung damage in mice *in vivo*. In conclusion, our data demonstrated that UFM24 inhibits oxidative stress in human neutrophils through inhibition of PDE4 activity. UFM24 also exhibited significant protection against endotoxin-induced acute lung injury in mice. UFM24 has potential as an anti-inflammatory agent for treating neutrophilic lung damage.

Key words : acute lung injury; 6-hydroxy-5,7-dimethoxy-flavone; neutrophil; oxidative stress; phosphodiesterases 4

PP-36

Celastrol represses MPP$^+$-induced dopaminergic neuronal death via mitophagy activation

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Parkinson's disease (PD) is a common neurodegenerative disease, in which the progressive loss of dopaminergic neurons in the substantia nigra pars compacta causes dopamine depletion in the striatum further leads to the primary motor symptoms of resting tremor and bradykinesia. Mitochondria are double membrane-bound organelles in the cytoplasm of cells. Main functions of mitochondria are including energy production, calcium homeostasis, apoptosis, etc. Previous research has shown that an impaired capability of neurons to remove damaged mitochondria results in cytochrome c release, which leads to dopamine neuron apoptosis in PD. Autophagy inhibits neuron apoptosis by removing damaged mitochondria and abnormal protein aggregations. Mitophagy is the selective degradation of mitochondria by autophagy. Previous studies using gene transfer technology have demonstrated that overexpression of *PINK1* and *DJ1* exert dopamine neuroprotection against MPTP-induced dopaminergic neurotoxicity in mice. PINK1 is a mitochondrial serine/threonine-protein kinase; DJ1 is an antioxidant and cytoprotective protein. Both can induce mitophagy and thus play a neuroprotective role in neurons. In this study we found celastrol altered the LC3 conjugation system and increased PINK1 and DJ1 expression. Following treatment with MPP$^+$ (mitochondria complex I inhibitor), celastrol demonstrated neuroprotection by maintaining mitochondria membrane potential, enhancing damaged mitochondria clearance by mitophagy and anti-apoptosis against MPP$^+$-induced neurotoxicity. Our study indicates that celastrol activates mitophagy and provides therapeutic benefit in PD.

關鍵字/Key words：Autophagy; celastrol; mitophagy; Parkinson's disease

PP-37

細胞凋亡對靈芝揮發性代謝物生成之影響

Effect of Apoptosis on Production of Volatile Metabolites in *Ganoderma lucidum*

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Ganoderma lucidum is an important medicinal fungus, with anti-cancer, liver protection, anti-inflammatory, immune regulation and other important pharmacological activities. Secondary metabolites, including alkaloids, glycosides, terpenes, tannins, sterols, volatile ingredients, essential oils, are active components in plants and fungi. Regulation of secondary metabolites biosynthesis and how to produce more secondary metabolites are critical for medical purpose. To our knowledge, broad-spectrum secondary metabolites biosynthesis affected by apoptosis has never been investigated in fungi and plant. To evaluate the effect of apoptosis signaling on production of broad-spectrum volatile components, fungal mycelium of *G. lucidum* was incubated with aspirin for 1-6 days to induce apoptosis; headspace solid-phase microextraction (HS-SPME) combined with gas chromatography (GC) and gas chromatography mass spectrometry (GC-MS) was carried out to analyze the production of volatile secondary metabolites. The results showed that 37 volatile components were identified and much more secondary metabolites were produced during apoptosis induction. The total volumetric content of the control group had the highest total peak area (PA) value on the first day. There was no significant difference of PA value in mycelium incubated with aspirin for 1 to 6 days. The main volatile components were 3-octanone, benzaldehyde and 1-octen-3-ol in control. However, the main components of apoptosis-induced mycelium were benzaldehyde, β-barbatene and hexana. Aspirin induced more benzaldehyde, β-barbatene and β-caryophyllene than control. Benzyl alcohol, 2-undecanone, (E) -2-octenal, o-tolualdehyde, nonanal and benzyl acetate were identified only in mycelium incubated with aspirin. Taken together, this study proved that apoptosis induced various secondary metabolites production and this approach is potential for pharmaceutical application in medicinal fungi and plant.

關鍵字/Key words：

Apoptosis, *Ganoderma lucidum,* ganoderic acids, headspace solid-phase microextraction (HS-SPME), volatile secondary metabolites

PP-38

3, 5, 6, 7, 8, 3', 4'-heptamethoxyflavone Impairs Dendritic Cell Maturation and Has Antiarthritic Effect in Murine Collagen-Induced Arthritis.

3, 5, 6, 7, 8, 3', 4'-heptamethoxyflavone 可抑制樹狀細胞成熟並且具有抗關節炎之功效於膠原蛋白誘導關節炎小鼠模式

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The aim of this study was to investigate the effect of 3, 5, 6, 7, 8, 3', 4'-heptamethoxyflavone, a citrus flavonoid, on dendritic cell (DC) maturation, as well as its potential as a therapeutic agent in a murine model of collagen-induced arthritis (CIA). 3, 5, 6, 7, 8, 3', 4'-heptamethoxyflavone significantly impaired lipopolysaccharide (LPS)-induced DC maturation as shown by decrease in the secretion of inflammatory cytokines, the expression of costimulatory molecules and the T cell proliferation ability of DCs when given at noncytotoxic doses. In addition, the decrease of LPS-induced MAPK and NF-κB signaling activation may contribute to the inhibitory activity of 3, 5, 6, 7, 8, 3', 4'-heptamethoxyflavone. In mice with CIA, the i.p injection of 3, 5, 6, 7, 8, 3', 4'-heptamethoxyflavone ameliorated the severity of arthritis, reduced the levels of anticollagen Type II (CII) IgG and limited the proliferation of T cells, observed as a lower frequency of Th1 and Th17 cells in the spleen after restimulation with CII. In conclusion, this study shows for the first time that 3, 5, 6, 7, 8, 3', 4'-heptamethoxyflavone can manipulate the immunostimulatory properties of DCs and thus represents a potential therapeutic for\the treatment of rheumatoid arthritis in humans.

