Gypenosides Inhibited N-acetyltransferase Activity of Human Cervical Cancer Cells and *Nisseria Gonorrhoreae in Vitro* and Distribution and Metabolism of 2-aminofluorene in Spraque-Dawley Rats *in Vivo*

Tsan-Hung Chiu

Major professor: Jung-Chou Chen

Institute of Chinese Medical Science, China Medical College

Gypenosides is a major compound of *Gynostemma pentaphyllum* (thumb) *Makino,* exit the anticancer activity and induced apoptosis from pharmacological studies *in vitro* and *in vivo*. It is well known that arylamine carcinogens should be metabolized by N-acetyltransferase (NAT) to form the activated metabolites, and then to connect with DNA and to form DNA-adducts, finally lead to cancer development. These studies are focused on the effects of gypenosides on the metabolism of arylamine carcinogen *in vitro* and *in vivo.*

In vitro, to examine and measure the changes of level of acetylated 2-aminofluorene (2-AF) and non-acetylated 2-AF by using High Pressure Liquid Chromatograph (HPLC) after human cervix cancer cells with or without co-treatment of various concentrations of gypenosides for various time periods. We also used RT-PCR and cDNA microarray to examine the effect of gypenosides on NAT gene expression from human cervix cancer cell line. In addition, we also examined gypenosides affect the growth and NAT activities in bacteria strain *Nisseria Gonorrhoreae.* Finally, examined the effect of gypenosides of the metabolism of 2-AF from Spraque-Dawley (SD) rats *in vivo.*

The results from the present studies indicate that NAT is presented in human cervix cancer cells and the NAT can acetylate 2-AF and gypenosides did affect NAT activity in these examined cell lines. This effect is dose-dependent and gypenosides is a uncompetitive inhibitor. The results from the RT-PCR and cDNA microarray also indicated that gypenosides

affect NAT mRNA gene expression which may lead to decrease NAT activity, 2-AF metabolism and DNA-adduct formation. Gypenosides also inhibited the growth and NAT activity in bacteria strain *N. Gonorrhoreae* and this effect is dose-dependent. As the concentration of gypenosides up to 450 μg/ml, the inhibition of growth was up to 85%. For NAT in *N. Gonorrhoreae*, the gypenosides is also a uncompetitive inhibitor. *In vivo* studies, gypenosides affect 2-AF acetylation, metabolism and distribution of SD rats after co-treated with AF and gypenosides for 24 hours.

The exact mechanism of gypenosides affect 2-AF metabolism and NAT activity is unclear, but the data clear show gypenosides after oral treatment did also decrease the DNA-adduct formation.

***Key Words*：** Gypenosides, cDNA microarray, human cervix cancer cell line, DNA-adduct formation, 2-aminofluorene, N-acetyltransferase, NAT mRNA,