Chinese Herbal Formulas Every Western Practitioner Should Know—Part 1

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Abstract

Four important herbal formulas from Chinese medicine are discussed from the standpoint of their uses in Western medicine. The research supporting their efficacy for a wide range of conditions and safety are reviewed. Xiaŏ chái hú tāng (sho-saiko-tō), sì jūn zĭ tāng (shikunshi-tō), bŭ zhōng yì qì tāng (hochu-ekki-tō), and sháo yào gān căo tāng (shakuyaku-kanzo-tō) are discussed in sufficient depth for Western practitioners of natural medicine to begin to incorporate them into their practices.

Introduction

Chinese and other East Asian traditional herbal medicine systems are ancient and well-documented, and they provide many effective therapies. Formulae from these systems have been around for hundreds or thousands of years and have been refined to a state of high utility, but are sadly little known in the West. These formulas originated in China but were avidly taken up into Japanese and Korean traditional medicines and have been studied in all three countries in modern times.

This article, together with a second article in the next issue of the Journal, illuminates some of the most useful formulas. This is by no means a comprehensive review of Traditional Chinese Medicine (TCM) and offers only a small glimpse into the potential of these medicines (Table 1).

The formulas are discussed using a Western medical approach to make the information more useful to Western herbal practitioners. Readers who seek a traditional Chinese concept of these formulas should consult *Chinese Herbal Medicine: Formulas and Strategies, 2nd edition,* by Scheid et al.[1] or similar works. Unless otherwise noted, all historical and modern components and amounts of the formulas discussed come from Scheid et al.'s text. Note that Chinese names mentioned in this article are given with the family name first and given name second.

Minor Bupleurum Decoction (Xiăo Chái Hú Tāng)

This ancient formula was first described in the work *Discussion of Cold Damage* (Shāng Hán Lùn) by Zhāng Jī (circa 220 AD). The components of Minor Bupleurum, both the original and a typical modern form, and dosing are listed in Table 2. Minor Bupleurum is an important hepatoprotective, antifibrotic, antiviral, and inflammation-modulating formula.[2] Indications for this formula are summarized in Table 3.

Minor Bupleurum Decoction (MBD) has been the subject of several large clinical trials for preventing hepatocellular carcinoma in patients with chronic hepatitis B. In a randomized but open trial involving 260 patients with chronic hepatitis B who had cirrhosis, half of the participants received MBD (7.5 g daily) and the other half of the participants were given standard medications.[3] The trial period was 5 years. The incidence of hepatocellular carcinoma was lower in the MBD group, although the difference from the control group just missed statistical significance (in patients without hepatitis B–surface antigen present, the difference was significant). Five-year survival rates were similarly different, just barely missing statistical significance unless only the group that was hepatitis B surface antigen–negative was considered.

This trial confirms the results from an earlier, very similar, trial in 260 patients with chronic hepatitis B that ran for 34 months.[4] Note that this earlier trial may actually have been the first 34 months of the first trial, as the details are somewhat similar, but, because the older study was published only in Japanese, it is difficult to be certain.

In a case series of 11 patients with chronic hepatitis B, co-infected with hepatitis D, treatment with MBD (dose unknown)

Table 1. Summary of Four Formulas

Chinese name	Japanese name	Korean name	English translation
Xiāo Chái Hú Tāng	Sho-saiko-tō	So-Si-Ho-Tang	Minor Bupleurum Decoction
Sì Jūn Zǐ Tāng	Shikunshi-tō	Sa-Gun-Ja-Tang	Four-Gentlemen Decoction
Bǔ Zhōng Yì Qì Tāng	Hochu-ekki-tō	Bo-Jung-Ikki-Tang	Tonify the Middle, Augment Qi Decoction
Sháo Yào Gān Cǎo Tāng	Shakuyaku-kanzo-tō	Baekjak-Kamcho-Tang	Peony and Licorice Decoction

Table 2. Minor Bupleurum Decoction Ingredients and Dosing

Traditional Herb	Modern Herb	Traditional Amount	Modern Amount
Bupleurum falcatum (thorowax) root	Same	24 g	12 g
Scutellaria baicalensis (Baikal skullcap) root	Same	9 g	9 g
Pinellia ternata (pinellia) cooked rhizome	Same	24 g	9 g
Zingiber officinale (ginger) fresh rhizome	Same	9 g	9 g
Panax ginseng (Asian ginseng) root	*Codonopsis pilosula* (dang shen) root	9 g	18–27 g
Glycyrrhiza uralensis (licorice) prepared root	Same	9 g	6 g
Zizyphus spinosa (jujube) fruit	Same	12 pieces	4 pieces

The original traditional formula recommended mixing the herbs with 12 cups of water and simmering until only 6 cups remained, filtering out the remaining marc (solid herbs), then simmering further until only 3 cups remained. The final dose was 1 cup, three times per day, taken warm. Today, the ingredients are more simply simmered in enough water to just cover them (roughly 250–500 mL) for 20–30 minutes. Three cups of this decoction are drunk warm each day. The typical dose of the granulation form of the formula is 2.5 g, two or three times per day, using the ratios in the modern formula.