Keywords: 3, 5, 6, 7, 8, 3', 4'-heptamethoxyflavone, dendritic cells, T cells, collagen induced arthritis

PP-39

5-hydroxyl-isosinulaflexiolide K Inhibits Dendritic Cell Functions and Attenuates Allergic Contact Hypersensitivity

5-hydroxyl-isosinulaflexiolide K 具有抑制樹狀細胞功能及減緩皮膚接觸性過敏之症狀

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The dendritic cells (DC) maturation process plays a key role in initiating T cell responses and maintaining immune tolerance. Accordingly, DCs are considered key targets for the immunomodulatory effects. In this study, the effect of 5-hydroxyl-isosinulaflexiolide, a new cembranoid isolated from the cultured soft coral *Sinularia flexibilis*, on lipopolysaccharide (LPS)-induced murine bone marrow-derived DCs was explored. The different cytokine productions, phenotypes, cytokine secretion and the lymphocyte activation of DCs were examined by ELISA and Flow cytometry. The experimental results showed that the cytokine production, the major histocompatibility complex class II (MHC class II) and costimulatory molecules (CD40, CD80) expression of *DCs stimulated by LPS were significantly decreased by* 5-hydroxyl-isosinulaflexiolide *in a dose-dependent manner*. In addition, 5-hydroxyl-isosinulaflexiolide reduced the propensity to stimulate the autologous T cell proliferation of LPS-induced DCs. Furthermore, we found that topical medication of 5-hydroxyl-isosinulaflexiolide decreased the 2,4-Dinitro-1-fluorobenzene induced skin contact hypersensitivity (CHS) in mice model. These novel findings provide new insight into the immunopharmacological function of 5-hydroxyl-isosinulaflexiolide and its effects on DCs.

Keywords: dendritic cells, 5-hydroxyl-isosinulaflexiolide, soft coral, contact hypersensitivity (CHS)

PP-40

Lobocrassin B Induces Apoptosis of Human Lung Cancer and Inhibits Tumor Xenograft Growth

Lobocrassin B 可誘導人類肺癌細胞自然凋亡及抑制異種移植腫瘤之生長

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Lobocrassin B, a natural cembrane-type compound isolated from the soft coral *Lobophytum crassum*, has been shown to have significant biological effects, including anticancer activity. As the most common cause of cancer mortality worldwide, lung cancer remains a major concern threatening human health. In the current study, we conducted in vitro experiments to demonstrate the inhibiting effect of Lobocrassin B on CL1-5 and H520 human lung cancer cells growth and to explore the underlying mechanisms, as well as in nude mice bearing CL1-5 tumor xenografts. Lobocrassin B exerted cytotoxic effects on lung cancer cells, as shown by decreasing cell viability, and inducing apoptosis, oxidative stress and mitochondrial dysfunction. In addition, the increased level of Bax, cleaved caspase-3, -9 and -8, and the suppression of Bcl-2 were observed in the Lobocrassin B treated cells. Moreover, in vivo assays verified the significance of these results, revealing that Lobocrassin B inhibited CL1-5 tumor xenograft growth and that inhibitory effects were accompanied by a marked increase in tumor cell apoptosis. In conclusion, the results suggested that Lobocrassin B could be a potential anticancer compound for its propensity to inhibit growth and induce apoptosis in human lung cancer cells.

Key words: Lobocrassin B, lung cancer, apoptosis, mitochondria, caspase, xenograft

PP-41

Dihydrosinularin Induces ATM-mediated DNA Damage Causes G2/M Cell Cycle and Apoptosis of Human Lung Cancer and Suppresses Tumor Xenograft Growth

Dihydrosinularin 可透過 ATM 間接誘導之 DNA 損傷進而造成人類肺癌細胞 G2/M 細胞週期停止及細胞凋亡並且抑制異體移植腫瘤之生長

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In this study, we evaluated the cytotoxic effect of dihydrosinularin, an active compound isolated from the cultured soft coral *Sinularia flexibilis*, on the human non-small cell lung cancer cells (NSCLC), CL1-5 and H226, and to subsequently explore the underlying molecular mechanisms. From the results of our study, cell viability was obviously inhibited by dihydrosinularin in a dose-dependent manner. In addition, our results suggested that dihydrosinularin triggered DNA damage and subsequently induced cell cycle G2/M arrest. Western results further showed that dihydrosinularin can up-regulated p-H2A.X, p-ATM, p-Chk2, and p-cdc25c (Ser216) expression coupled with down-regulated cyclin B1 expression. Moreover, we also observed that cell apoptosis induced by a high dose of the dihydrosinularin. After 48 hr treatment, increased expression of cleaved PARP was observed. Moreover, in vivo assays verified the significance of these results, revealing that dihydrosinularin inhibited H226 tumor xenograft growth. Taken together, our findings demonstrated that dihydrosinularin possesseed anti-NSCLC activity, and therefore is a potential candidate for NSCLC treatment.

Keywords: dihydrosinularin, non-small cell lung cancer cells (NSCLC), DNA damage, G2/M, xenograft

PP-42

Differentiated interaction **of harmine with the ATP-binding pocket of tyrosine kinases associates with inhibition of the secretion of tissue plasminogen activator**

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High mobility group box 1 (HMGB1) is secreted by activated innate immune cells and necrotic cells as a pro-inflammatory cytokine and thus represents a key target for the treatment of inflammatory diseases. Here we report that μM levels of harmine significantly attenuates the release of tissue-type plasminogen activator (tPA) from the human endothelial cell line, EA.hy926, induced by exogenous HMGB1, respectively. Of noted, the inhibition induced by harmine alone was paralleled by not only a decrease of the phosphorylation of C-terminal Src kinase (Csk), epidermal growth factor receptor (EGFR), ephrin type-A receptor 6 (EphA6), developmental tyrosine ***kinase*** (Dtk) and tyrosine-protein kinase receptor UFO (Axl) but also by an increase of the phosphorylation of anaplastic lymphoma kinase (ALK), Janus kinase 3 (JAK3), lymphocyte-specific protein tyrosine kinase (LCK), REarranged during Transfection (RET), and activated CDC42 kinase 1 (ACK1) (receptor) tyrosine kinases. Moreover, molecular docking stimulations reveal that harmine has graded higher affinities towards the ATP-binding pockets of the inhibited than the activated kinases. Given these effects, harmine holds promising as a pharmacophore against the proinflammatory cytokine, HMGB1.

關鍵字/Key words：High mobility group box 1, harmine , tissue-type plasminogen activator, tyrosine kinases

PP-43

以工業化製程生產關節炎之治療天然物，AG-02 RA1

Industrial Process to Produce AG-02, A Natural Product of Arthritis Treatment

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AG-02 RA1 is a diterpenoid structural based natural product isolated from Labiatae family with various biological activities such as anti-inflammatory, anti-cancer, anti-oxidation and many more. Based on our previous studies developed over the years, studies showed that AG-02 RA1 is an excellent and new botanical drug candidate for treating arthritis. The potential application of AG-02 RA1 urgently required the scale up of the manufacturing process of this natural product. Prior to the scale up, several solvents were investigated for optimizing the recovery of AG-02 RA1 selectively by the extraction method. In this poster, we present the manufacturing process of AG-02 RA1 from the herb of 60 kg batch size. The process was started from the decoloring after adsorbing colored impurities using active carbon after refluxing of the herb materials in solvent, was then continued with the extraction of the decoloring elute by solvent, followed by the concentrated *in vacuo* to remove solvents. AG-02 RA1 with >90% purity was finally obtained after solid phase extraction, and its yield was 73.2% of the theoretical yield.

