CGCM 2018

17th Meeting of the Consortium for Globalization of Chinese Medicine
Borneo Convention Centre, Kuching | 8 - 10 August 2018

Session Natural Products II (Cancer, Virus and Inflammation)

August 9, 2018, 13:45 – 16:15

Session Natural Products II

6b. Natural Products II		Title	Name of Institute
Chairman	Rudolf Bauer	Prof.	University of Graz (Austria)
Co-Chairman	Ding Qu	Prof.	Jiangsu Provincial Academy of Traditional Chinese Medicine
	Fang-Rong Chang	Prof.	Kaohsiung Medical University
	Clara Bik-San Lau	Prof.	The Chinese University of Hong Kong
	Zhengtao Wang	Prof.	Shanghai University of TCM
Panelist	Hongxi Xu	Prof.	Shanghai University of TCM
	Sarita Saraswati	Dr.	King Saud University, Riyadh
	Shu-ling Fu	Prof.	National Yang-Ming University

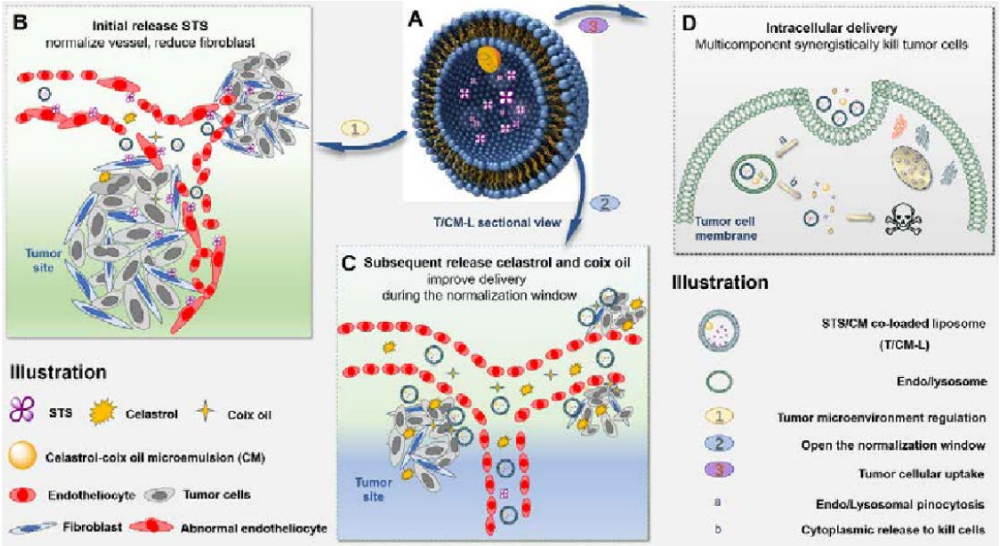
- 30 abstracts submitted, only 16 posters were presented
- 15 submitted abstracts were selected for discussion session
- only 5 followed the invitation and presented
- gap was filled with a general discussion on why drug development from natural products is not more successful

Session Natural Products II

Sequential-released liposome enhances anti-breast cancer efficacy of sodium tanshinone IIA sulfonate and celastrol-based microemulsion

Ding Qu*, Congyan Liu, Mengmeng Huang, Yuping Liu, Yan Chen
Jiangsu Provincial Academy of Traditional Chinese Medicine, Nanjing

A multicomponent-based liposomal system (T/CM-L) composed of sodium tanshinone IIA sulfonate (STS) and a small-sized celastrol-loaded micro-emulsion (CM) showed a synergistic anti-breast cancer activity through initial-released STS for normalization of tumor microenvironment and subsequent-released CM for eradication of tumor cells. T/CM-L is demonstrated as a “small-in-large” structure, staged-release characteristic, high cell apoptosis ratio and coordinated cytotoxicity against MCF-7 cells.



STS was released from T/CM-L rapidly to repair the abnormal vessel and to reduce the number of fibroblasts. Then celastrol was unloaded slowly after crossing over the barrier of microemulsion and liposome to kill tumor cells, resulting in an enhancement on the anti-breast tumor activities. T/CM-L exhibited a low systemic toxicity commonly occurred in the mono-treatment of celastrol.

