

### P20-P6-2 Effects of San'oshashinto on ischemia/reperfusion-induced cardiac dysfunction and serum lipid level in ovariectomized rats

Mayuko Sakanashi<sup>1</sup>, Makiko Sakanashi<sup>2</sup>, Katsuhiko Noguchi<sup>1</sup>, Toshihiro Matsuzaki<sup>1</sup>, Junko Nakasone<sup>1</sup>, Matao Sakanashi<sup>1</sup>

<sup>1</sup>Dept. Pharmacol., Sch. Med., Fac. Med., Univ. the Ryukyus, 207 Uehara, Nishihara-cho, Nakagami-gun, Okinawa 903-0215, Japan,

<sup>2</sup>Dept. Anesth., Univ. the Ryukyus Hosp., 207 Uehara, Nishihara-cho, Nakagami-gun, Okinawa 903-0215, Japan

The effects of San'oshashinto (SST) on serum lipid level and mechanical changes in reperfused ischemic hearts of menopause model rats were investigated.

Female Wistar rats (9-week-old) were ovariectomized (OVX) and administered 750 mg/kg/day of SST suspension or tap water (control group) orally. After 4 weeks, the blood was collected to measure serum lipid. The heart was isolated to set on a Langendorff apparatus and exposed to global ischemia for 30 min and reperfusion for 60 min. Changes in left ventricular (LV) function and myocardial contents of high-energy phosphates were measured.

In SST group: (1) ischemic contracture was significantly attenuated and LV end-diastolic pressure was significantly decreased, (2) cardiac dysfunction after reperfusion tended to be ameliorated, (3) myocardial ATP content was significantly higher than that in control group though there were no significant differences in inorganic phosphate and creatine phosphate contents, and (4) total cholesterol and LDL cholesterol were significantly decreased.

Results indicate that SST showed cardioprotective properties in OVX rats accompanied by an increase in ATP production and a decrease in serum lipid.

### P20-P6-4 Effect of novel dietary oil, green nuts oil, on plasma lipids

Mari Okimoto<sup>1</sup>, Yukiko Naito<sup>1</sup>, Shigehiro Tachibana<sup>1</sup>, Mami Furuya<sup>2</sup>, Toru Fukumitsu<sup>1</sup>, Tomoko Nagata<sup>2</sup>, Naoki Ohara<sup>1,4</sup>

<sup>1</sup>Lab. Pharmacol., Hatano Research Institute, Food and Drug Safety Center, Ochiai 729-5, Hadano, Kanagawa 257-8523, Japan, <sup>2</sup>Lab. Pathol., Hatano Research Institute, Food and Drug Safety Center, Ochiai 729-5, Hadano, Kanagawa 257-8523, Japan, <sup>3</sup>Lab. toxicol. II, Hatano Research Institute, Food and Drug Safety Center, Lab. toxicol. II, Hatano Research Institute, Food and Drug Safety Center, <sup>4</sup>Open Res. Center, Kinjyo Gakuin Univ., 2-1723 Omori, Moriyama-ku, Nagoya, Aichi 463-8521, Japan

Green nuts (*plukenetia volubilis* L.) oil is a novel dietary oil and rich in omega-3 fatty acids. Omega-3 fatty acids are known to reduce plasma lipids and to be preventive of inflammatory diseases. In the present study, we intended to examine the effects of green nuts oil on plasma lipids and oxidative stress (urinary 8-isoprostane level), and at the same time, to evaluate the safety of green nuts oil. F344 rats of both sexes were divided into 2 groups, respectively, and fed diets containing 6 w/w% green nuts oil or soybean oil (control) for 26 weeks. After the feeding period, both plasma level of total cholesterol and LDL cholesterol were decreased in the green nuts oil group of both sexes. Free cholesterol and HDL cholesterol level were decreased only in the female green nuts oil group. Urinary 8-isoprostane level was also decreased in the female green nuts oil group. There were no serious abnormalities in toxicological examinations. In conclusion, these results indicated that green nuts oil intake for 26 weeks in rats decreases plasma cholesterol levels and oxidative stress, and reveals no abnormalities in clinical and pathological signs.