關鍵字/Key words：Diterpenoid, Industrial Process, Botanical Drug, Solid Phase Extraction, arthritis

PP-44

The Anti-oxidant And Anti-melanogenesis Effects Of AC

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ABSTRACT

AC is a kind of traditional chinese medicine for the treatment of food and drug, which is rich of different biological active ingredients, such as terpenoids, benzenoids, lignans, superoxide dismutase (SOD). Superoxide dismutase is a strong antioxidant, it can suppress oxidative stress by reducing agent of superoxide. In our experiment, we investigated AC anti-oxidant effects. We examined hydrogen peroxide free radical scavenging activity and reducing power to evaluate the antioxidant activity.

Exposure of the skin to UV radiation increased ROS, melanin synthesis and pigmentation. Melanin determines skin color of human. However, the overproduction of melanin in the skin results in hyperpigmentation disorders such as melasma, freckles, age spot and skin cancer.

In animal experiment, UVB-induced hyperpigmentation in the C57BL/6 mice ear skin was significantly reduced by topical application of AC for 5 weeks. The results showed AC has no toxicity and it significantly inhibited melanin index of C57BL/6 mice ear skin. These results indicated that AC is promising candidates for development as antioxidant and whiting agents.

Key words: AC, superoxide dismutase (SOD), antioxidant, melanin

PP-45

咸豐草萃取物之抗氧化能力及對癌細胞的抑癌活性分析

The Analysis of Antioxidation and Anti-cancer Activity of Bidens Pilosa Var. Radiate

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Abstract :

The formation of cancer is related to the DNA damage. Human body using mitochondrion to proceeds oxidation reaction for the energy that can maintain physiological function. In this reaction also produces free radicals. Free radicals, in the normal physiological circumstances, catalyzed by the relevant enzymes, produce superoxide anion free radicals to remove bacteria or infected cells; in other words, the body must have a certain amount of free radicals to prevent disease. If it is affected by the abnormal environment will produce free radicals. Once the number of free radicals in the body more than the range of the normal defense of the human body, it will produce a "free radical chain reaction"; under the vicious cycle, the body's function gradually damage, followed by a variety of diseases. Free radicals can damage the molecular in the cell because of the unstable electronics propriety that grabs the electrons of other molecules in the cell. In the case of this reaction occurring in the nucleus that will cause DNA damage, cell growth will be affected and cause cancer. According to the former research shows the Bidens pilosa var. radiate extracts have excellent antioxidant ability and the effect of inhibiting the growth of cancer cells. The previous studies show that Bidens pilosa var. radiate contains rich flavonoids and phenolic acids are indeed excellent anti-oxidation and anti-inflammatory ingredients. In this experiment, we use the cytotoxicity and antioxidant ability of the extracts from Bidens pilosa var. radiate to treat the lung cancer, breast cancer, prostate cancer of the cell lines. Expecting the extract from Bidens pilosa var. Radiate possess superior antioxidant ability, the effect of inhibiting growth and migration of cancer cell lines.

Keyword: free radicals , antioxidant ability, cytotoxicity, lung cancer, breast cancer, prostate cancer

PP-46

樹葡萄籽乙酸乙酯萃取物之抑癌活性

The anti-cancer activity of the ethyl acetate extract from Jaboticaba

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Abstract

The jaboticaba (*Myrciaria cauliflora*) belonging to the family Myrtaceae is native to Brazil. The Jaboticaba fruit is about 2-3 cm in diameter, with the color ranging from wine-red to black. The previous studies showed the aqueous extract of seed from jaboticaba exhibit cytotoxicity on human oral cancer cells. In this study, the extract of the seeds from jaboticaba exhibited strong antioxidant activity using DPPH assay (IC_{50} = 21.55 ng/ml). Treatment with extracts of seeds of jaboticaba retarded MDA-MB-231 cell proliferation and reduce Hep-3B, PC-3 cell survival rate by WST-1 assays. The anti-migration activity of extracts from jaboticaba was also investigated using wound-healing assay. G1 phase arrest was observed in MDA-MB- 231 cancer cells treated with extracts of jaboticaba by flow cytometry. Several regulatory proteins involved in G1 phase arrest and apoptosis were also evaluated by western blotting.

關鍵字/Key words：Jaboticaba, Cell cycle arrest, Cell apoptosis

PP-47

Evaluation and Application of Indigenous Thraustochytrids from Mangrove Regions of Taiwan as Sources of Natural Health and Supplementary Products

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Thraustochytrids are a group of marine osmoheterotrophic, straminipilan protists that grow in the neritic and oceanic water, especially in mangrove region, and probably play an important role as saprobes. The high content of ω-3 polyunsaturated fatty acids (PUFA) make thraustochytrids as a candidate source for commercial docosahexaenoic acids (DHA) and eicosapentaenoic acid (EPA). To search indigenous thraustochytrids with commercial value, we tried to collect the indigenous species of thraustochytrids from mangrove regions of Taiwan and analyze their levels of PUFA (such as DHA and EPA) and carotenoids (such as astaxanthin). Besides, to clarify more medicinal application of thraustochytrids, we tried to screen the various bioactivities of the extracts of isolated thraustochytrids by established bioassays, such as acetylcholinesterase TLC and NS2B protease expression assays. Interestingly, the preliminary results suggested that the ethyl acetate (EtOAc) extracts of several species of thraustochytrids have certain components with a clear inhibitory activity toward acetylcholinesterase (AChE), which is responsible for the breakdown of acetylcholine (Ach) in the neural synapse to lead"cholinergic deficit hypothesis" of Alzheimer's disease. In the poster, we would like to show the aforementioned results about the study on the indigenous thraustochytrids from mangrove regions of Taiwan.

關鍵字/Key words：Thraustochytrids, PUFA, DHA, EPA, Carotenoids, Astaxanthin, Acetylcholinesterase TLC assay, NS2B protease expression assay

PP-48

SC9 提高口腔癌細胞經由氧化壓力誘導之 G2/M 停滯與細胞凋亡

SC9 Induces Oxidative Stress-Mediated G2/M Arrest and Apoptosis in Oral Cancer Cells

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Soft corals-derived natural product, SC9, was antiproliferative against some cancers but its effect and detailed mechanism on oral cancer cells remain unclear. The subject of this study is to examine the anti-oral cancer effects and underlying detailed mechanisms in terms of cell viability, oxidative stress, cell cycle analysis, and apoptosis analyses. In MTS assay, SC9 dose-responsively decreased cell viability of three oral cancer cells (Ca9-22, HSC-3, and CAL 27) but only little damage to oral normal cells (HGF-1). This cell killing effect was rescued by the antioxidant *N*-acetylcysteine (NAC) pretreatment. Abnormal cell morphology and induction of reactive oxygen species (ROS) were found in SC9-treated oral cancer Ca9-22 cells, however, NAC pretreatment also recovered these changes. SC9 arrested the Ca9-22 cells at G2/M phase and dysregulated the G2/M regulatory proteins such as cdc2 and cyclin B1. SC9 dose-responsively induced apoptosis on Ca9-22 cells in terms of flow cytometry (annexin V and pan-caspase analyses) and western blotting (caspases 3, 8, 9 and poly (ADP-ribose) polymerase (PARP). These apoptotic changes of SC9-treated Ca9-22 cells were rescued by NAC pretreatment. Taken together, SC9 induces oxidative stress-mediated antiproliferation, G2/M arrest, and apoptosis against oral cancer cells and may be a potential marine drug for anti-oral cancer therapy.