Table 3. Indications for Minor Bupleurum Decoction

Indication	Type of supporting evidence
Chronic hepatitis B, to prevent hepatocellular carcinoma in particular	Clinical trials
Chronic hepatitis B, with or without hepatitis D co-infection	Case series
Chronic hepatitis C	Clinical trial
Acute tonsillitis	Case series
Seizure disorders not responding to antiseizure drugs alone	Clinical trials

for 3 months was associated with conversion to hepatitis B-DNA negativity in 2 patients, conversion to being hepatitis B e antigen (HBeAg) negative in 7 patients (a very good prognostic finding), and serum alanine aminotransferase (ALT) levels normalizing in 5 patients.[5]

In a cohort of 14 children with chronic hepatitis B, MBD treatment (dose unknown) was associated with HBeAg clearance in 7 patients within 6 months.[6] In a comparison group of 22 untreated children, only 22% had cleared HBeAg. Adverse effects were not seen in these trials.

Somewhat confirming these findings was a larger double-blind randomized trial in 222 patients with chronic hepatitis B that ran for 3 months.[7] One hundred and sixteen patients were given a dose of 5.4 g MBD per day, compared to a placebo-level dose of just 0.5 g per day given to 106 patients. The full-dose MBD was associated with significant reduction in serum aminotransferase levels and a trend toward greater clearance of HBeAg, compared to the low-dose MBD. No serious adverse effects occurred in this trial.

In the only published clinical trial involving patients with chronic hepatitis C that was located, 24 patients who were not candidates for interferon treatment were given 2.5 g of MBD three times daily for 1 year.[8] Serum aspartate aminotransferase levels improved in 16 patients, and ALT levels improved in 18 patients. Five patients had substantial improvement in their liver biopsy results, compared to baseline findings. Viral load levels improved in 7 patients, rose in 10 patients, and were indeterminate in 7 patients. This promising initial open trial needs to be confirmed in a randomized clinical trial with a control group.

MBD with 10 g of added gypsum and 3 g of *Platycodon grandiflorum* (balloon flower) root, and using *Panax* not *Codonopsis* (a formula called shosaiko-tō-ka-kikyo-sekko in Japanese), was effective for decreasing recurrence of acute tonsillitis

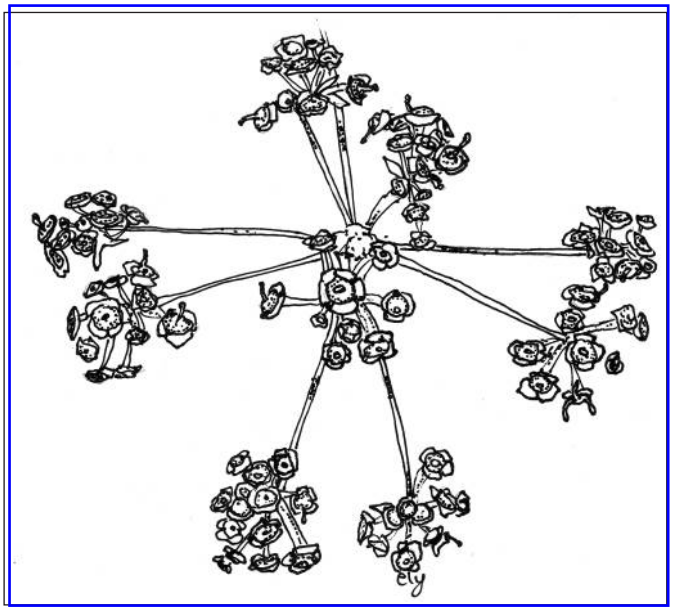
in 7 of 10 patients with recurrent infections in one case series.[9] This allowed some patients to avoid having tonsillectomies. The efficacy of this treatment should also be confirmed in a controlled trial.

The current authors have previously reviewed research on this formula for patients with seizure disorders that were not responding to conventional antiseizure medications.[10] The formula was used simultaneously with various antiseizure medications safely. MBD should be considered as an add-on therapy in this setting and not as a replacement for medications.

MBD is generally very safe. There are troubling reports of some patients with hepatitis taking MBD and interferon-α concomitantly and developing interstitial pneumonitis.[11] This complication has been reported to occur, albeit very rarely, in patients taking MBD or interferon alone as well, but the combination seems to increase the risk.

Any patient who is taking MBD and who develops unexplained cough, dyspnea, or fever should have a chest film taken. If the chest film shows any abnormality, coupled with findings of high serum C-reactive protein (CRP) and leukocytosis, MBD should be stopped and corticosteroids administered to the patient.[12] This problem may be caused by allergy to MBD as opposed to some kind of inherent immune- or pulmonary toxicity, which would help explain the rarity of the problem and its prompt resolution with corticosteroid therapy.[13] However, patients with preexisting liver disease have a higher risk of developing pneumonitis and a higher risk of dying from this condition, and, thus, should not be given MBD.[14]

MBD can increase the duration of effect of corticosteroids; therefore, somewhat lower doses of such medications than usual should be used in patients undergoing therapy with MBD.[15] This is a well-established result of the *Glycyrrhiza uralensis* (licorice) in the formula. Because of the presence of this herb in substantial amounts, patients' blood pressure (BP) should also be monitored, and they should be encouraged to eat a high-potassium diet to prevent glycyrrhizin-induced pseudohyperaldosteronism.



