

Front Line of Kampo Pharmacology

Review of Research Presentations on Kampo Medicines 5

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This series will introduce the recent research and studies relating to Kampo medicines presented at academic conferences. This installment of the series provides presentations made at The 28th Annual Meeting of Medical and Pharmaceutical Society for WAKAN-YAKU held in Toyama on August 27-28, 2011.

Quality control of crude drugs and their discrimination

Doui, et al. of Kanazawa University have clarified that when Ginger is heat-processed, the content amounts of shogaol and gingerol, which are the ingredients that change by processing, correlate with the values measured by a colorimeter based on the property that the color of heat-processed ginger changes depending on the heating method used and/or the heating time applied. They reported that colors can be used for quality evaluation.

Pharmacokinetics of crude drug components

Ochiai, et al. of Hoshi University reported that they have investigated the absorption of hydroxy- α -sanshool (α -HS) and hydroxy- β -sanshool (β -HS) contained in *Zanthoxylum* fruit (Japanese pepper) in the digestive tract with the finding that α -HS becomes the ground substance or matrix of the excrete type transporter and the digestive tract absorption is in the state of being controlled, and when daikenchuto (Major Middle-Strengthening Decoction) which includes *Zanthoxylum* fruit is used, the transporter becomes inhibited and the digestive tract absorption is promoted.

Horii, et al. of Kracie Pharmaceutical, Ltd. reported that they have investigated differences between the extract form and the liquid form of kakkonto (*Pueraria* Decoction) in the digestive tract absorption of ephedrine and pseudoephedrine contained in kakkonto with the findings that there were no differences in the absorption but plasma concentration-time curves were equivalent.

Basic pharmacological study on crude drugs and Kampo formulas

Fujikawa, et al. of Fukuoka University reported that they have observed that in a cerebral ischemia-reperfusion-induced rat model, spatial memory disturbance improved by continuous oral administration of yokukansan (Liver-Inhibiting Powder), which further enhanced the releasing amounts of acetylcholine from the hippocampus, inhibiting neural cell death.

Nakada et al. of University of Toyama reported that they have used kamikihito (Modified Back to the Spleen Decoction) in a Alzheimer's disease model in transgenic mice that had excessive expression of mutant type human genes neuron-specifically induced, with the results that the ability of object-recognition memory significantly improved with a significant decrease in β -amyloid deposition in the hippocampus.

Ouchi, et al. of University of Toyama reported improvements in carelessness-like behaviors in mice exposed to isolation-rearing stress by the continuous administration of sansoninto (Wild Jujube seed Decoction). And they suggest that sansoninto possibly has effects on attention deficit hyperactivity disorder (ADHD).

Kitamura, et al. of University of Toyama reported that they have evaluated the actions of Kampo medicines for neuropathic pain, a side-effect of the

anticancer drug paclitaxel or vincristine, with the findings that shakuyakukanzoto (Peony and Licorice Decoction) and goshajinkigan (Life-Preserving Kidney-Qi Pill) are very useful.

Yoshihisa, et al. of University of Toyama observed that keishibukuryogan (Cassia Twig and Tuckahoe Pill) inhibited the production of inflammatory cytokines when lipopolysaccharide (LPS) was induced to activate in human dermal endothelial cells, suggesting that this formula is effective for microvascular inflammation in patients with dermal inflammatory diseases.

Tamiya, et al. of Osaka City University observed that the administration of tokiinshi (Angerica Decoction, Antipruritus) yielded an increase in the water containing of the stratum corneum and a significant decrease in trans epidermal water loss, suggesting the possibility of this formula to revitalize the turnover time of the stratum corneum slowed down with age and to improve the moist-retention ability and the skin barrier function.

Aburada, et al. of Hoshi Pharmaceutical University observed that in the mice fed the diet containing the extracted matters from gypsum, the expression of aquaporin 3 mRNA in the skin increased. They also observed similar effects in the mice fed CaSO₄, a main ingredient of gypsum.

Namaki, et al. of Gifu Pharmaceutical University reported that maoto (Ephedra Decoction) inhibits airway inflammation provoked by the activation of toll-like receptor ligands in the mouse trachea.

Tachi, et al. of Nagoya City University observed that bofutsushosan (Divaricate Saposchnikovia Miraculous Powder) controlled Niemann-Pick C1-like protein responsible for the absorption of cholesterol in the small-intestinal epithelial cells.

They found the crude drugs of Ginger and Platycodi Radix have the activity, suggesting that bofutsushosan inhibits the absorption of cholesterol while eating

Bai, et al. of Nagoya City University administered shichimotsukokato (Seven Herbs Decoction For Hypertension) to 5/6 nephrectomized rats and observed it had no effects on renal functions but produced a significant improvement in renal hypertension, explaining this improvement mechanism where dimethylarginine dimethylaminohydrolase (DDAH) is induced, lowering the concentration of asymmetric dimethylarginine in blood.