關鍵字/Key words：Soft corals, ROS, oral cancer, G2/M arrest

PP-49

LH suppresses hepatitis C virus replication via JNK/c-Jun-C/EBP-mediated down-regulation of cyclooxygenase-2 expression

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Hepatitis C virus (HCV) chronically infects 2–3% people of the world's population, which leads to a high risk of cirrhosis and hepatocellular carcinoma (HCC). Drug resistance remains a serious problem to limit the effectiveness of among US Food Drug Administration (FDA)-approved direct-acting antiviral (DAA) drugs against HCV proteins. The objective of our research is to discover new antivirals from natural products to supplement current therapeutics. In this study, we demonstrated that LH, isolated from Formosan soft coral Lobophytum crassum, significantly reduced HCV replication in replicon cells and JFH-1 infectious system in a dose-dependent manner. We further demonstrated that the inhibition of LH on HCV replication is due to suppression of HCV-induced cyclooxygenase-2 (COX-2) expression. Based on COX-2 promoter-based reporter analysis, we identified CCAAT/enhancer-binding protein (C/EBP) as a key transcription factor for down-regulation of COX-2 by LH, in which LH decreased phosphorylation of c-Jun NH2-terminal protein kinase and c-Jun and, ultimately leading to reduction of HCV-induced C/EBP expression. The combination treatment of LH with currently used HCV drugs synergistically reduced HCV RNA replication, indicating that LH exhibited high potency to serve as a supplementary therapeutic agent for HCV-infected patients.

Keywords

HCV; cyclooxygenase-2; mitogen activated protein kinase; c-Jun NH2-terminal protein kinase; CCAAT/enhancer-binding protein

PP-50

4-Acetylantroquinonol B 藉由抑制 MAPK 及 NFκB 活化而減少因脂多糖引發的細胞激素釋放及敗血症 /

4-Acetylantroquinonol B inhibits lipopolysaccharide-induced cytokine release and alleviates sepsis through of MAPK and NFκB suppression

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Background: Antrodia cinnamomea is an indigenous medicinal mushroom in Taiwan, commonly used for the treatment of cancers and inflammatory disorders. 4-acetylantroquinonol B (4AAQB) is one of the active component isolated from the mycelium of A. cinnamomea. However, whether 4AAQB exhibits anti-inflammatory effect is not clear.

Methods: The anti-inflammatory activity of 4AAQB was examined by ELISA to measure the pro-inflammatory cytokines production in lipopolysaccharide (LPS)-simulated RAW264.7 cells, peritoneal macrophages and in mice. The effect of 4AAQB for MAPK kinase molecules phosphorylation in LPS-stimulated RAW264.7 macrophage including ERK, JNK and p38 were evaluated. The *in vivo* efficacy of 4AAQB was also demonstrated.

Results: In the present study, we found that 4AAQB exhibits anti-inflammatory effects inhibit tumor necrosis factor-α (TNF-α)/interleukin-6 (IL-6) releasing and LPS-stimulated phagocytes migration without affect cell growth. In addition, the MAPK kinase molecules phosphorylation in LPS-stimulated RAW264.7 macrophage including ERK, JNK and p38 was inhibited by 4AAQB. The phosphorylation of NFκB subunit p65 and IkBa were also decreased after 4AAQB treatment. Furthermore, 4AAQB attenuates the cytokine production in LPS-induced and CLP-induced septic mice.

Conclusion: These results showed that 4AAQB exhibited anti-inflammatory property both *in vitro* and *in vivo*, suggesting that 4AAQB may be a therapeutic candidate which used in inflammatory disorders treatment.

關鍵字/Key words：Antrodia cinnamomea, 4AAQB, Anti-inflammation, MAPK, NFκB

PP-51

Demethoxycurcumin impairs cell migration and invasion of human cervical cancer HeLa cells *via* PI3K/AKT and NF-kB signaling pathways

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Abstract

Dimethoxycurcumin (DMC) is one of the lipophilic analog of curcumin, possesses several biological activities such as anti-inflammation and anti-cancer activities. No available information to show DMC inhibits metastasis of human cervical cancer cells in vitro. The aim of the present study is to investigate the molecular mechanisms associated with DMC inhibits cell migration and invasion of human cervical cancer HeLa cells. DMC affect cell migration and invasion in HeLa cells were investigated by wound healing mobility assay and Boyden chamber migration and invasion assay. Results indicated that DMC inhibited cell migration and invasion in concentration dependently. Results from western blotting indicated that DMC decreased the protein expressions of focal adhesion kinase (FAK), growth factor receptor bound protein 2 (GRB2), matrix metallopeptidase 9 (MMP-9), matrix metallopeptidase 2 (MMP-2), 14-3-3, phosphoinositide-3-kinase (PI3K), The serine–threonine kinase Akt, nuclear factor kappa B (NF-kB p65), hosphorylated c-Jun NH2-terminal kinase (p-JNK 1/2), phosphorylated extracellular signal-regulated kinase (p-ERK), phosphorylated p38 (p-p38), urokinase-type plasminogen activator (uPA) and ras homolog family member A (Rho A) in HeLa cells. Based on those observations, we suggest that DMC could be used as a novel anti-cancer metastasis of human cervical cancer in the future.

Key word: Dimethoxycurcumin , HeLa cells

傳統中藥組 |

Traditional Chinese Medicine

PC-01

The antioxidant activity and ingredients of endemic *Cirsium* species in Taiwan in comparison with Cirsium Herba

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Cirsium species (Asteraceae) have been used for hepatoprotection medicine in Taiwan and called as ''ji-jiao-ci''. However, previous research has few investigations to explore their ingredients and pharmacological activity. In the present study, the four widely used species (*C. arisanense*, *C. kawakamii*, *C. brevicaule*, and *C. japonicum* var *australe*) were selected and their three parts of plants (leaves, roots, flowers) were extracted by methanol and water respectively. Our first aim is to compare the antioxidant ingredients and scavenging activities among those plant parts. The result showed that methanol extracts of *Cirsium* species had higher phenolic and phenylpropanoid contents and better antioxidant potencies than aqueous extracts. Among the four species, the flower of *C. japonicum* var *australe* (CJFM) was the most active part in scavenging 2,2-Diphenyl-1-Picrylhydrazy (DPPH), 2,2'-azino-bis(3-ethylbenzothiazoline-6 sulphonic) acid ($ABTS^{\bullet+}$), hypochlorous acid (HOCl). There is a significant relationship between the antioxidant activities and the contents of the phenolic and phenylpropanoid ingredients. Second aim, we want to compare their chromatographic fingerprints and analyze the contents of ingredients by high performance liquid chromatography (HPLC). All species parts possess different chromatographic fingerprints. CJFM has more contents of silibinin α and silibinin β than other plants. In conclusion, these results show that CJFM has the best free radical-scavenging activity among all species parts and phenolic and phenylpropanoid compounds are major free radical-scavenging active ingredients of *Cirsium* species.

