A105 Immunomodulating antitumor activities of an acidic polysaccharide from Korean red ginseng (*Panax ginseng* C.A. Meyer)

J.D. Park [a], Y.S. Kim [a], H.J. Shin [a], K.M. Park [a], Y.S. Kwak [a], T. Toida [b] and R.J. Linhardt [c]

[a] Div. Of Ginseng Efficacy, KT&G Central Research Institute, Daeduk Science Town, 305-345, Korea. [b] Dept. of Analytical Chemistry, Faculty of Pharmaceutical Sciences, Chiba University, Chiba 263-8522, Japan. [c] Div. of Medicinal and Natural Products Chemistry, University of Iowa, Iowa city, Iowa 52242, USA

A red ginseng acidic polysaccharide (RGAP) with immunomodulating antitumor activities was isolated from Korean red ginseng. The molecular weight of RGAP was estimated to be 12 - 450 kDa by gel filtration chromatography. RGAP was found to increase survival rate and to inhibit of tumor growth significantly in a dose dependent manner in mice transplanted with tumor cells. RGAP significantly promoted nitric oxide (NO) production from peritoneal macrophages both *in vivo* and *in vitro*. Western blot analysis exhibited a newly synthesized inducible nitric oxide synthase (iNOS) protein band in the RGAP treated group. It seems likely that immunomodulating antitumor activities of RGAP are mainly mediated by NO production of macrophage. RGAP was further purified by ultrafiltration and anion exchange chromatography on DEAE-sepharose, followed by gel filtration on Sephacryl S-300 to give an active fraction (GFP) with stronger NO production in murine macrophages. GFP increased survival rate ten times compared to RGAP in male ICR mice transplanted with sarcoma 180 and also showed more potent tumoricidal activities of natural killer cells than RGAP. Sugar composition (mol %) of GFP was found to be arabinose, rhamnose, xylose, galacturonic acid, mannose, galactose, glucose (10:9:1:25:8:20:27) by GC/MS. Additionally, combined treatment of paclitaxel (5 or 15 mg/kg) and RGAP (25 mg/kg) resulted in 28.6 % or 48.2 % increase in life span of ICR mice bearing sarcoma 180 tumor cells, while no obvious effect was shown in single paclitaxel treatment. When a combination of paclitaxel 10 mg/kg) and RGAP (100 mg/kg) was intraperitoneally given to C57BL/6 mice implanted with B16 melanoma, the tumor weight per mouse also decreased by 76.3 %, suggesting RGAP might be used as an adjuvant in medicinal application of paclitaxel. The results suggest that clinical trials of RGAP in immunotherapy against cancer are highly feasible.

A106 New flavans, spirostanol sapogenins, and a pregnane genin from *Tupistra chinensis* and their cytotoxicity

Fang-Rong Chang, [a] Wen-Bin Pan, [a,b] Li-Mei Wei, [a,b] and Yang-Chang Wu [a]

[a] Graduate Institute of Natural Products, Kaohsiung Medical University, Kaohsiung 807, Taiwan. [b] Fooyin Institute of Technology, Kaohsiung County 831, Taiwan.

Three new flavans [tupichinol A-C (**1-3**)], five spirostanol sapogenins (**4-8**), [including three new ones, tupichigenin D-F (**4-6**)], and a new pregnane genin [tupipregnenolone (**9**)], together with sixteen known compounds, were isolated from the underground parts of *Tupistra chinensis*. The structures of the new compounds were elucidated by spectroscopic analysis and chemical evidence. The structures and relative stereochemistry of **1** and **8** were further confirmed by single-crystal X-ray crystallographic analysis. Cytotoxicity of the isolated compounds and some acetyl derivatives against human gastric tumor (NUGC) cells and nasopharyngeal carcinoma (HONE-1) cells were tested. Among them, $^{25(27)}$-pentrogenin, **10**, and ranmogenin A showed cytotoxity against NUGC cells, having inhibition of 100%, 96%, and 80% at a concentration of 50 μM, respectively. $^{25(27)}$-pentrogenin showed cytotoxity against HONE-1 cells, having inhibition of 100% at a concentration of 50 μM.

Acknowledgements: The National Science Council of the Republic of China.

References: 1. Pan W.B.; Chang F.R., et al. (2000) J. Nat. Prod. 63: 861-863. **2.** Pan W.B.; Chang F.R., et al. (2000) Chem. Pharm. Bull. 48: 1350-1353. **3.** Niwa T, et al. (2001) J. Agric. Food. Chem. 49: 177-182.