Bupleurum falcatum (thorowax). Drawing © 2013 by Eric Yarnell, ND, RH (AHG).

Finally, one small study in healthy volunteers found that 2.5 g of MBD twice daily could decrease CYP1A2 activity by ~ 16% on average within 5 days. This could extend the potency or toxicity of drugs that are a substrate for this enzyme (e.g., amitriptyline, fluvoxamine, haloperidol, naproxen, or tacrine) if taken simultaneously with the formula (unless the dose of the drug was lowered).[16]

Table 4. Four-Gentlemen Decoction Ingredients and Dosing

Traditional herb	Modern herb	Traditional amount	Modern amount
Panax ginseng (Asian ginseng) root	*Codonopsis pilosula* (dang shen) root	1 part	6–27 g
Glycyrrhiza uralensis (licorice) prepared root	Same	1 part	3–6 g
Wolfiporia extensa (hoelen, fu ling) sclerotium	Same	1 part	6–9 g
Atractylodes macrocephala (bai zhu) rhizome	Same	1 part	6–9 g

The original formula recommended grinding all of the herbs into powders in equal parts and taking 6 g as a draught in plain or lightly salty water, three times per day. The modern formula is simmered in 250–500 mL of water for 20–30 minutes, and 1 cup is drunk three times per day. The granulation dose (of modern amounts of the herbs) is 2.5 g, two to three times per day.

Table 5. Indications for Four-Gentlemen Decoction

Indication	Type of supporting evidence
Major surgery support	Clinical trials
Immunosuppressed states	Clinical trials
Ionizing radiation protection	Preclinical studies; clinical practice
Anemia caused by major surgery, chemotherapy, or radiation therapy	Clinical trial

Table 6. Tonify the Middle to Augment Qi Decoction Ingredients and Dosing

Traditional Herb	Modern herb	Traditional amount	Modern amount
Panax ginseng (Asian ginseng) root	*Codonopsis pilosula* (dang shen) root	0.9 g	9–12 g 18–36 g
Astragalus membranaceus (astragalus) root	Same	3 g	12–24 g
Atractylodes macrocephala (bai zhu) rhizome	Same	0.9 g	9–12 g
Glycyrrhiza uralensis (licorice) prepared root	Same	1.5 g	3–6 g
Angelica sinensis (dong quai, dang gui) wine-washed root	Same	6 g	6–12 g
Citrus reticulata (Mandarin orange) pericarp	Same	0.9 g	6–9 g
Cimicifuga foetida (skunk bugbane) root	Same	0.9 g	3–6 g
Bupleurum falcatum (thorowax) root	Same	0.9 g	3–9 g

The original formulation consisted of grinding the herbs, then simmering them until 2 bowls of liquid cooked down to 1 bowl (smaller bowls were recommended for weaker patients). The liquid was strained and taken three times per day, warm, between meals. The modern formula is simmered in 250–500 mL of water for 20–30 minutes, and 1 cup is drunk three times per day. The dose of modern recipe granulation is 2.5 g, three times per day.

Table 7. Indications for Tonify the Middle to Augment Qi Decoction

Indication	Type of supporting evidence
Allergic rhinitis	Clinical trials
Atopic dermatitis	Clinical trials
Chronic obstructive pulmonary disease	Clinical trials
Male infertility	Case series
Cancer fatigue	Single clinical trial
MRSA infections	Case studies

MRSA, methicillin-resistant *Staphylococcus aureus*.

Four-Gentlemen Decoction (Sì Jūn Zǐ Tāng)

This formula comes from the *Formulary of the Pharmacy Service for Benefiting the People in the Taiping Era* (Tài Píng Huì Mín Hé Jì Jú Fāng) by the Imperial Medical Bureau (1107 AD). This is an extremely common and preeminent tonifying formula in Chinese medicine. Given the relative simplicity of the formula (its ingredients and dosing are given in Table 4), combined with its importance and efficacy, this formula is often combined with other formulae for helping patients with a wide range of problems. For a summary of uses of Four-Gentlemen Decoction (FGD), see Table 5.

FGD has immunomodulating benefits, for example, after major surgery. In a single-blinded trial, 59 patients with gastric cancer undergoing surgery were randomized to either parenteral or enteral nutrition. The enteral group was then randomized to FGD or no additional treatment.[17] The diet was started the second day after surgery in all groups. FGD was administered by nasogastric tube, 100 mL daily, for 8 days postsurgery. Albumin, transferrin, and T-cell subset levels were all higher in patients who received FGD versus what occurred in the other 2 groups.

In a similar trial, patients with a variety of gastrointestinal (GI) cancers were randomized in the same manner.[18] Treatment was given for 1 week after surgery in this trial. Total T-lymphocytes and various subset levels were higher in the FGD group, compared to the control groups. Serum interleukin (IL)–2 concentration was significantly higher and IL-6, tumor necrosis factor–α (TNF-α), and CRP concentrations were significantly lower in the FDG group, compared to controls.