關鍵字/Key words：*Cirsium* species; antioxidant; Total phenolics; phenylpropanoid; silibinin

PC-02

The Ethanol Extraction of Prepared *Psoralea corylifolia* Induces Apoptosis and Autophagy and Alteres Genes Expression Assayed by cDNA Microarray in Human prostate cancer PC-3 Cells

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Psoralea corylifolia Linn. is an important medicinal plant with thousands of years of clinical application. It has been widely used in many traditional Chinese medicine formulas for the treatment of various diseases such as leucoderma and other skin diseases, cardiovascular diseases, nephritis, osteoporosis, and cancer. *P.corylifolia* can kidney yang, Gujing reduction of urine. Documented its estrogen-related diseases have a considerable effect common with traditional Chinese medicine theory should permit, we look forward to psoralen in prostate cancer in men may also have further effect. *P. corylifolia* was extracted frequently with 95% ethanol at room temperature. The combined all ethanol extracts were filtered and evaporated under reduced pressure (PCE). For this experiment, the crude extracts were dissolved in dimethyl sulfoxide (DMSO). We analyzed the chemical compounds by High Performance Liquid Chromatography (HPLC). We determined the percentage of cell viability and cell cycle by flow cytometer. Then also uesd the 4,6-Diamidino-2-phenylindole (DAPI) nucleic acid stain to check the apoptotic cells. After that, the cDNA microarray assay used for gene expression in prostate cancer cells following exposure to prostate cancer PC-3 cells. Further, we uesd Western blotting to indicate the extrinsic and the intrinsic apoptotic pathway associated protein expression in prostate cancer.In this report, we found the PCE inhibited the human prostate cancer PC-3 cells growth and induced apoptosis in a

dose-dependence and the cell cycle arrest. Then, some gene expression following the cell cycle stagnation and apoptosis. We demonstrated the molecular mechanisms underlying PCE-induced antitumor activity in PC-3 cells *in vitro*, which is involved in p53 activation. Understanding the manner of PCE-affected cell cycle progression and apoptotic pathways will promote the development of treatment of the human prostate cancer in the future.

Keywords: Prostate cancer, *Psoralea corylifolia*, Apoptosis, PC-3, Autophagy, Gene expression

PC-03

Rapid and Sensitive DNA-based Molecular Method for the Authentication of *Fallopia multiflora*

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Abstract:

Fallopia multiflora (FM) is known for useful tonic herbal medicine and had been reported that having many biological functions on hair-blacking, liver and kidney-tonifying and anti-aging. Thus, it widely utilizes in many fields such as production of health food, cosmetic application or functional ingredients. Because of its large consumption and its claimed benefits, however, the problem of the authenticity and the substitution of FM are getting more and more emerged such as fake FM or its adulterants appeared in the herbal market. This not only the effectiveness of herbal materia is affected but also the consumers' anxiety are raised. Currently, numerous well-known methods for the authentication of FM such as morphological and microscopic identification and chemical chromatographic profiling have been frequently used in the previously reports. Even though some ways have practically used, however, more precisely, sensitive or rapidly way for the detection of FM is still needed. In this study, a DNA-based molecular method was developed for the authentication of FM; and four primers which specifically annealed distinct six DNA regions of ribosomal sequences were designed and used for DNA amplification. Results were showed that the DNA amplifications were produced successfully by using FM isothermal primers when the sample containing FM, and the adulterants did not displayed the DNA amplification. Optimal amplification conditions including sensitivity, specificity and time for reaction were also determined herein. Taken together, the isothermal DNA amplification method for the authentication of FM presented herein was sensitive, specific and rapidly. It shows its potential application for the authentication of herbal materia such as FM in the future.

Key words: *Fallopia multiflora* , authentication, DNA-based molecular method

PC-04

中藥不良反應提示系統的追蹤與研究

A Follow-up Study on the Adverse Drug Reaction Reporting System of Traditional Chinese Medicine

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OBJECTIVES : Adverse drug reactions system of traditional Chinese medicine is a very important part of drug safety in patients. This study mainly explored the database of prompt system in hospital, analyzed the effectiveness and maintenance of the system, so that the safety monitoring of traditional Chinese medicine will be institutionalized, and the safety medication of people will be enhanced as well.

MATERIALS AND METHODS : Retrospective design was used in this study. From January 2016 to June 2017, people who went to the hospital and received Chinese medicine prescriptions were used as subjects, and the drug adverse reactions on the computer screen of traditional Chinese medicine indicated by physicians were collected. Then the data was tracked and analyzed.

RESULTS: Between January 2016 and June 2017, there were total 1,639 prescriptions. After statistical analysis, there were 13 prompt screens,which were, respectively: Rhei Rhizoma、Cannabis Fructus、Polygonati Odorati、Cinnamomi Cortey、Agrimoniae Herba、Paeoniae Rubra Radix、Periostracum Cicadae、Lycii Fructus、Puerariae Radix、Aismatis Rhizoma、Gui Zhi Tang, a total of 11 pieces of data for research. In the total 11 drugs found in this study, Only 3 pieces of drug information: Rhei Rhizoma, Cannabis Fructus, Periostracum Cicadae, were the correct information, the other 10 pieces of drug information were wrong,which indicating that the correct rate of the prompt screen was only 23.07%.

CONCLUSIONS：Information technology is a two-edged sword. Information equipment can be used to reduce waste, and enhance the safety medication of the people.

Key words：Adverse Reaction, Traditional Chinese Medicine, Safety

PC-05

Water Extract of Liuwei Dihuang Attenuates Lipopolysaccharide-Induced Inflammation in Primary microglia Cultures and Methylglyoxal-Induced atrophy in Myotubes

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Drug development on neurodegeneration and skeletal muscle atrophy caused by inflammation and metabolic diseases has its importance and urgency. Liuwei dihuang (LWDH) is a widely used traditional Chinese medicine (TCM) composed of dihuang (*Rehmannia glutinosa*), shanyao (*Dioscorea opposite*), shanzhuyu (*Cornus officinalis*), zexie (*Alisma orientalis*), hoelen (*Poria cocos*) and mudanpi (*Paeonia suffruticosa*), has been employed as an anti-aging prescription to improve declined function. Our previous studies reveal that water extract of LWDH (LWDH-WE) possesses protection on dopaminergic neurons through enhancing antioxidant defense and decreasing apoptotic death, and it also possesses multi-protective properties on neurons and muscle tissue against deficiency of survival motor neuron protein. In this study, we investigated the protective effects of LWDH-WE on lipopolysaccharide (LPS)-induced inflammation in primary microglia cultures and methylglyoxal-induced inhibition of protein synthesis in C2C12 skeletal muscle myotubes. The present results indicated, in primary cultures of rat microglia, LWDH-WE attenuated LPS-induced inflammatory and oxidative factors. In C2C12 myotubes, we also found that LWDH-WE upregulated protein synthesis signaling and attenuated methylglyoxal-induced myotubes atrophy. These results suggest that LWDH-WE might provide protection under inflammation and skeletal muscle atrophy.

