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医工薬融合 GCOE Seminar Series

*Center for Medical System Innovation
through Multidisciplinary Integration
The University of Tokyo*

Indigenous-guided Investigation of the Northern Kaanju Medicinal Plant, *Dodonaea Polyandra*

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Date: Wednesday, March 27, 2013

Time: 13:00 - 14:00

**Venue: W5 5F. Seminar room, Faculty of Pharmaceutical Sciences Bldg.,
the University of Tokyo**



In a collaborative research venture between the Chuulangun Aboriginal Corporation and University of South Australia, an Indigenous-guided investigation of the Northern Kaanju medicinal plant, *Dodonaea polyandra*, traditionally used to relieve pain and discomfort from toothache and infection, has been the subject of investigation. Crude extracts initially screened in a model of acute inflammation showed significant inhibition of 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced mouse ear oedema, prompting activity-guided fractionation of the extracts. Several novel compounds identified from this work were elucidated as benzyl ester furanoclerodane diterpenoids, a class of compound not particularly recognized for anti-inflammatory effects. Furthermore, in a chronic model of mouse ear inflammation, which resembles the pathobiology of psoriasis, one compound (DP8)

significantly reduced ear thickness and flaking (scaling) of skin.

Using *in silico* and *in vitro* approaches, the mechanism of action of DP8 is being elucidated. The compound abrogates the secretion of several pro-inflammatory cytokines including IL-1 β , IL-6 and TNF- α from THP-1 monocytes and neonatal human epidermal keratinocytes. IL-1 β from mouse ear tissue homogenate is reduced by 78 % following treatment with 0.4 mg/ear after 6 hr. Histological examination of DP8-treated ear tissue shows a significant reduction in ear thickness and neutrophil infiltration when compared to non-treated controls. The enzymatic activity of a common inflammatory target cyclooxygenase-1 and 2 is not significantly affected by treatment with DP8. Furthermore, protein kinase C which is activated by TPA is not inhibited by the active compound. DP8 is unable to suppress the production of the inflammatory mediator, nitric oxide, in LPS-activated RAW264.7 mouse macrophages.

D. polyandra grows uniquely as distinct separate male and female individuals. Research on the chemistry of a male individual yielded four labdane diterpenoids as major components that were not identified in previous work. Chromatographic analysis of extracts from different individuals has shown that chemical profiles vary with plant gender. Additionally, chemical variability studies indicate that the levels of active compounds differ between individual plants growing within the same location. For one active constituent (DP5), location of growth may affect the amount of the compound produced by this plant species.

Further chemical studies have revealed prenylated flavonoids as non-active constituents, however these may play a supportive role in the efficacy displayed by the active diterpenoids.

Organizer: GCOE Program Center for Medical System Innovation through Multidisciplinary Integration, the University of Tokyo

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Cooperation: Graduate Program for Leaders in Life Innovation, the University of Tokyo

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