FGD and related formulas have additional benefits for patients with cancer who are undergoing surgery. A modification of FGD known as Jiā Wèi Sì Jūn Zǐ Tāng, or Augmented Four-Gentlemen Decoction (AFGD) has *Angelica sinensis* (dong quai, dang gui) root, 9 g; *Ligusticum chuanxiong* (Chinese lovage) root, 6–9 g; *Citrus* x *aurantium* (bitter orange) pericarp, 6–9 g; *Cyperus rotundus* (purple nutsedge) rhizome, 6–9 g; and *Cinnamomum cassia* (cassia cinnamon) bark, 3–9 g; in addition to the ingredients in FGD. A group of 65 patients with advanced hepatocellular carcinoma were randomized to receive AFGD or standard therapy alone after hepatectomy.[19] The results of a standard test used to assess reserve liver function after surgery were superior in the AFGD group, compared to the controls.

FGD combined with a formula known as Xiǎo Chéng Qí Tāng (Minor Order the Qi Decoction)—which adds *Rheum palmatum* (rhubarb) root, 15 g; bitter orange, 15 g; and *Magnolia officinalis* (magnolia) bark, 15 g—has been studied for an

ability to prevent bowel obstruction. One trial randomized 248 patients to receive a 100-mL total of the two formulas by nasogastric tube twice daily or standard care only after surgery.[20] The herbs significantly reduced the risk of postoperative adhesive small-bowel obstruction, compared to what occurred in the control group.

FGD should be considered for patients who are exposed to ionizing radiation. Two rodent studies have confirmed that FGD is radioprotective, particularly of immune function.[21,22] Note that the Four-Substance Decoction (discussed in the next issue's article) was a superior radioprotective agent in one of these studies.

Shí Quán Dà Bǔ Tāng (Juzen-Taiho-Tō), the All-Inclusive Great Tonifying Decoction (AIGTD), is a combination of FGD and Four-Substance Decoction (Sì Wù Tāng). Four-Substance Decoction contains *Rehmannia glutinosa* (rehmannia) cooked root, *Paeonia lactiflora* (white peony) root without bark, *Angelica sinensis* (dong quai, dang gui) cooked root, and *Ligusticum chuanxiong* (Chinese lovage) root. The amounts are the same for the separate formulas (Four-Substance Decoction will be discussed in the future). AIGTD is a strong tonic for the immune system and bone marrow. The first written description of this formula was in the text *Transmitted Trustworthy and Suitable Formulas* (Chuán Xìn Shì Yòng Fāng) by Wú Yǎn-Kuí (1180 AD).

In one clinical trial of 18 Japanese women undergoing major hip surgery, all of the women donated blood for autologous transfusion during surgery should it be needed prior to the operations.[23] Half of the group was randomly assigned to take AIGTD, 7.5 g daily, for 21 days prior to surgery, the other half had no additional therapy. Hemoglobin levels were significantly lower in the untreated group, compared to the AIGTD group, and the rate of hemoglobin decline was lower in the AIGTD group than in the control group after surgery.

FGD is very safe but, because of its significant licorice content, BP should be monitored in patients taking the formula long-term, and a high-potassium diet is warranted to prevent pseudoaldosteronism. If AIGTD causes any insomnia or agitation, the dose can be reduced, and the formula should be avoided in the evening.

Tonify the Middle to Augment Qi Decoction (Bǔ Zhōng Yì Qì Tāng)

This formula was first mentioned in *Clarifying Doubts About Damage from Internal and External Causes* (Nèi Wài Shāng Biàn Huò Lùn) by Lǐ Gǎo (1247 AD). The components are listed in Table 6. This formula is based on the MBD. Tonify the Middle to Augment Qi Decoction (TMAQD) has immunomodulating properties as well as being antiallergic and inflammation-modulating; the formula's uses are summarized in Table 7. TMAQD does not have the liver focus that MBD does.

TMAQD has been studied for use in patients with various allergic conditions. In one trial, 60 patients with dust mite–induced allergic rhinitis were randomized to receive TMAQD, 12 g per day, or Ping Wei San (PWS), 4.5 g per day.[24] PWS is not typically used to treat allergic disorders and contains bai zhu, *Magnolia officinalis* (magnolia) bark, *Citrus* spp. (citrus) peel, *Zingiber officinale* (ginger) rhizome, *Zizyphus spinosa* (jujube) fruit, and licorice root. While TMAQD improved symptom scores, compared to baseline, PWS did not (unfortunately, the 2 groups were not directly compared for this measure). TMAQD decreased immunoglobulin E (IgE) and IL-4 levels, compared to PWS. In another cohort of patients with recalcitrant atopic dermatitis, an unknown dose of TMAQD lowered eosinophil levels significantly and showed a trend toward lower IgE levels, compared to baseline.[25]

In a double-blinded, randomized trial of 77 patients with atopic dermatitis, 2.5 g of TMAQD, tid, was able to lower doses of topical corticosteroids and tacrolimus necessary to control symptoms significantly better than placebo.[26] Symptoms were nonsignificantly lowered in the treatment group, compared to controls. A very similar study of 84 patients had similar results.[27] At least one other double-blinded trial has confirmed the value of TMAQD in patients with atopic dermatitis, but no details of this Japanese-language trial were available.[28]

In a double-blinded randomized trial of 35 patients with chronic obstructive pulmonary disease (COPD), half were given 2.5 g of TMAQD tid and half were given placebo. All patients were taking the same inhaled medications.[29] CRP and TNF–α levels fell significantly in the treatment group, compared to baseline, but did not change in the placebo group. Serum prealbumin levels rose in the TMAQD group but not in the control group. An unfortunate weakness of this trial was the failure to use between-group comparisons.