Key words: liuwei dihuang, inflammation, protein synthesis, microglia, skeletal muscle

PC-06

從形態與化學成分探討台灣地區市售谷精草品質

Eriocauli Flos Sold in Taiwan by Morphological and Chemical Analyses

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Eriocauli Flos (Gujingcao; EF), the dried capitulum with peduncle of *Eriocaulon buergerianum* Koern. (Eriocaulaceae), is a Chinese herbal medicine for treating eye diseases and inflammation. However, several species of *Eriocaulon* genus are used as the same source of EF in different areas of China. To examine the species of EF used in Taiwan and establish the quality control platform, morphological and chemical analyses were performed. Ten major compounds, including apigenin (**7**) and its 7-*O*-β-D-glucopyranoside (**1**) and 7-*O*-[6-*O*-*E*-coumaroyl]-β-D-glucopyranoside (**6**), hispidulin (**8**) and its 7-*O*-β-D-glucopyranoside (**2**) and 7-*O*-[6-*O*-*E*-coumaroyl]-β-D-glucopyranoside (**5**), jaceosidin (**9**) and its 7-*O*-β-D-glucopyranoside (**3**), and toralactone (**10**) and its 9-*O*-*β*-D-glucopyranosyl(1→6)-*β*-D-glucopyranoside (**4**), were isolated and identified from commercially available EF as chemical markers. Morphological investigation showed that there are two kinds of EFs sold in Taiwan herbal market. Most of them are capitulum without peduncle. A simultaneous H(U)PLC analyses of above multiple components (**1-10**) in commercially available EFs, collected from different ares of Taiwan, indicated their differences not only in morphology but also in chemical profile between capitulum with and without peduncle. Further, comparing with an authentic *E. buergerianum*, we found both morphology and the chemical profile vary greatly from collected samples to authentics. In terms of the morphological investigation, the samples without peduncle are closer to the EF species which recorded in Hong Kong Pharmacopoeia. To ensure the correct EF materia medica used in Taiwan and guarantee their therapeutic efficacy in clinical practice, further monitoring is necessary.

Key words：Eriocauli Flos; capitulum; peduncle; morphology; chemical constituents

PC-07

Influence of cytokinins on *in vitro* regeneration of bulblets in *Fritillaria cirrhosa* - an important Chinese medicinal herb

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Abstract

Fritillaria cirrhosa D. Don growing at 3200 to 4500M height, belonging to family Liliaceae is a perennial herb, mainly distributed in Sichuan province of China, and is categorized as threatened species. The bulbs of *F. cirrhosa* herb are highly effective in relieving cough and eliminating phlegm in the traditional Chinese medicine. In China, the production of *Fritillaria* preparations has been developed into a large-scale industry of about US $400 million a year. However, the low propagation rate (two bulblets per year) is a serious limitation for large-scale cultivation. In the present study, we have investigated the role of cytokinins (growth regulators) on *in vitro* regeneration of bulblets using bulb scale sections as explants. A high frequency (4.7 per explant) of bulblets was induced in the scale sections on solid Murashige and Skoog's medium supplemented with 0.1 mg/L BA. Cultures were incubated under 16 h white fluorescent light (40 μmol m^{-2} s^{-1}) at 20◦C. Regenerated bullets developed leaves and roots in 12 weeks of culture. Tissue cultured bulblets contained bioactive compounds.

Keywords: *Fritillaria cirrhosa,* bulb scale sections, cytokinins

PC-08

Studies on the chemical constituents with anti-cancer activity in ethyl acetate-soluble layer from *Ganoderma tsugae*

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Ganoderma (known as Lingzhi) has been recognized as a medicinal mushroom for over 2000 years. It is used for promoting health and longevity in China, Japan, and other Asian countries. Many studies about chemical composition, cultivation, and effects on *Ganoderma* are still being conducted worldwide. *G. tsugae* (GT), one of the popular *Ganoderma* species and as famous as *G. lucidum* (GL), is commonly used as dietary supplement for health benefits, including immunomodulation, antioxidant, and anti-cancer effects. Based on our previous studies, GT extracts could inhibit a wide variety of cancer cells growth and metastasis, including HER2-overexpressing breast and ovarian cancers, human epidermoid carcinoma, lung adenocarcinoma, and colorectal carcinoma. However, the study on those ingredients responsible for anti-cancer bioactivities of GT remains to be investigated. In this study, the powder of GT was immersed in 95% ethanol and the extract was partitioned against ethyl acetate (EA), n-butanol (Bu) to give GT-EA, GT-Bu and GT-aqueous layers sequentially. Subsequently, the cytotoxicity of each layer was monitored by MTT assay on ovarian SK-OV-3 cancer cells. The preliminary results showed that GT-EA had a growth inhibition effect on SK-OV-3 cells better than that of GT-Bu and GT-aqueous layers. In addition, the GT-EA layer is currently undergone with a serial and repeated column chromatography in order to obtain the active components against cancer activities. The final goal of this study is to find some novel chemical constituents or leads isolated from GT for anti-cancer activities and used for clinical treatments for cancers in the future.

Key words：*G. lucidum*, *G. tsugae*, natural products, SKOV-3, anti-cancer components

PC-09

Water extract of *Cordyceps militaris* may amelioate depression-like behavior in chronic unpredictable mild stress rats model via regulating ROCK2/Akt pathway

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Abstract

According to world health organization's report, depression may be the first contribution of global burden disease in 2030. Due to the side effect in treatment and the low reception of drug, the new strategy of preventing depression is required. *Cordyceps militaris* has been known as a precious Chinese herb in Asia. Researchers had found amounts of neuroprotection effects in recent years such as it could significantly decrease the immobility time in forced swimming test of mice. Modern scientists have confirmed that the main active compounds in *Cordyceps militaris* including cordycepin, poly-saccharides, nucleoside and sterols. The aim of this study is to evaluate the anti-depression effect of *Cordyceps militaris* precisely. In unpredictable chronic mild stress (UCMS) animal model, *Cordyceps militaris* maintained the amount of water intake and food intake to prevent weight loss in stress condition. It was observed that *Cordyceps militaris* (125, 250 and 500 mg/kg bw/day) significantly increased the crossing number and total travel distance in open field test. Besides, it also increased the sucrose preference of rats. Low dosage of *Cordyceps militaris* (125 mg/kg bw/day) significantly decreased the IL-1β in serum. In brain cortex, low dosage of *Cordyceps militaris* (125 mg/kg bw/day) might altered the serotonin turnoverate and dopamine turnoverate. In Western blotting, the data showed that *Cordyceps militaris* (125, 250 and 500 mg/kg bw/day) decreased the ROCK2 protein expression and up-regulated the Akt protein expression in cortex. In conclusion, we found that *Cordyceps militaris* could ameliorate depressive-like behavior of UCMS-treated rats by not only decreasing the pro-inflammatory cytokine IL-1β in serum but also regulating the ROCK2/Akt pathway in brain.

