

The special features of Japanese Kampo medicine

Kenji Watanabe, Pengfei Gao

Center for Kampo Medicine, Keio University, School of Medicine, Tokyo, Japan

The history of Kampo medicine: Ancient Chinese herbal medicine was introduced into Japan since the 5th century. The term *Kampo* literally means “method from Han-period China” (2nd century AD). The basic therapeutic handbook for the clinical usage of herbal prescriptions was the *Shang han lun*. It was during the Edo-period from 1600 onward, that the specific Japanese characteristics of Kampo medicine were shaped. Japanese clinicians moved away from the highly theoretical and speculative nature of Chinese medicine as not being adequate to meet the problems of every day practice. The complaints of the patient and his bodily symptoms were again put into the center of consideration. This individual symptom profile, the Kampo diagnosis (*sho*), directly led to the selection of the appropriate herbal prescription. As additional diagnostic tool, a refined abdominal palpation technique (*fukushin*) was developed. **Recent development of Kampo:** Since the founding of the Japan Society of Oriental Medicine in 1950, its membership increased from 98 to more than 8000 today, of which more than half are medical doctors. 148 different Kampo formulae are covered by the Japanese national health insurance system. Only licensed physicians are allowed to prescribe Kampo drugs. In the past 30 years, extensive basic research revealed the high quality of the Kampo extracts with respect to toxins, pesticides, microbes, and heavy metals. In the same period, significant scientific evidence has been accumulated to understand the pharmacology of Kampo formulae. Moreover, most clinical studies on Kampo are guided by an evidence based medicine (EBM) approach. For example, the Kampo drug *Daikenchu-to* is currently being investigated in a multicenter, double-blinded, placebo-controlled study involving 80% of nation-wide university hospitals to study its benefits and mechanisms of action. **The future of Kampo:** Over the last few years, the U.S. Food and Drug Administration started to pay attention to Kampo due to its high quality and standardized ingredients. The U.S. National Center for Complementary and Alternative Medicine (NCCAM) has also allocated greater funds for research in herbal medicine. Based on recent studies, like the *Daikenchu-to* study in Japan, Kampo drugs may emerge as leading candidates for the next series of international clinical and experimental research.

Maintaining the redox-balance intact: Treatment with Gosha-jinki-gan prevents oxidative stress reactions and induces soluble guanylate cyclase activation in rat diabetic retinopathy

Silke Cameron^{1,2,3,4}, Toshihiko Hanawa¹, Makoto Suematsu², and Kenji Watanabe³

¹Oriental Medicine Research Center of the Kitasato Institute, Tokyo 108-8642; ²Department of Biochemistry and Integrative Medical Biology, Keio University School of Medicine, Tokyo 160-8582; ³Department of Oriental Medicine, Keio University School of Medicine, Tokyo 160-8582; ⁴current address: Department of Gastroenterology and Endocrinology, Georg-August University, 37099 Goettingen, Germany

Introduction: Diabetic complications are recognized as major health burden in the Western world. However, the diagnosis of diabetic complications is delayed as symptoms are non-specific. Strategies to prevent hyperglycemia-induced cytotoxic reactive oxygen species in the retina include the prevention of free radical production and the activation of radical-scavenging capacities. This study examined the effect of the standardized Japanese herbal extract product *Gosha-jinki-gan* (GJG) in comparison to insulin treatment in the rat retina.

Methods: Diabetes was induced in male Wistar rats by single injection of streptozotocin (STZ 50 mg/kg i.p.). At 6 and 12 weeks, eye-cups were removed for immunohistochemistry. Regional lipid peroxidation and nitrosyl stress were tested with the anti-acrolein (Ab5F6) and the anti-nitrotyrosine antibody (NO₂-Y) respectively. The gas-mediated activation of soluble guanylate cyclase (sGC) was examined using the function-sensing antibody MoAb 3221 and compared to the function-insensitive MoAb 28131 antibody. The induction of NO-product ion was tested with the anti-iNOS-antibody. **Results:** At 6 weeks after STZ injection, iNOS induction became evident in Müller's glial cells, coinciding with overproduction of nitrotyrosine. At 12 weeks, lipid peroxidation was enhanced significantly in the untreated diabetic group. In both treatment groups, staining intensities with the NO₂-Y and anti-acrolein-antibodies were significantly reduced. As an early treatment effect, GJG – but not insulin - enhanced sGC activation, as compared to the non-diabetic control. **Conclusion:** In our model of experimental diabetic retinopathy, GJG reduces nitroxidative stress and lipid peroxidation. We further propose that the high glucose turnover in the insulin-treated model disturbs the intracellular redox equilibrium, one result of which might be the impaired sGC activation.