Another randomized trial involved 7 patients with COPD who took either 2.5 g of TMAQD tid or standard inhaler medications alone.[30] Symptoms were reduced in the TMAQD group, compared to baseline, but not in the control group. The number of common colds and the number of acute COPD exacerbations were significantly lower in the TMAQD group, compared to the control group. No adverse effects of TMAQD were observed.

TMAQD was studied in a trial of male infertility. In 22 men with idiopathic infertility, TMAQD (dose unknown) elevated levels of soluble Fas, which is associated with increased sperm counts.[31] Further research is needed but this does provide a promising lead.

In a preliminary open trial, 40 patients with cancer-related fatigue were randomly assigned to take TMAQD or to a wait-list (no treatment, but told they were eligible for potential future assignment to the treatment group) for 2 weeks.[32] Fatigue was reduced considerably in the treatment group, compared to the wait-list control group.

Two separate reports suggest that TMAQD may have a role for patients with methicillin-resistant *Staphylococcus aureus* (MRSA) infections not responding to antibiotics. In one report, 5 bedridden patients with cerebrovascular disease and dementia with MRSA, and not responding to multiple antibiotics, were treated with TMAQD, 5 g qd.[33] In all 5 cases, MRSA was cleared, and the patients' general health improved without adverse effects.

Table 8. Peony and Licorice Decoction Ingredients and Dosing

Herb	Traditional amount	Modern amount
Paeonia lactiflora (bai shao, white peony) root without bark	12 g	30–100 g
Glycyrrhiza uralensis (licorice) prepared root	12 g	10–30 g

In both cases, the herbs are simmered together in 250 mL of water for 20–30 minutes. One cup is drunk three times per day. A typical granulation dose is 2.5–5 g tid.

Table 9. Indications for Peony and Licorice Decoction

Indication	Type of supporting evidence
Hemodialysis muscle cramps	Clinical trials
Colonoscopy- or ERCP-associated spasms	Clinical trials
Paclitaxel-associated myalgia/arthralgia	Clinical trials
FOLFOX-associated neuropathies	Single clinical trial
Hyperprolactinemia	Case series and case studies
Dysmenorrhea	Case series
Ureteral colic	Case series

ERCP, endoscopic retrograde cholangiopancreatography; FOLFOX 5-fluorouracil/folinic acid plus oxaliplatin.

In the other report on 34 patients with asymptomatic bacteriuria involving MRSA, TMAQD was given at a dose of 2.5 g tid for 24 weeks.[34] None of the patients took antibiotics during this time. Twelve untreated patients with MRSA bacteriuria comprised a control group. Of the 34 patients who were given TMAQD, 12 had eradication of MRSA and, in 10, the colony count fell below 10^2 colony-forming units (CFU)/mL. Urinary bacteria levels were significantly lower in the TMAQD group, compared to controls. Other reports, the details of which are not accessible, appear to confirm the value of TMAQD for clearing MRSA infection.[35,36]

This formula is very safe. As it contains licorice, it has the same cautions as the first two formulas mentioned above in terms of pseudoaldosteronism.

Peony and Licorice Decoction (Sháo Yào Gān Cǎo Tāng)

This simple formula was first described in the *Discussion of Cold Damage* (Shāng Hán Lùn) by Zhāng Jī (circa 220 AD). Because there are just two herbs in the combination (see Table 8), it is perhaps one of the most accessible and understandable formulas to practitioners who are used to single medicines. This formula has been particularly researched as a spasmolytic for smooth and skeletal muscle, for neuropathies, and as an agent to reduce excessive prolactin levels; the formula's uses are summarized in Table 9.

In 5 patients undergoing hemodialysis with recurrent muscle cramps, 6 g of Peony and Licorice Decoction (PLD) were given daily for 4 weeks.[37] Two patients had their cramps resolve and 2 patients had significant reduction of their cramps. In 61 patients undergoing hemodialysis who were having muscle cramps, giving 2.5 g of PLD led to resolution of the cramps in 54/61 patients in an average of 5.3 minutes.[38] In a double-blinded, randomized trial of 101 patients with muscle cramps related to liver cirrhosis, PLD was compared to placebo.[39] The PLD dose was 2.5 g three times daily. After 2 weeks, cramp severity and frequency was significantly reduced compared to placebo. However, some patients had weight gain and BP elevations in the PLD group (7 of 61) consistent with licorice-induced pseudoaldosteronism.

Two trials have assessed the effect of PLD solution being sprayed directly on spasmodic bowel during invasive imaging procedures. In one, PLD was compared to saline in 101 patients undergoing colonoscopy.[40] Subjects were randomly assigned to the treatment or the saline group. Based on video measurements, PLD significantly decreased the spasms, compared to saline. In a similar trial involving 50 patients undergoing endoscopic retrograde cholangiopancreatography, all had 5 g of PLD dissolved in saline sprayed on the duodenal papilla, and 38/50 (76%) had relief from spasms.