Keywords: *Cordyceps militaris*, anti-depression, ROCK2, unpredictable chronic mild stress

PC-10

Research and Development of A New Drug by *Ru-Yi-Jin-Huang-San*

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【Introduction】 In modern medicine, the compliance of patients to use drugs is an important issue. Consequently, the research and development of drugs mainly focuses on the convenience of using drugs. When the level of convenience of using drugs increases, the willingness of patients to use the drugs also increases.

Ru-Yi-Jin-Huang-San, a Chinese medicine external preparation, Wai-Ke-Zheng-Zong《外科正宗》, which is a hamous Chinese medical books, can provide some useful effects, such as detoxification, dehumidification and stasis, and swelling and pain. It is the widely used drug in Traumatology therapy in Chinese medical. Particularly, some water is usually added to make it paste, and then it is smeared on the non-woven fabric. Finally, the drug is pasted on the affected area. However, this process is not very convenient, which affects the compliance of patients to use this drug. **【Materials and Methods】** In this research, 1200 milliliters of R.O. water is added to 120 grams of *Ru-Yi-Jin-Huang-San*. Then, the induction cooker is used to heat them for 90 minutes. After that, 400 milliliters of the liquid are filtered by the filter paper. Next, 12 milliliters of Glycerin and 4 grams of Carbopol #940 are put into the liquid. After stirring them evenly, 8.8 milliliters of Triethanolamine is slowly dripped into the liquid. During this process, the litmus paper is used to examine the *pH* value of the liquid until it becomes neutral. Finally, 0.6 milliliter of Mentha Arvensisiol is added into the liquid for generating the new drug. **【Results】**The *pH* value of *Ru-Yi-Jin-Huang-San* based on the traditional approach is acidic, and it is used by pasting to the affected area, which is

likely to make patients allergy. On the contrary, since the *pH* value of the new drug is neutral, the discomfort feeling of patients during the pasting step can be reduced. Moreover, these two pasting ways can be used consequently to enhance the treatment effect. Furthermore, as the new drug belongs to the gel type, the convenience of using it will not be influenced by the size of the affected area and joint parts. It can even simplify the process of using the new drug by some patients who are old or move with difficulty. **【Conclusions】** Due to the advancement of the research and development of the technology, the R&D of traditional Chinese medicines should also keep up to date for patients to use the drugs more conveniently. Consequently, the compliance and efficacy of the patients to use the drugs can be improved.

Key words：Ru-Yi-Jin-Huang-San · gel · Wai-Ke-Zheng-Zong.

PC-11

利用不同檢測參數來探討地黃炮製加工之變化規則性

The Regularity of Variation on the Processing of *Rehmannia glutinosa* using Different Monitoring Parameters

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Abstract

Shu Di Huang, the root of *Rehmannia glutinosa* has to be processed by nine cycles of rice wine immersing, steaming and drying before using in clinical applications. In order to understand the chemical changes regularity from the processing, a comprehensive analysis of Rehmanniae radix was made using different monitoring parameters including the chemical and physical analysis.

The results indicated that catalpol and verbascoside levels gradually decreased during processing, whereas 5-HMF and manninotriose were found to be higher in processed roots. In addition, delayed luminescence (DL), a physical analysis, refers to a decaying long-term ultraweak photon emission after exposure to light, and its decay kinetics under certain conditions is a sensitive indicator reflecting the internal structural and chemical/physiological state of a biological system. Therefore, it has been found that the metabolic profile changed gradually through the processing cycles and their differences became smaller after the fifth processing cycle when we applied DL monitoring system on the processing of Rehmanniae radix.

Key words: *Rehmannia glutinosa*、Processing、Delayed luminescence

PC-12

2D Sepbox System Separation and Molecular Networking Relationship for Traditional Chinese Medicine

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Because of the various bioactivities of natural products, many researchers and chemists have highly interested in Traditional Chinese Medicine. Traditional Chinese Medicine has been used as clinical drugs for thousands of years and a large number of natural products have been purified as medicinal synthesis templates for new drug development. However, the purification of active compounds always spends a lot of time and manpower, and produced many wastes as well. Therefore, good separation models with suitable tools can faster the timeline of this kind of research. In this research, we demonstrated the speedy purification from the crude extract to pure compounds by 2D Sepbox System in one week.

Besides, to avoid the reduplicative work, molecular networking by LC-MS/MS was developed as a new research strategy to identify secondary metabolites in Traditional Chinese Medicine. In this method, we can fine the active or novel compounds rapidly by calculating the MS/MS data of tandem mass spectra and database comparison.

關鍵字/Key words： LC-MS/MS, Molecular Networking, 2D Sepbox System

PC-13

Cinnamomum cassia extracts suppress human lung cancer cells invasion by reducing u-PA/MMP expression through the FAK to ERK pathways

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Abstract

Cinnamomum cassia exhibits antioxidative, apoptotic, and cytostatic properties. These activities have been attributed to the modulation of several biological processes and are beneficial for possible pharmaceutical applications. However, the potential of C. cassia in retarding lung adenocarcinoma cells metastasis remains ambiguous. We determined whether C. cassia extract (CCE) reduces metastasis of human lung adenocarcinoma cells. The results showed that CCE treatment (up to 60 μg/mL) for 24 h exhibited no cytotoxicity on the A549 and H1299 cell lines but inhibited the motility, invasiveness, and migration of these cells by repressing matrix metalloproteinase (MMP)-2 and urokinase-type plasminogen activator (u-PA). CCE also impaired cell adhesion to collagen. CCE significantly reduced p-focal adhesion kinase (FAK) Tyr397, p-FAK Tyr925, p-extracellular signal-regulated kinases (ERK)1/2, and Ras homolog gene family (Rho)A expression. CCE showed anti-metastatic activity of A549 and H1299 cells by repressing u-PA/MMP-2 via FAK to ERK1/2 pathways. These findings may facilitate future clinical trials of lung adenocarcinoma chemotherapy to confirm the promising results.