Effects of Japanese Kampo medicines on histopathological findings in diabetic animal models

Takeshi Sakiyama, Chizuko Hashimoto, Shigeko Ohnuma, Mieko Funatsu, Mamoru Tadokoro

Department of General Internal Medicine and Diagnostic Pathology, St Marianna University School of Medicine, Kawasaki, Kanagawa, Japan

Aim: Many patients with Diabetes Mellitus (DM) and its co-morbidities like metabolic syndrome are treated with ethical traditional Japanese Kampo drugs (JKd) in Japan. Their efficacy for patients or diabetic animal models is reported elsewhere. However, reports on the influence of JKd on histopathological findings are few. Here we focus on histopathological effects of several JKd on genetic diabetic animals. **Material and Methods:** Wister fatty rats, db/db mice and ob/ob mice were used as DM II and DMI models, respectively. The DMII animal models orally received the JKd *Boi-ogi-to* at a concentration of 2,5g/l for free intake, a control group only water. The DMI animal models received the JKd *Hachimi-jio-gan* or *Gosha-jinki-gan*, there was also a control group. All animals were continuously monitored and finally examined histopathologically after 3, 6 or 12 months of treatment for *Boi-ogi-to* and 3, 6 or 9 months of treatment for *Hachimi-jio-gan* or *Gosha-jinki-gan*, respectively. **Results:** As for DMII, the *Boi-ogi-to* group of Wister fatty rats showed a clear reduction of their blood glucose levels and their body and liver weights in comparison with the control group. The histochemical examination of the liver revealed that the ability of glycogen storage was better in the *Boi-ogi-to* group than in the control group. As for db/db mice, the *Boi-ogi-to* group also showed a decrease both in body and liver weights, but there was no remarkable histochemical change in the liver. As for DMI animals, there were no significant clinical and histochemical differences between the *Hachimi-jio-gan* or *Gosha-jinki-gan* groups and the control group. However, in the pancreatic beta-cells of JKd treated animals, a tendency was detected of keeping granules and showing few degranulation in electron-microscopic findings. **Conclusion:** JKd show effects in diabetic animal models which can be demonstrated not only biochemically but also histopathologically.

Efficacy of *Hange-koboku-to* on patients with functional dyspepsia with special reference to gastrointestinal function

Tetsuro Oikawa, Go Ito, Toshihiko Hanawa

Oriental Medicine Research Center, Kitasato University, Tokyo, Japan

Background: Limited evidence is available as to whether Kampo medicine modifies gastrointestinal function in humans. *Hange-koboku-to* (HKT), a traditional Kampo formula, is classically considered one of the representative formulations to improve abdominal bloating. **Methods:** Thirty patients with functional dyspepsia (FD) (12 men and 18 women, mean age 54.5 years) were enrolled. We administered HKT to the patients with FD for 2 weeks. Before and after this administration, the gastric emptying rate (GER) was estimated with regard to gastric motility using ultrasonography. The bowel gas volume was calculated from a plain abdominal radiogram from the standpoint of bowel gas retention, and was shown as gas volume score (GVS). We also assessed the gastrointestinal symptoms of the FD patients using the gastrointestinal symptom rating scale. **Results:** GER in FD patients was significantly lower than in the healthy subjects. GER in FD patient showed a significant increase after medication with HKT. GVS in FD patients was significantly higher than that in the healthy subjects. Administration of HKT in the FD patients showed a significant decrease of GVS. Gastrointestinal symptoms improved significantly in the FD patients after the administration of HKT. **Conclusion:** These results suggest that HKT improves both gastrointestinal function and symptoms in FD patients.

