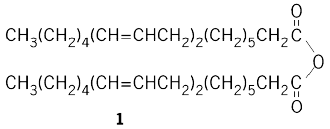
A111 Isolation of inhibitory compounds on melanin biosynthesis in cultured B-16 mouse melanoma cell lines from the cortex of *Machilus thunbergii*

J.K. Son [a], *H.W. Chang* [b], *S.J. Kang* [b], *H. Lee and* S.H. Lee [a]

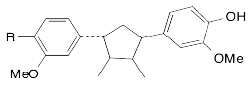
[a] College of Pharmacy Yeungnam University, Kyongsan 712-749, Korea. [b] LG Chemical Ltd./Research Park, Taejon 305-343, Korea.

Melanin polymer is biosynthesized in the melanosome of melanocyte, which is a determinant of human skin color and involved in localized hyperpigmentation such as melasma, ephelide and lentigo. Thus, the biosynthesis inhibitors have been of great concern as cosmetics to have skin-whitening effects on the local hyperpigmentation.

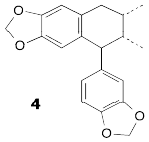
During the search for new inhibitory components on melanin polymer biosynthesis from natural sources, methanol extracts of 100 higher plants were tested for the inhibitory effect on melanin biosynthesis in cultured B-16 mouse melanoma cell lines. Among them, the methanol extract of *Machilus thunbergii* cortex exhibited potent inhibitory effect on melanin polymer synthesis in B-16 mouse melanoma cell lines. Subsequently, we isolated four active compounds from the methanol extract of *M. thunbergii* cortex by the activity guided fractionation. The structures of isolated compounds were identified as linoleic acid anhydride (**1**), (-)-nectandrin A (**2**), nectandrin B (**3**) and machilin A (**4**). And they exhibited IC_{50} value on melaninpolymer formation in cell lines of 120 μg/ml (**1**), 105 μg/ml (**2**), 123 μg/ml (**3**) and 140μg/ml (**4**). Kojic acid as a reference compound exhibited IC_{50} value of 250 μg/ml.



1



R=OMe (**2**)
R=OH (**3**)



4

Acknowledgement: This research was supported by a grant (PF002109-01) from Plant Diversity Research center of 21st century Frontier Research Program funded by Ministry of Science and Technology of Korea government.

A112 Chemoprevention activity of some Southeast Asian plants

C.C. Lee [a], *P.J. Houghton* [b] *and G. Steventon* [c]

[a] Pharmacy Dept, King's College London, 150 Stamford St, London SE1 8WA, UK. [b] Pharmacy Dept, King's College London, 150 Stamford St, London SE1 8WA UK. [c] Pharmacy Dept, King's College London, 150 Stamford St, London SE1 8WA, UK.

The induction of Phase 2 metabolism enzymes, such as gluthathione S-transferases (GST), quinone reductase and sulfotransferases, have been used to indicate chemopreventive potential at the initiation stage of carcinogenesis (1). We have optimised a simple *in vitro* model for assaying the GST induction activity of plant extracts using the human liver hepatoma cell line, HEP G2. GST activity was obtained based on the method of Habig et al. (1974) (2).

The plants tested are reputed to have anticancer properties in SEA.

Crude plant extracts were prepared in methanol, dichloromethane and water. Cells were treated with extracts 24 hours after plating at 250, 25 and 2.5 μg/ml. GST activity was read 48 hours after incubation. Active crude extracts underwent further bioassay-guided fractionation to produce several pure compounds.

Dichloromethane extracts of Thai *Alpinia offinarum*, Thai and Malaysian *Alpinia galanga* and *Cayratia japonica* exhibited significant induction activity at 25 μg/ml compared to solvent controls. The induction ratios were 1.87 fold, 1.65 fold, 1.38 fold and 1.34 fold, all $P \leq 0.05$ analysed with One way Anova, respectively. Malaysian *Jasminum sambac* induced 2.09 fold activity at 250 μg/ml. Phenobarbitone sodium was used as the positive control, yielding an induction of 1.56 fold ($P \leq 0.05$) at 4 mM. A total of 8 compounds have been isolated from fractionation of the Thai *Alpinia officinarum* and the Malaysian *Cayratia japonic*a and are under investigation.

Acknowledgements: Overseas Research Scheme.

References: 1. Lee S.K., et al. (1999) Anticancer Res. 19: 35-44. **2.** Habig W.H., et al. (1974) J. Biol. Chem. 249 (22): 7130-7139.