In 21 women with ovarian cancer being treated with paclitaxel and carboplatin chemotherapy causing muscular pain, PLD was tried at a dose of 7.5 g daily for 8 days.[41] In 9 cases (43%), pain was significantly relieved. A group of 50 patients with non–small cell lung cancer, who were treated with paclitaxel and carboplatin, were randomized to take PLD 2.5 mg tid or to no additional treatment.[42] Treatment started before paclitaxel and carboplatin infusion and continued for 21 days.

Grades of myalgia and arthralgia were significantly worse in the control group, compared to the PLD-treated group. Duration of pain was significantly longer in the control group, compared to the PLD group. Significantly more control patients

needed to take nonsteroidal anti-inflammatory drugs for pain control, compared to the PLD group. This allowed the PLD group to have significantly more cycles of chemotherapy, resulting in better outcomes.[42]

Twenty four patients with metastatic colon cancer undergoing chemotherapy with 5-fluorouracil, folinic acid, and oxaliplatin were treated with PLD at an unknown dose.[43] None of the patients developed grade 3 neurotoxicity, and only 10 patients developed grades 1–2 neurotoxicities, which is significantly less than usual. The response rate was 65%, which is typical for these drugs, so there was no indication that PLD interfered with the treatment.

Several case reports have been published in which PLD was able to reverse or mitigate hyperprolactinemia in patients who were taking antipsychotic drugs.[44] In the most recent case, a 23-year-old woman with schizophrenia, who was taking olanzapine, developed hyperprolactinemia-induced amenorrhea. This condition was reversed by taking PLD 7.5 g daily.[45] Although her urinary homovanillic acid (metabolite of dopamine) levels rose during PLD therapy, this patient's psychotic symptoms did not worsen.

In a case series of 11 patients with antipsychotic drug-induced hyperprolactinemia, PLD (dose unclear) significantly decreased average serum prolactin levels compared to baseline.[46] Potassium levels were unchanged, no adverse effects occur, and schizophrenic symptoms remained well-managed. In a case series, 20 men being treated with an unnamed antipsychotic drug who had hyperprolactinemia, and 10 who had low libido, were given PLD 2.5 mg tid for 4 weeks.[47] Five of the 20 men had a decrease in serum prolactin by 50% or more, and 3/10 of the patients with low libido had improvement in sexual desire.

Long-term use of PLD, because of the licorice component, can lead to renal potassium wasting and sodium retention, pseudoaldosteronism, and hypertension. Therefore BP and/or serum or urinary potassium levels should be monitored regularly (monthly, up to every 3 months in patients who are stable after long-term use of the formula) in patients taking PLD for more than 30 days consecutively. It should not be used with thiazide diuretics or corticosteroids without careful monitoring as these medications can also cause potassium wasting.[48] Patients using the formula long-term should eat foods rich in potassium to help avoid this problem.

Conclusion

These four formulae have a wide range of uses for Western practitioners based on a range of types of evidence. All of them arguably have far more empirical history of use than any conventional pharmaceutical in use, given their origination hundreds or thousands of years ago and continuous use ever since. Many of these formulae have been the subject of clinical trials and have been proven to be helpful.

It should also be noted that increasing numbers of these herbs are being grown in North America, which makes the use of these formulas more ecologically sound.[49] In some cases local herbs (for example, *Paoenia brownii* [Brown's peony] from California for *P. lactiflora*) could be substituted for herbs from China. While this has not strictly been studied, it is clinically effective in the author's limited experience having tried this in some cases.

These herbal formulas are useful tools and should be known better by Western practitioners who are looking to expand their therapeutic options. More formulas will be considered in the next article. ■

References

1. Scheid V, Bensky D, Ellis A, Barolet R. Chinese Herbal Medicine: Formulas and Strategies, 2nd ed. Vista, CA: Eastland Press, 2009.

2. Shimizu I. Sho-saiko-to: Japanese herbal medicine for protection against hepatic fibrosis and carcinoma. J Gastroenterol Hepatol 2000;15(suppl):D84–D90.

3. Oka H, Yamamoto S, Kuroki T, et al. Prospective study of chemoprevention of hepatocellular carcinoma with sho-saiko-to (TJ-9). Cancer 1995;76:743–749.

4. Yamamoto S, Oka H, Kanno T, et al. Controlled prospective trial to evaluate syosakiko-to in preventing hepatocellular carcinoma in patients with cirrhosis of the liver [in Japanese]. Gan To Kagaku Ryoho 1989;16(4[pt2-2]):1519–1524.

5. Chen NL, Gu F, Jia KM. Chronic active hepatitis with superinfection of delta virus and hepatitis B virus: Treatment with Chinese traditional medicine [in Chinese]. Zhonghua Nei Ke Za Zhi 1990;29:144–146,189.

6. Tajiri H, Kozaiwa K, Ozaki Y, et al. Effect of sho-saiko-to (xiao-chai-hu-tang) on HBeAg clearance in children with chronic hepatitis B virus infection and with sustained liver disease. Am J Chin Med 1991;19:121–129.