### P20-P6-3 Inhibitory effect of piperlongumine on platelet aggregation via glycoprotein VI

Masaya Iwashita<sup>1,2</sup>, Yuiko Nasu<sup>1</sup>, Masaki Saito<sup>1,2,3</sup>, Norimichi Nakahata<sup>1,2,3</sup>

<sup>1</sup>Dept. Cell. Signal., Grad. Sch. Pharmaceut. Sci., Tohoku Univ., Aoba, Aramaki, Aoba-ku, Sendai, Miyagi 980-8578, Japan,

<sup>2</sup>Tohoku Univ. Int. Adv. Res. Edu. Org., Aoba, Aramaki, Aoba-ku, Sendai, Miyagi 980-8578, Japan, <sup>3</sup>21st Century COE Program CRESCENDO, Grad. Sch. Pharmaceut. Sci., Tohoku Univ., Aoba, Aramaki, Aoba-ku, Sendai, Miyagi 980-8578, Japan

*Piper longum* L. has been used as a crude drug for the treatment of the disorder of peripherally poor blood circulation in Asia. In a previous study, we revealed that piperlongumine (PLG), a constituent of *Piper longum* L., was a thromboxane A<sub>2</sub> (TXA<sub>2</sub>) receptor antagonist which inhibited platelet aggregation. Thereafter, we showed that collagen-induced platelet aggregation was inhibited by PLG at lower concentrations than U46619-induced one. In the present study, we examined the inhibitory mechanism of PLG on collagen-induced platelet aggregation. Because collagen-induced platelet aggregation was mediated TXA<sub>2</sub> generation, we examined the effect of PLG on collagen-induced TXA<sub>2</sub> generation and arachidonic acid liberation. As the result, PLG inhibited collagen-induced TXA<sub>2</sub> generation and arachidonic acid liberation. It is suggested that collagen-induced platelet aggregation is mainly mediated via glycoprotein VI (GPVI). Then, we examined the effect of PLG on GPVI agonist convulxin-induced platelet aggregation, phosphatidylinositol hydrolysis and protein phosphorylation. As the result, PLG inhibited the aggregation, phosphatidylinositol hydrolysis and Syk phosphorylation. In conclusion, PLG is a valuable antiplatelet drug with a novel mechanism of action.

### P20-P6-5 Ginsenoside metabolite IH 901 reduced foam cell formation *in vitro*

Jia Yi, Li Xiao-Hui

Dept. Pharm., Third Mil. Med. Univ., Chongqing 400038, China

The current experiment explored the roles of IH 901 on the formation of foam cell sourced from rat peritoneal macrophage. Compared with model group, the formation of foam cell was significantly reduced by IH 901 treatment (50  $\mu$ M and 25  $\mu$ M), while the amount of living cells of 50  $\mu$ M group was lessened compared with other groups. Compared with model group, the contents of total cholesterol, cholesterol ester and CE/TC ratio were significantly reduced in IH 901 50  $\mu$ M and 25  $\mu$ M groups ( $p < 0.05$ ). Meanwhile, there was obvious difference among IH 901 groups. The concentrations of TNF- $\alpha$  and IL-1 in IH 901 high and middle dose groups were reduced remarkable compared with model group. The changes of expression of NF- $\kappa$ B, perilipin and CD36 showed the similar tendency of the results above. There were no noticeable difference between model group and IH 901 low dose group. In conclusion, IH 901 could reduce the formation of foam cell sourced from rat peritoneal macrophage dose dependently. The mechanism may depend on the effects of IH 901 reducing the inflammation reaction of macrophage and the expression of perilipin in foam cell. (supported by National Natural Science Foundation of China No. 30470465, No. 30371768 and No.30672641)