A reflection on the place of a Kampo practitioner in an action research project team – the Westminster University Menopause study

Ann Bradford

University of Westminster, London, United Kingdom

Background: Action research is a form of research in which practitioners reflect systematically on their practice, implementing informed action to bring about improvement in practice. At Westminster University a grant has been given to carry out action research looking at how acupuncture and herbs may help women with menopausal symptoms. Women who fit the study criteria are recruited to have 12 sessions of treatment; the treatment received by the patient is decided by the practitioner (and according to the practitioners practice modality). Monthly meetings are arranged whereby the researcher practitioners discuss problems and progress and practitioner's approaches to treatment. One of the aims of the study is to find out if a group of practitioners share a similar approach to patients with similar symptoms and if this is reflected in the formulae prescribed and treatments given. In the case of the Westminster study, of the seven practitioners participating, only one practitioner uses Japanese Kampo herbal medicine.

Outline: A brief presentation on the current 'action research' menopause study being carried out at Westminster University and a reflection on the place of Japanese Kampo medicine in this study when the other participating practitioners use Chinese herbal medicine

Efficacy of ethical Japanese Kampo extracts on influenza infection

Tomoaki Ishikawa¹, Yukiji Sakaeyama^{2,3}, Yuki Ishikawa¹, Takeshi Sakiyama^{1,3}

¹Ishikawa Clinic, Hino, Tokyo, ²Sakaeyama Clinic, Machida, Tokyo, ³St Marianna University School of Medicine, Kawasaki, Kanagawa, Japan

Background: Since the first case of new pandemic influenza (new-flu) from Mexico was broadcasted, world-wide spread has been reported including in Japan. Previous influenza episodes such as the Spanish flu in 1918 had been cared and treated with Japanese Kampo drugs (JKd) with recognized effects at a time where anti-viral drugs were not available. Japanese Kampo doctors have always used JKd for influenza on the basis of longstanding experiences and knowledge. Recently, pharmacological effects of crude drugs, such as *Mao* (Ephedra Herb) and *Keishi* (Cinnamon Bark) have been demonstrated with respect to an inhibition of the viral reproduction. **Aim:** In order to clarify the effectiveness of JKd against seasonal influenza (season-flu) and new-flu, we characterized the different clinical signs and symptoms (s&s), the choice of adequate JKd, and their effects. **Materials and Methods:** 52 patients with season-flu and 110 patients with new-flu were studied for their s&s, and the selection of the adequate JKd under the characteristic Kampo diagnosis was discussed. While season-flu was mainly treated with *Mao-to*, patients with new-flu were treated with several JKd such as *Mao-to*, *Kakkon-to*, *Shosaiko-to* et al, according to their s&s. **Results:** Most patients with flu-infection were teenagers both in season-flu and new-flu. Elevated fever was mainly 38-38.9°C in cases of season-flu which was alleviated within 2 days (72.2%) by using *Mao-to*. However, after the fever went down some patients needed a subsequent treatment by other JKd. Many patients with new-flu showed several different s&s, which initially could be interpreted in most cases as “three yang stage” by Kampo diagnosis with relatively low grade fever. On the contrary, patients with season-flu often showed “tai yang stage” with high fever. According to their s&s, various kinds of JKd were medicated for each patient, which finally led to a restoration of health. **Conclusion:** Patients with season-flu and new-flu were cured without remarkable side effects by applying JKd according to established Kampo diagnostics. Although the therapy with anti-viral drugs is popular to treat both influenza types in Japan, several problems such as appearance of virus resistance against anti-viral drugs and unclear neurological side-effects are not dissolved yet. On the contrary, JKd show few side effects and there is no resistance problem. The treatment should follow adequate Kampo diagnostic procedures.

Comparison of *Rikkunshi-to* and *Koso-san* for patients with functional dyspepsia and irritable bowel syndrome