7. Hirayama C, Okumura M, Tanikawa K, et al. A multicenter randomized controlled clinical trial of shosaiko-to in chronic active hepatitis. Gastroenterol Jpn 1989;24:715–719.

8. Deng G, Kurtz RC, Vickers A, et al. A single arm phase II study of a Far-Eastern traditional herbal formulation (sho-sai-ko-to or xiao-chai-hu-tang) in chronic hepatitis C patients. J Ethnopharmacol 2011;136:83–87.

9. Goto F, Asama Y, Ogawa K. Sho-saiko-to-ka-kikyo-sekko as an alternative treatment for chronic tonsillitis to avoid surgery. Complement Ther Clin Pract 2010;16:216–218.

10. Yarnell E, Abascal K. An herbal formula for treating intractable epilepsy: A review of the literature. Altern Complement Ther 2000;6:203–206.

11. Nakagawa A, Yamaguchi T, Takao T, Amano H. Five cases of drug-induced pneumonitis due to sho-saiko-to or interferon-alpha or both [in Japanese]. Nihon Kyobu Shikkan Gakkai Zasshi 1995;33:1361–1366.

12. Hatakeyama S, Tachibana A, Morita M, et al. Five cases of pneumonitis induced by sho-saiko-to [in Japanese]. Nihon Kyobu Shikkan Gakkai Zasshi 1997;35:505–510.

13. Ishizaki T, Sasaki F, Ameshima S, et al. Pneumonitis during interferon and/or herbal drug therapy in patients with chronic active hepatitis. Eur Respir J 1996;9:2691–2696.

14. Sato A, Toyoshima M, Kondo A, et al. Pneumonitis induced by the herbal medicine sho-saiko-to in Japan [in Japanese]. Nihon Kyobu Shikkan Gakkai Zasshi 1997;35:391–395.

15. Homma M, Oka K, Ikeshima K, et al. Different effects of traditional Chinese medicines containing similar herbal constituents on prednisolone pharmacokinetics. J Pharm Pharmacol 1995;47:687–692.

16. Saruwatari J, Nakagawa K, Shindo J, et al. The in-vivo effects of sho-saiko-to, a traditional Chinese herbal medicine, on two cytochrome P450 enzymes (1A2 and 3A) and xanthine oxidase in man. J Pharm Pharmacol 2003;55:1553–1559.

17. Cai J, Wang H, Zhou S, et al. Effect of sijunzi decoction and enteral nutrition on T-cell subsets and nutritional status in patients with gastric cancer

after operation: A randomized controlled trial [in Chinese]. Zhong Xi Yi Jie He Xue Bao 2008;6:37–40.

18. Liang C, Zhang SH, Cai ZD. Effects of early intestinal application of sijunzi decoction on immune function in post-operational patients of *[sic]* gastrointestinal tumor [in Chinese]. Zhongguo Zhong Xi Yi Jie He Za Zhi 2005;25:1070–1073.

19. Zhang B, Huang G, Zhang Y, et al. Clinical observation on prevention of "jia wei si jun zi tang" from damage of hepatic reserving function after intervention of liver cancer [in Chinese]. Zhong Yao Cai 2004;27:387–389.

20. Wu C, Wang N, Wu C. Clinical observation of integrative medicine for treatment of adhesive ileus [in Chinese]. J Linyi Med College 2003;25:101–102.

21. Hsu HY, Yang JJ, Lian SL, et al. Recovery of the hematopoietic system by si-jun-zi-tang in whole body irradiated mice. J Ethnopharmacol 1996;54:69–75.

22. Lee SE, Oh H, Yang JA, et al. Radioprotective effects of two traditional Chinese medicine prescriptions: Si-wu-tang and si-jun-zi-tang. Am J Chin Med 1999;27:387–396.

23. Kishida Y, Nishii T, Inoue T, et al. Juzentaihoto (TJ-48), a traditional Japanese herbal medicine, influences hemoglobin recovery during preoperative autologous blood donation and after hip surgery. Int J Clin Pharmacol Ther 2009;47:716–721.

24. Yang SH, Yu CL. Antiinflammatory *[sic]* effects of bu-zhong-yi-qi-tang in patients with perennial allergic rhinitis. J Ethnopharmacol 2008;115:104–109.

25. Kobayashi H, Mizuno N, Teramae H, et al. The effects of hochu-ekki-to in patients with atopic dermatitis resistant to conventional treatment. Int J Tissue React 2004;26:113–117.

26. Furue M, Tanaka Y, Kobayashi M, et al. Efficacy of kanebo hochuekkito in patients with atopic dermatitis and qikyo—a multicenter, double-blind trial [in Japanese]. Arerugi 2005;54:1020.

27. Kobayashi H, Ishii M, Takeuchi S, et al. Efficacy and safety of a traditional herbal medicine, hochu-ekki-to in the long-term management of kikyo (delicate constitution) patients with atopic dermatitis: A 6-month, multicenter, double-blind, randomized, placebo-controlled study. Evid Based Complement Alternat Med 2010;7:367–373.