Key words: FAK; ERK; metastasis; lung cancer; Cinnamomum cassia

PC-14

The components isolated from active LJMWB crude fraction of *Leonurus japonicas*

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Leonurus japonicus Houtt (Chinese motherwort) belongs to Labiatae and is a flowering plant native to Asia. *L. japonicus* had been traditionally used to treat various diseases such as menstrual disturbances, dysmenorrhea, and amenorrhea. The methanol extract of the dried plant was partitioned into EtOAc-soluble (LJME) and aqueous extracts (LJMW), the latter one were further partitioned into *n*-BuOH-soluble fraction (LJMWB). Based on the bioassay results, LJMWB has significant anti-melanogenesis and antioxidant effects. The chromatographic fractionation of the LJMWB extract led to isolation of one new alkaloid (**1**), one liganoside (**2**), five flavonoids, apigenin 7-*O*-β-glucopyranoside (**3**), nicotiflorin (**4**), quercetin 3-*O*-rutinoside (**5**), ilixanthin (**6**), hirsutrin (**7**). Their structures were elucidated by nuclear magnetic resonance. Currently, the isolated compounds are still undergoing bioassay.

Keywords : *L*eonurus *japonicas*, anti-melanogenesis, antioxidant

PC-15

The Study on Five Fruits Phytochemicals based on the Concepts of Five Colors in TCM and the Roles of TCM Dietary Therapies

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Abstract

Huangdineijing pointed out that "the five colors correspond with the five viscera, as the color green is associated with the liver , and the red with the heart, the yellow with the spleen, the white is with the lung and, the black is with the kidney". Huangdineijing showed the importance of fruits in our daily diet: "grains are as nutrition, and fruits are as sustenance". Sun Simiao's Beijiqianjinyaofang also mentioned that before taking any medicines, the food must be used as dietary treatment first, and if it is not effective, then. medicines could be given afterwards. From the concepts of TCM, we understand the importance of daily diet which has been regarded as medicines and so has fruit been. Recent studies have revealed that phytochemicals are proved to be very good antioxidants in medical treatments and they are found mainly in fruit and vegetables, which can be categorized into 5 colors by their appearances. In addition to being an antioxidant, phytochemicals can provide more such as hormonal actions, stimulation of enzymes, interference with DNA replications and so forth, which may help to prevent or cure some human diseases, inflammations, and even cancers. The study focus on the top 5 different color fruits produced in the world. They are banana, apple, grape, pear and lemon/lime, according to FAO 2016 statistics. We analyzed the phytochemicals of the chosen five fruits, to investigate if phytochemicals from each color can have clinical effects on their matched organs based on the color theories in TCM. The dietary habits of eating fruits are also taking into consideration, as most of the phytochemicals are in their peels, and obviously the peels are always discarded. The figures of ORAC or ABTS are used to evaluate antioxidant capabilities by 3 different groups: the fruit flesh, the whole fruit (with peel), and the whole fruit fermented (a better way to eat whole

fruit). The results showed the antioxidant ability is higher in the whole fruit group than flesh only. The study suggested to eat the whole fruit with peel in that way, the phytochemicals can be used as preventive dietary medicines to treat the clinical conditions such as inflammation and cancer with their associated viscera.

關鍵字/Key words：五色 五果 五臟 植化素 食療/ TCM Five Colors, Five Fruits, Five Viscera, Phytochemicals Dietary Therapy

PC-16

cAMP 對靈芝細胞凋亡及靈芝酸生合成之影響

Effect of cAMP on Apoptosis and Ganoderic Acids Biosynthesis in *Ganoderma lucidum*

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Ganoderma lucidum is a well-known traditional Chinese medicine, it contains many active ingredients and widely used in anti-tumor, hepatoprotection and anti-inflammatory. In addition, it has been used as a functional food. However, the biosynthetic regulation of its active ingredients (ganoderic acids, GAs) is poorly understood. Apoptosis signaling in relation to secondary metabolite biosynthesis in plants and fungi also remains a mystery. In this study, we use the phosphorylterase inhibitor, caffeine, and adenylate cyclase activator, NaF, to increase intracellular cAMP (3 ', 5'-cyclic adenosine monophosphate) and induce apoptosis. TUNEL and HPLC analysis was used to evaluate cell apoptosis and ganoderic acids production, respectively. Our results showed that incubation with NaF and caffeine induced apoptosis and increased ganoderic acids production. It suggests that cAMP *signaling* controls apoptosis and ganoderic acids biosynthesis in *Ganoderma lucidum*, and apoptosis induction is a potential approach to induce secondary metabolites in fungi.

關鍵字/Key words：

Apoptosis, *Ganoderma lucidum,* ganoderic acids, cAMP *signaling*, caffeine, NaF

PC-17

菊花木對缺血/再灌流造成心臟失能的保護效果

Protection of Bauhinia championii Againt Ischemia/Reperfusion-Induced Cardiac Dysfunction

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BACKGROUND: Bauhinia championii (BENTH.) BENTH. (BC), is one of the commonly used medicinal herbs in Taiwan. The stem of this plant has been used in treatment of different pains and rheumatoid arthritis. With known nociceptive action, it may have potential to alternate the characteristics of different ion channels. Therefore, this study aims to investigate the effect of boiling water extracts of BC (BCW) on cardiac arrhythmia and myocytes lose in an isolated mice heart model.

MATERIALS AND METHODS: Isolated hearts from 8-12 weeks male C57BL/6JNarl mice were performed with ischemia (30 min)/reperfusion (60 min) (I/R) by left anterior descending artery (LAD) ligation on Langendorff-perfused apparatus. Lead II electrocardiogram (ECG) was also continuously monitored. BCW (10 mg/L) was pretreated 15 min before reperfusion. After reperfusion, hearts were removed for infarct size analysis by 2,3,5-triphenyltetrazolium chloride (TTC) assay. To further determine the underlying mechanism, ventricular myocytes of mice were enzymatically isolated and then action potential, sodium current (INa), L-type calcium current (ICa), and transient outward potassium current (Ito) were recorded using the whole-cell patch clamp technique.

RESULTS: BCW not only decreased the frequency and duration of different types of ventricular arrhythmias, but also reduced infarct size induced by I/R. By patch clamp technique in current-clamp mode, we've found time to peak of action potential was prolonged and action potential amplitude (APA) was reduced in BCW treated cardiomyocytes. On the other hand, the current density of INa, but not ICa and Ito was significantly decreased by BCW in voltage-clamp mode.

CONCULSION: The present study indicates that BCW may prevent I/R-induced ventricular arrhythmias by inhibiting sodium channel. Since most of the clinical antiarrhythmic remedies have their own serious side effects, to develop a novel therapeutic agent against

lethal arrhythmia is still needed. BC, in this concern, will be a new candidate for the treatment of myocardial infarction and ventricular arrhythmia.

關鍵字/Keywords：Ischemia/Reperfusion; Infarct size; Arrhythmia; Ion channel; *Bauhinia championii*

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