Chiba, et al. of Meijyo University administered juzentaihoto (Ten Strong Tonic Herbs Decoction) to hapten applied mice and then removed and transferred their lymphnodes into naïve mice, which caused the inflammatory activity to appear, reporting that juzentaihoto has the action of inducing regulatory T cells.

Hoshina, et al. of University of Toyama reported that in vitro, ogikenchuto (Astragalus Middle-Strengthening Decoction) has the ability to enhance presentation of antigen when dendritic cells are sensitized by ovalbumin, suggesting that the formula may be useful as an adjuvant for oral vaccines. Likewise, Yamada, et al. of University of Toyama reported on the same activity of juzentaihoto (Ten Strong Tonic Herbs Decoction) and their successful isolation of its effective ingredient of 1,2,3,4,6-penta-O-galloyl- α -D-glucose contained in Paeoniae Radix.

Fukui, et al. of University of Tokushima reported that the extracted matter from Sophorae Radix inhibits the production of interleukin-4 released from rat basophilic leukocytes and they have isolated the effective ingredient of trifolirhizin.

Hyuga, et al of Kitasato University reported that maoto (Ephedra Decoction) inhibits the ability-to-move of human breast cancer cells stimulated by the hepatic growth factor and Ephedra Herba contained in the formula causes the inhibition of tyrosine kinase.

Yamada, et al. of Yokohama City University observed increased flows of the intraorbital posterior ciliary arteries and extraocular arteries in rabbits after the administration of shosaikoto (Minor Bupleurum Decoction), suggesting that this formula is useful for obstructive [angitis](#) in patients with various types of cancer.

Yamaguchi, et al. of Fukuoka University reported that yokukansan (Liver-Inhibiting Powder) improves anxiety-like behaviors in rat cerebral ischemia-reperfusion injury models, explaining that the improvement is caused by the 5-HT_{2A} receptor mediated mechanism.

Iwaoka, et al. of Hyogo University of Health Sciences removed and cultured rat dorsal root ganglia with an addition of Euodiae Fructus thereon and observed the increasing of Ca²⁺ concentration in neurons, suggesting that the analgesic effect is permitted by the mechanism of mediating TRPV1 activation action. They also reported they have isolated the effective ingredient of evodiamine.

Oda, et al. of University of Toyama liberated various crude drugs for the cells having TRP channels expressed forcibly and observed the action of activating TRPV1 in Rhubarb and isolated the effective ingredient of senidine, which, they found, was unrelated to the purging effect of Rhubarb.

Takayama, et al. of Fukuyama University investigated mechanisms of the purging action of daiokanzoto (Rhubarb and Licorice Decoction) in mice with the findings that liquiritin contained in

Licorice promotes the action of sennoside A and individual types of antibiotics significantly inhibit the purging action of sennoside A.

Endo, et al. of Kitasato University administered rikkunshito (Six Gentlemen Decoction) to mice and observed an increased activity of gastric motility and emptying in healthy mice and, on the contrary, an inhibiting effect in food-deprived mice, reporting that rikkunshito has complex mechanisms with multiple points of action.

Jo, et al. of University of Toyama reported that peripheral edema in rats induced when pioglitazone is administered can be improved by the use of goreisan (Poria Powder with Five Herbs).

Ito, et al. of Kitasato University have clarified the antidepressant action of kososan (Cyperus and Perilla Leaf Powder) using a stress-induced depression-like mouse model, reporting that the regulation of orexin and neuropeptide Y nervous system network in the brain is involved in the mechanism. Nagai, et al. further made proteome analysis of mouse serum and observed a decreased level of complement C3 due to kososan. Okuda, et al. conducted proteome analysis of hippocampi of the mice and reported that tropomyosin α -1 chain can be recovered.

Yamamoto, et al. of University of Toyama isolated CD4⁺ Tcells, which recognize OVA, from mouse lymphatic tissues and showed that kakkonto (Pueraria Decoction) inhibits the proliferation of cells when stimulated with OVA. They reported that the action of improving food allergies can be expected in kakkonto.

Kigasawa, et al. of University of Toyama clarified that in mice, byakkokaninjinto (White Tiger plus Ginseng Decoction) inhibits the differentiation of femoral bone marrow cells into mature dendritic

cells and reported that this formula has the action of immune regulation.

Nishimoto, et al. of Kitasato University analyzed active ingredients of immunoregulatory factors induced by having hochuekkito (Middle-Reinforcing and Qi-Benefiting Decoction) act on rat duodenum-derived epithelial cell lines and then isolated four types of sugar chains with a molecular weight of 37,000-40,000/each.

Kimura, et al. of University of Toyama evaluated curative effects of kigikenchuto (Angelica Root Middle-Strengthening Decoction) in a rat model with pressure ulcers induced by applying repetitive pressure, observing the enhanced growth of new blood vessels and increased actin-positive myofibroblastic cells. They suggest that the formula is potentially useful for pressure ulcer treatment.

Yanagihara, et al. of Osaka City University reported that hochuekkito (Middle-Reinforcing and Qi-Benefiting Decoction) improves skin hazards in hairless mice caused by ultraviolet radiation through the antioxidant action of the formula.