Heidrun Reissenweber

Research Unit for Japanese Phytotherapy (Kampo), University of Munich, Germany

Introduction: In modern industrialized societies about 20% of the population suffer from functional gastrointestinal disorders. Often patients present with an overlap of symptoms of the upper gastrointestinal tract accompanied by diarrhea-type irritable bowel syndrome. For the treatment of this condition Kampo medicine has shown considerable value in Japan. Depending on the individual symptom profile (*sho*) of the patient, several traditional formulae may be applied, finding *Rikkunshi-to* on the first place. Due to its high contents of Ginseng, this formula is most efficacious for patients with *ki-deficiency* presenting with weakness, fatigability and feeling of coldness in combination with their gastrointestinal complaints of epigastrical fullness and pain, nausea, and diarrhea. In contrast, our clinical experience shows that patients with symptoms of *ki-stagnation*, who present with nervousness, depression, neurotic tendency and dizziness, in combination with their leading gastrointestinal complaints of epigastric pain, bloating and occasional diarrhea, gain more benefit from the treatment with the formula *Koso-san*, containing Cyperi rhizome and Perillae folia. We here present data of our clinical observations comparing *Rikkunshi-to* and *Koso-san* in outpatients in Germany. **Methods:** 38 patients, mean age 51(±6), with the Western diagnosis of an overlap of functional dyspepsia accompanied by diarrhea-type irritable bowel syndrome who either fitted to the *sho* of *Rikkunshi-to* or the *sho* of *Koso-san* were evaluated according to a five-scale functional gastrointestinal disorder score. The symptoms evaluated were: epigastric fullness, epigastric pain, nausea, abdominal pain, bloating and diarrhea. For each symptom intensity and frequency from 0 to 4 were scored. In the *Rikkunshi-to* subgroup additionally fatigability and coldness were evaluated, in the *Koso-san* subgroup nervousness and depression were scored. Primary endpoint was the change in the functional gastrointestinal disorder score. **Results:** In both subgroups (*Rikkunshi-to* 15 patients, *Koso-san* 13 patients) the symptoms were evaluated before treatment, after 4 weeks, 8 weeks and 12 weeks of treatment. A clinically meaningful improvement of symptoms by more than 55% was found after 12 weeks of treatment in both subgroups with slight but specific differences. **Conclusion:** This clinical observation with a limited Western study population takes the individualized treatment approach of Kampo medicine into account, breaking down a Western diagnosis into subgroups according to the traditional diagnostic approach. Thus it contributes to the current discussion of finding an adequate research methodology in CAM clinical research.

Effectiveness of Kampo medicine in Western Countries: two case reports

Ulrich Eberhard

Kampo Clinic, Madrid, Spain

The application of Japanese Kampo phytotherapy in daily clinical practice in a Western environment will be demonstrated by means of two clinical cases. In both cases, Kampo was applied to patients suffering from diseases of the musculoskeletal system (rheumatoid arthritis in one female and osteoarthritis in another). Both patients had been diagnosed and treated conventionally by Western medicine before attending Kampo consultation. The specific Kampo diagnostics (*shoho*-determination) was applied for diagnosis and treatment according to traditional practice. Due to Kampo therapy, both patients' pain could be controlled and the RA patient became independent from modern antiinflammatory or antirheumatic drugs. The set of symptoms which the patients presented improved during the course of application of several classical Kampo prescriptions (*Eppi-ka-jutsu-to*, *Yokui-nin-to*, *Keishi-bukuryo-gan*, *Boi-ogi-to*). Besides the apparent effectiveness of Kampo prescriptions, both cases show a characteristic feature of Kampo-Medicine which is of great importance for the process of the treatment: the adaptation of the prescription (*shoho*-adaptation) during the treatment according to the change of the clinical picture.

Evaluating the efficacy and effectiveness of Kampo - methodological considerations

Claudia M. Witt

Institute for Social Medicine, Epidemiology and Health Economics, Charité University Medical Center, 10098 Berlin, Germany

Kampo is “whole medical systems” and uses a complex approach for the diagnosis and treatment. According to NCCAM whole medical systems are systems that are built upon complete systems of theory and practice and have evolved prior and separate from the conventional medical approach. In addition, most of them use an individualized treatment approach. For clinical studies, whole medical systems have to be broken down to single interventions to allow for comparison with a placebo. Furthermore, in these so-called efficacy studies the interventions are mainly applied in a standardized manner, whereas in practice they are usually tailored to the individual patient. When developing a treatment protocol for a clinical study, the theoretical basis of the medical system and the available health service data on the usage in routine care should be considered, to assure that this trial reflects usual care. There are at least two options: 1) Individualized treatment protocols could be included into placebo-controlled trials. 2) Pragmatic clinical trials (PCT) are the adequate design for an evaluation of whole medical systems. A PCT is a randomized trial with the aim to inform decision making. The focus is on effectiveness instead of efficacy by using a less standardized treatment protocol, less narrow inclusion and exclusion criteria and patient centered outcomes. To conclude, randomized trials are the appropriate study design for testing efficacy or effectiveness of Kampo, however, within the trial; the traditional aspects of Kampo should be taken into account.

