Front Line of Kampo Medicine

Review 1 of Academic Meeting Concerning Pharamaceutical Sciences (2)

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This series introduce latest studies on Kampo medicines presented at the Society's meetings. The second installment of the series will provide the studies presented at The 27th Annual Meeting of Medicinal and Pharmaceutical Society of WAKAN-YAKU.

Quality preservation of crude drugs, Research for identification

Wu et al. of University of Toyama made analysis of diversity of ingredients contained in the products on the peony market and reported that most of the red peonies produced in China were originated from *Paeonia lactiflora* but some were originated from *P. veitchii*. And they further clarified that the red peony originated from *P. veitchii* contains slightly more amounts of paeoniflorin and pentagalloyl glucose than *P.lactiflora*, but ingredients of both spices are not different.

Studies on problems arising from preparing Kampo medicines

Himeno et al. of University of Toyama showed that when a Kampo formula was decocted and the decoction was heated again after being stored for ten hours at room temperature, no changes occurred in the amounts of the ingredients. And they reported there would be no problem if the amount/formula for a daily use was decocted at a time and then divided portions were taken.

Basic pharmacological research for Kampo medicines

Visasul et al. of Niigata University of Pharmacy and Applied Life Sciences reported the effectiveness of *shomyakusan (Generate the Pulse Powder)* for memory disturbance induced in mice when scopolamine was intraperitoneally administered.

Endo, et al. of Kitasato University reported that *saireito (Minor Bupleurum Decoction plus Poria Powder with five Herbs)* and *orengedokuto (Coptis Detoxificating Decoction)* had the effects on ulcerative colitis in mice induced by the oral administration of dextran sulphate.

Oka et al. of University of Toyama reported that they had administered *hachimijiogan* to the models of chronic renal impairment in 5/6 nephrectomized rats and observed renal protective effects by the activation of hypoxia inducing factor 1α. Kanako, et al. of University of Toyama examined renal protective effects of *keishibukuryogan (Cassia Twig and Tuckahoe Pill)* using the same models as above and reported that this Kampo formula had inhibitory effects on the kidney becoming fibrotic - stronger effects that cannot be seen from losartan. And Shibahara, et al. of the same University reported that they had performed gene expression analysis using the remaining portion of the kidney and found there were changes in the expression of the genes involved in kidney becoming fibrotic, such as matrix metallopeptidase or kallikrein. Moreover, Nakatsuka et al of the same University reported that they had administered the single medicinal herb *Rhubarb* to the same models, observing its inhibitory effects on kidney fibrosis, and it had the mechanisms different from those of *keishibukuryogan*.

Jyou et al. of University of Toyam reported that *goreisan (Poria Powder with Five Herbs)* had been administered to models of high blood

pressure induced by giving saline water to hemi-nephrectomized rats, resulting in significant increases in the expressions of Na^+/K^+-ATPase, beta-1 protein, aquaporin 1 and 2, through which *goreisan* improved kidney impairment.

Sakurai, eta al. of University of Toyama compared inhibitory effects for 50 types of protein kinase of 10 kinds of crude drug extracts composing *juzentaihoto (Ten Strong Tonic Herbs Decoction)* and suggested the comparison could be used as an omics research tool.

Kojima et al. of Musashino University reported that they had administered geniposide, which is a composing element of *gardenia fruit*, to spontaneously obese mice (TSOD mice) and observed the inhibitory effects on body weight gain, visceral fat accumulation and subcutaneous fat accumulation.

Yamabe et al. of University of Toyama observed the effects of lowering the levels of blood sugar and blood LDL in spontaneously diabetic mouse models (db/db mice) by administering *Kangen-karyu* (granules), and reported *Kangen-karyu* has the effects of improving diabetes. And, Park et al of the same University reported that they observed the effects of lowering levels of blood sugar, the effects of controlling triglyceride levels, and renal-protective effects by the administration of loganin contained in Asiatic Cornelian Cherry Fruit to the same models.

Kamei et al. of University of Toyama reported that significant declines was observed in increased levels of blood sugar and increased epididymal adipose tissue mass in rat models of obese fed a high-fat diet by the administration of *hachimijiogan*.

Kaminari et al. of Kracie reported that *bofutsushosan (Divaricate Saposhnikovia Miraculous Powder)* had been continuously administered orally to mice fed a high-fat diet, showing the inhibitory effects of weight gain and weight increase of white adipose tissues, suggesting that *bofutsushosan* has anti-obesity effects.

Cho et al. of University of Toyama reported that *chotosan* improved memory disturbance in aging promoted SAM mice and as the mechanisms, the improvement was due to its action of promoting NMDA-type glutamate receptor signals.

Aoki et al of Kitasato University reported that an increase in anti-virus antibody values was observed in influenza virus-infected mice by the administration of *maoto (Ephedra Decoction)*.