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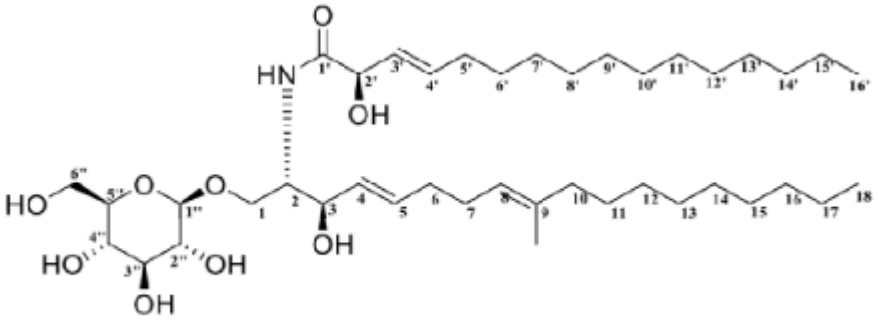
Deciphers on the Chemical Constituents and Biological Activities of the Fruiting Body of *Cordyceps militaris*.

Ching-Peng Chiu[1], Yi-Hong Tsai[1], Fang-Rong Chang[1,2,*]

[1]Graduate Institute of Natural Products, College of Pharmacy, Kaohsiung Medical University Kaohsiung;
[2]National Research Institute of Chinese Medicine, Ministry of Health and Welfare, Taipei

Three cerebrosides and six fatty acids were isolated and identified from the ethanolic extract of *C. militaris*. M-1 to 3 were cerebrosides firstly be reported as ingredients from C. militaris. M-1 is a new compound.

M-2 exhibited a promising potential against NO production at the IC50 value of 8.4 μg/mL. It inhibits the accumulation of pro-inflammatory iNOS protein and reduced the expression of COX-2 protein in LPS-stimulated RAW264.7 macrophages. M-2 also showed an anti-osteoarthritis activity via inhibiting monocyte/macrophage infiltration into synoviocytes, attenuating synovial inflammation and preventing cartilage damage by reducing MCP-1 expression in vitro and in vivo.



Cordycerebroside A (M-1), a new cerebrosides firstly be reported as ingredients from *C. militaris*.

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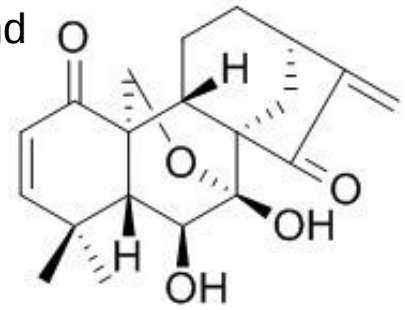
New potential roles of the natural diterpenoid eriocalyxin B in breast cancer

Xunian Zhou[1,2], Grace Gar-Lee Yue[2,3], Stephen Kwok-Wing Tsui[1], Kwok-Pui Fung[1,2,3], Handong Sun[4], Pema-Tenzin Puno[4,*], Clara Bik-San Lau[2,3,*]

[1]School of Biomedical Sciences; [2]Institute of Chinese Medicine; [3]State Key Laboratory of Phytochemistry and Plant Resources in West China, The Chinese University of Hong Kong,Hong Kong ; [4]State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Yunnan

Eriocalyxin B (EriB), has been isolated from *Isodon eriocalyx* var. *laxiflora* and has been reported to possess anti-tumor and anti-inflammatory activities. The anti-angiogenic activities of EriB were studied in human endothelial cells, zebrafish and mouse models, while the anti-tumor effects were evaluated in human breast cancer cells and breast xenograft mouse models.



EriB at 50 or 100 nM significantly suppressed vascular endothelial growth factors (VEGF)-induced cell proliferation, tube formation and cell migration.

It inhibited angiogenesis via down-regulation of VEGFR-2 signaling pathway in human endothelial cells.

EriB at 1.5 or 2.25 μM induced apoptosis and triggered autophagy by inhibition of Akt/mTOR/p70S6K signaling pathway, as well as coordinated the crosstalk between apoptosis and autophagy in both estrogen-positive and estrogen-negative human breast cancer cells.