Japanese Kampo Medicine within the Health Care System of Japan: the role of the Japan Society for Oriental Medicine

The Japan Society for Oriental Medicine (Takeshi Sakiyama, Kenji Watanabe, Kiichiro Tsutani, Katsutoshi Terasawa),

Minato-ku, Tokyo, Japan

Background: After the Meiji Restoration in 1868, a qualification in Western medicine became the precondition to gain a medical doctor's license in Japan. Therefore, the traditional Japanese Kampo Medicine (JKM) lost its institutional basis and declined. However, a few Kampo specialists and pharmacists preserved the traditional heritage. In modern society, a new interest in JKM emerged. At present, traditional Japanese Kampo drugs (JKd) are approved as ethical drugs and covered by the National Health Insurance. Almost 80% of modern medical doctors are using JKd in their daily practice. In 2001, education in JKM was officially included into the main curriculum of the medical education system, requiring students to study the basic concepts of JKM. Because integration into modern medicine is indispensable, JKM is required to establish a standardization of its traditional terminology. Suitable textbooks for graduate and post-graduate education have to be written and a standard for quality, safety and efficacy of JKd has to be established, the requirements for evidence based medicine have to be fulfilled, etc. **Aim:** Western medicine has developed supreme diagnostic procedures, but for many indications the treatment is only based on statistical efficacy for large patients' cohorts without paying enough attention to the individual condition. JKM has developed refined tools to determine the individual condition of the patient. In order to apply JKM within an international context, the requirements for safety, efficacy and quality of JKd have to be fulfilled. The Japan Society for Oriental Medicine (JSOM) has been engaged in the promotion of JKM for 60 years now. Here we present recent activities of JSOM:

1. Participation in WHO headed international cooperations to establish a standard terminology of traditional medicine 2007.
2. International cooperation to establish an ICD for traditional diagnostic entities.
3. Publication of textbooks of JKM for students and Kampo specialists.
4. Publication of an "Evidence Report of Kampo Treatment 2009", which contains 320 randomized controlled trials in Japanese and English on the JSOM website.
5. Analysis of profitability of JKM, for common diseases, senile disorders and so on – including a comparative study between JKd and synthetic products.
6. Task Force to create Clinical Practice Guidelines for Kampo products in Japan.
7. Many domestic activities including publishing the official journal of JSOM.

A patient-oriented evaluation system for Kampo Medicine by using a new medical interviewing system

Matsuura Keiko¹, Tokunaga Hideaki¹, Imazu Yoshinori¹, Nishimura Ko¹, Imoto Seiya², Yamaguchi Rui², Nagasaki Masao², Saito Ayumu², Miyano Satoru², Watanabe Kenji¹

¹Center for Kampo Medicine, School of Medicine Keio University, 35 Shinano-machi, Shinjuku-ku 160-8582, Tokyo, Japan. ²Human Genome Center, Institute of Medical Science, University of Tokyo, Japan

Background: Kampo medicine is characterized by individually prescribed tailored formulae. This treatment has the advantage of curing several symptoms at the same time with only one or a few formula. Mainly subjective complaints are taken into account for the selection of the right formula. However, how these subjective complaints should be evaluated is not established. **Purpose:** To introduce an evaluation system for subjective complaints that is referred to a medical interviewing system, and to show examples of practical use with this system. **Methods:** We developed a computer based medical interviewing system that can be easily used by touch panel. Kampo diagnosis is based on the concept of the “*sho*” diagnostic system, where a specific set of symptoms leads to the selection of a specific formula. The patient has to tell his complaints and states the severity of the symptom by visual analogue scale. The doctor then makes an input in the categories “*sho*”, “Western disease” and “Kampo prescription” based on his diagnosis. Thus, during the period from June 2008 until January 2009, 953 records were compiled from new patients at the Kampo Clinic of Keio University. **Results:** We report the results of our analysis of 97 records of patients who were diagnosed with “*Hie-sho*” (coldness). This disorder is considered to be effectively treated by Kampo medicine. First, we extracted frequent sets of “*sho*” that could be simultaneously diagnosed in coldness. By using Eclat algorithm (support > 0.5%), 4637 frequent sets of “*sho*” were defined. We then determined the specific sets for coldness by comparing them with the sets for non-coldness (856 records). For each set, we created a 2x2 contingency table and performed Fisher’s exact test. Using 0.1 as the cutoff for q-value, 79 frequent sets were identified as coldness-specific. These 79 sets were classified into 4 groups by cluster analysis. Now the corresponding Kampo prescriptions for these 79 sets were extracted and analyzed with respect to their efficacy after 3month of treatment by using Logistic and Elastic Net. **Conclusions:** We obtained new perspectives on Kampo medicine based on the data of this medical interviewing system. These perspectives enable us not only to give more consideration to the patient’s view, but also to differentiate between therapeutic implications.