Nagai, et al of the same University reported *shoseiryuto (Minor Blue Dragon Decoction)* inhibited antibody value from increasing and showed anti-inflammatory effects and the recovery of the decreased expression of aquaporin 5 in mouse models of airway inflammation induced by ovalbumin inhalation.

Nohara, et al of Meijo University produced frequently sneezing mouse models by nasally administering compound 4/80 to mice and reported the significant inhibitory effects of *shoseiryuto (Minor Blue Dragon Decoction)* and *maobushisaishinto (Ephedra, Aconite and Manchurian Wildginger Decoction)* on frequent sneezing.

Sekiya et al of Kitasato University orally administered *hochuekkito* to mice that was given methotrexate intraperitoneally and compared changes in temperature-controlled expressions of the immunorelated molecule mRNA and they clarified the effects of *hochuekkito* on

immune-enhancement of the intestinal tract.

Yamamoto et al of University of Toyama reported that they had examined the influence of *kakkonto (Pueraria Decoction)* in mouse model of food allergy induced by the oral administration of ovalbumin to mice and observed a significant increase in regulatory T cells, suggesting *kakkonto* has the improving effects on food allergy.

Kimura et al of Ehime University reported that the oral administration of flavonoid contained in Scutellaria Root improved impairment of the dermal layer induced by ultraviolet radiation to hairless mice.

Kimura et al. of University of Toyama reported that in the models of pressure ulcers produced by applying pressure to rats, *kigikenchuto* (*Kigi Middle-Strengthening Decoction*) showed the effect of improving pressure ulcers by suppressing the expression of MCP-1.

Munekata et al. of Keio University reported that the administration of *juzentaihoto (Ten Strong Tonic Herbs Decoction)* to mice increased the expression of interferon-stimulated gene 15 in the lamina propria mucosae of the large intestine, enhancing the production of interferon.

Onuma et al. of Tokyo University of Pharmacy and Life Sciences reported that in cultured hepatocytes of healthy rats treated with the extract of Rhizoma and Radix Forbes *Notopterygium*, enzymes involved in drug metabolism were induced and detoxication of foreign substances was promoted.

Yamada et al. of St. Marianna University School of Medicine reported that in the *yokukansan (Liver-Inhibiting Powder)* administered rabbits, blood flow increased in the orbital short posterior ciliary arteries with lowered ocular pressure.

Handa et al. of Fukuoka University reported that the administration of *yokukansan* to rat models of Alzheimer's induced by treated cerebral ischemia-reperfusion abnormalities + intracerebroventricular administration of amyloid-beta showed the complete recovery effects on memory impairment.

Ito et al. of Kitasato University reported that the antidepressant effects of *kososan (Cyperus and Perilla Leaf Powder)* were observed in the models of depression induced by the application of chronic mild stress to mice.

Hori et al. of Showa University observed that *kamishoyosan (Modified Merry Life Powder)* showed the improving effects on the spontaneous tunnel in menopausal models in ovariectomized mice, suggesting it is effective for unidentified complaints associated with menopause.

Kanayama et al. of The University of Tokushima observed the suppressing effects of *Kujin* Extract (*Sophora Angustifolia* Root Extract) on cytokine expression induced by stimulating rat basophil leukemia cells (RBL-2H3 cells) with IgE, and isolated maackian to identify it as an active ingredient.

Liu of Hokuriku University reported that *yokukansan (Liver-Inhibiting Powder)* showed the protective effects on apoptosis by treating rat PC12 cells derived from pheochromocytoma with Abeta 40.

Clinical research for Kampo drugs

Sato et al. of Oita University reported that the levels of neuropeptides were measured to

compare those before and after the single administration of *goshajinkigan* Extract (*Life-Preserving Kidney-Qi Pill* Extract) in healthy males, showing significant increases that were caused by the administration in the levels of vasoactive intestinal polypeptides and calcitonin gene-related peptides with slightly increased blood flow rates, blood pressures, and pulse rates.

Ozeki et al. of Osaka University reported that there was a significant correlation between stagnant water scores and parameters showing cardiac muscle function.

Watanabe et al. of Suwa Chuo Byoin reported on their experience in which they had made the single administration of *Astragalus* Root or *Hedysarum Polybotrys* Root to patients with chronic kidney disease with the result of a decline in serum creatinine levels in either of them.

Others

Kashu et al. of Hyogo College of Medicine conducted a drug lymphocyte stimulation test (DLST) by treating peripheral lymphocytes prepared from the blood withdrawn from healthy people with crude drug extracts, and clarified that the reactions were found significantly positive to "*Prepared Aconiti Daughter Tuber*" and "*Gardenia Fruit*." They reported that in drug allergy diagnosis, false-positive reactions to these two drugs are prone to be detected.