EriB treatment (10 mg/kg) in breast xenograft-bearing mice could induce autophagy and anti-angiogenic effects. Furthermore, a comprehensive transcriptome analysis in zebrafish embryos after EriB treatment (10 or 15 μM) has been performed.

The findings suggest great potential of this natural compound to be developed as an anti-cancer agent or adjuvant for breast cancer treatment.

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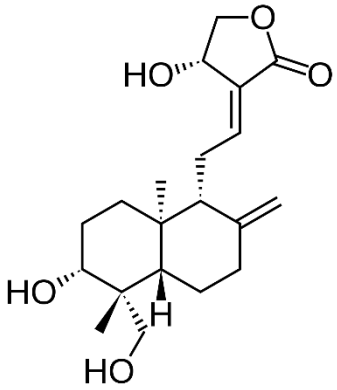
Andrographolide inhibits LPS-induced inflammation by suppressing TLR4-mediated NF-kB and MAP Ks signaling pathways in macrophbages

Na-mi Kim, Peeraphong Lertnimitphun, Yue Lu, Yi-wen Jiang, Hong-sheng Tan, Hong-xi Xu*
School of Pharmacy ,Shanghai University of Traditional Chinese Medicine, Shanghai

Andrographolide (Andro) is a natural compound extracted from *Andrographis paniculata* (Burm. f.) Nees.
The authors investigated the molecular mechanisms of Andro in Lipopolysaccharide(LPS) stimulated murine macrophage cell line RAW264.7 cells, human macrophage cell line U937 cells and murine bone marrow derived macrophages (BMDM).



The results suggest that the anti-inflammatory effect of Andro was attributed to the down-regulation of TLR4-triggered MyD88-dependent signaling pathways, thereby attenuating TLR4 mediated the activation of NF-κB and MAPK signaling and the release of pro-inflammatory cytokines.

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Andrographolide and its potent derivative exhibits multiple anticancer effects against imatinib-resistant chronic myeloid leukemia cells by downregulating Bcr-Abl oncoprotein

Hsin-Chia Liao[1], Yi-Ju Chou[2], Ching-Cheng Lin[1], Sheng-Hung Liu[3], Audrey Oswita[4], and Shu-Ling Fu[*1, 2]

[1]Institute of Traditional Medicine, National Yang-Ming University, Taipei; [2]Program in Molecular Medicine, National Yang-Ming University and Academia Sinica, Taipei; [3]Department and Institute of Pharmacology, [4]Department of Life Sciences and Institute of Genome Sciences, National Yang-Ming University, Taipei

- Andrographolide and the per-acetylated derivative NCTU-322 downregulated Bcr-Abl oncoprotein through an Hsp90-dependent mechanism.
- Andrographolide and NCTU-322 induced multiple effects on both KBM5 and KBM5R cells, including differentiation, apoptosis, and mitosis-arrest.
- Epression profile of myeloid cell-surface markers, which indicates that both compounds could promote monocytic and granulocytic lineage differentiation of KBM5 and KBM5R.
- The data demonstrated that andrographolide and NCTU-322 inhibit Bcr-abl function via a mechanism different from imatinib and both compounds could eliminate imatinib-sensitive and imatinib-resistant CML cancer cells through multiple mechanisms.
- Our finding support that both andrographolide and NCTU-322 are promising therapeutic agents for CML treatment.

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General discussion: why is drug development from natural products not more successful

- Drug market is highly competitive (market protection)
- Besides drug development, establishment of dietary supplements may also be a goal
- Many studies are basic research aiming to explain the activity of medicinal plants
- Development of multi-compound/extract preparations may be more promising
- A focus should be put on diseases in which conventional medicine is not successful
- Development of medicinal products for new pharmacological targets may be more promising (→ research on new targets based on Chinese medicine theory is needed)

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Conclusions and major outcome of the session:

- 14 of 30 posters were not presented
- only 5 of 15 invited authors gave oral presentation in the discussion session
- highlights of the presentations were new promising findings in the research on tanshinone IIA, celastrol, Cordiceps, eriocalycin B, and andrographoilide
- 40-50 participants attended the discussion session
- intensive general discussion strategies and hurdles of drug development out of natural products