Comparison of the educational systems for traditional medicine in Japan and China

Pengfei Gao, Kenji Watanabe

Center for Kampo Medicine, Keio University, School of Medicine, Tokyo, Japan

Background: Kampo medicine is the term for the Japanese kind of traditional medicine. It is rooted in ancient Chinese medicine and has been modified in Japan in a unique way. There are different education systems for medical students and doctors with respect to traditional medicine in Japan and China. **Aim:** To compare the educational systems for traditional medicine between Japan and China. **Results:** In Japan, all medical students have to study modern Western medicine. There is no special college or university only for training in Kampo medicine. However, Kampo medicine has been integrated into the core curriculum of undergraduate medical education in all medical colleges since 2001. Thus, all students obtain a basic knowledge of Kampo medicine. In addition, there are several institutions which offer postgraduate education in Kampo medicine and thoroughly trained Kampo specialists have been increasing in recent years. In China, there are 23 special colleges or universities for Traditional Chinese Medicine (TCM). The proportion of teaching hours in TCM is two third, in Western medicine it is one third, it takes five years to graduate. Even in medical colleges which specialize on Western medicine, students usually have 80 hours' of TCM courses. In Japan, Kampo education puts a special focus on the study of Han-dynasty (2nd century AD) medical works. Especially Zhang Zhongjing's work *Shanghan-zabing-lun* (Treatise on Febrile and Miscellaneous Diseases) is extensively studied and still influences daily practice. In China, TCM doctors rely in their daily clinical work on traditional theories of Chinese medicine such as the Yin-Yang theory, the Five-elements-theory or the relationship between meridians and organs. **Conclusion:** Traditional medicine has become an integral part of the health care systems both in Japan and China which is reflected in different educational systems. In order to improve the quality of traditional medical education ideas should be exchanged.

Kampo: ours, or theirs? A model for disentangling Japanese Kampo Medicine from Traditional Chinese Medicine

Gretchen De Soriano

Medical Anthropology Research Group, Green Templeton College, Oxford University, Oxford, United Kingdom

Kampo is said to be *the traditional medicine of Japan* which is a curious statement, given that the title, *Kampo*, denotes *the Medicine of the Han* which surely began in China during the historical period known as the Han Dynasty. How then could there be *Japanese Kampo Medicine*? A study of other medical systems reveals traditional British medicine to be firmly rooted in Greek and European tradition. What is currently called *Traditional Chinese Medicine* differs from other forms of Chinese medicine currently practiced in China, yet this one form is called *Traditional*. The traditional Mayan medicine *curandero* practices indigenous needling techniques which resemble acupuncture, thought to be Asian in origin. These examples demonstrate that what is called a traditional medicine of any one country is notoriously difficult to define. Medical Anthropologists study the cultural and social aspects which humanise medicine, rather than focus on biomedical properties. Anthropologists expect a medical tradition to be *meaningful* to a population, and recognise the traditional medicine of a region by looking at a different set of criteria from that of a medical historian, who might be informed primarily by the historical records. This paper proposes a model: that a nation's *traditional medicine can become visible — and therefore acknowledged — when it clashes with an established medicine practice*. We tentatively explore this through examples of the medical systems recognised as Traditional British, Traditional Mayan, Traditional Chinese and Traditional Japanese. As evidence we examine writings from scholars — both medical anthropologists and medical historians — from contemporary practice and fieldwork.