28. Kobayashi H. Clinical evaluation of hochuekkito in the treatment of atopic dermatitis: A multicenter, double-blind, randomized, placebo-controlled study [in Japanese]. Nihon Yakurigaku Zasshi 2008;132:285–287.

29. Shinozuka N, Tatsumi K, Nakamura A, et al. The traditional herbal medicine hochuekkito improves systemic inflammation in patients with chronic obstructive pulmonary disease. J Am Geriatr Soc 2007;55:313–314.

30. Tatsumi K, Shinozuka N, Nakayama K, et al. Hochuekkito improves systemic inflammation and nutritional status in elderly patients with chronic obstructive pulmonary disease. J Am Geriatr Soc 2009;57:169–170.

31. Furuya Y, Akashi T, Fuse H. Effect of bu-zhong-yi-qi-tang on seminal plasma cytokine levels in patients with idiopathic male infertility. Arch Androl 2004; 50:11–14.

32. Jeong JS, Ryu BH, Kim JS, et al. Bojungikki-tang for cancer-related fatigue: A pilot randomized clinical trial. Integr Cancer Ther 2010;9:331–338.

33. Itoh T, Itoh H, Kikuchi T. Five cases of MRSA-infected patients with cerebrovascular disorder and in a bedridden condition, for whom bu-zhong-yi-qi-tang (hochu-ekki-to) was useful. Am J Chin Med 2000;28:401–408.

34. Nishida S. Effect of hochu-ekki-to on asymptomatic MRSA bacteriuria. J Infect Chemother 2003;9:58–61.

35. Seki T, Matsumoto T, Deguchi H, et al. Evaluation of the efficacy of hochuekkito in preventing MRSA colonization and infection [in Japanese]. Kampo Igaku 1999;23:196–197.

36. Ueda T, Yamashita K, Nakamori Y, et al. Study of the MRSA carriage–preventing effect of hochuekkito (TJ-41): 1st report. Progress Med 1999;19:1000–1003.

37. Hinoshita F, Ogura Y, Suzuki Y, et al. Effect of orally administered shaoyao-gan-cao-tang (shakuyaku-kanzo-to) on muscle cramps in maintenance hemodialysis patients: A preliminary study. Am J Chin Med 2003;31:445–453.

38. Hyodo T, Taira T, Takemura T, et al. Immediate effect of shakuyaku-kanzo-to on muscle cramp in hemodialysis patients. Nephron Clin Pract 2006;104: c28–c32.

39. Kumada T, Kumada H, Yoshiba M, et al. Effect of shakuyaku-kanzo-to (Tsumura TJ-68) on muscle cramps accompanying cirrhosis in a placebo-controlled double-blind parallel study [in Japanese]. Rinsho Iyaku 1999;15:499–523.

40. Ai M, Yamaguchi T, Odaka T, et al. Objective assessment of the antispasmodic effect of shakuyaku-kanzo-to (TJ-68), a Chinese herbal medicine, on the colonic wall by direct spraying during colonoscopy. World J Gastroenterol 2006;12:760–764.

41. Fujii K, Okamoto S, Saitoh K, et al. The efficacy of shakuyaku-kanzo-to for peripheral nerve dysfunction in paclitaxel combination chemotherapy for epithelial ovarian carcinoma [in Japanese]. Gan To Kagaku Ryoho 2004;31:1537–1540.

42. Yoshida T, Sawa T, Ishiguro T, et al. The efficacy of prophylactic shakuyaku-kanzo-to for myalgia and arthralgia following carboplatin and paclitaxel combination chemotherapy for non–small cell lung cancer. Support Care Cancer 2009;17:315–320.

43. Hosokawa A, Ogawa K, Ando T, et al. Preventive effect of traditional Japanese medicine on neurotoxicity of FOLFOX for metastatic colorectal cancer: A multicenter retrospective study. Anticancer Res 2012;32:2545–2550.

44. Yamada K, Kanba S, Yagi G, Asai M. Herbal medicine (skakuyaku-kanzo-to) in the treatment of resperidone-induced amenorrhea [letter]. J Clin Psychopharmacol 1999;19:380–381.

45. Hori H, Yoshimura R, Katsuki A, Nakamura J. Herbal medicine (shakuyaku-kanzo-to) improves olanzapine-associated hyperprolactinemia: A case report. J Clin Psychopharmacol 2013;33:122–123.

46. Yamada K, Kanba S, Murata T, et al. Effectiveness of skakuyaku-kanzo-to in neuroleptic-induced hyperprolactinemia: A preliminary report. Psychiatr Clin Neurosci 1996;50:341–342.

47. Yamada K, Kanba S, Yagi G, Asai M. Effectiveness of herbal medicine (skakuyaku-kanzo-to) for neuroleptic-induced hyperprolactinemia [letter]. J Clin Psychopharmacol 1997;17:234–235.

48. Kinoshita H, Okabayashi M, Kaneko M, et al. Shakuyaku-kanzo-to induces pseudoaldosteronism characterized by hypokalemia, rhabdomyolysis, metabolic alkalosis with respiratory compensation, and increased urinary cortisol levels. J Altern Complement Med 2009;15:439–443.

49. Schafer P. The Chinese Medicinal Herb Farm: A Cultivator's Guide to Small-Scale Organic Herb Production. White River Junction, VT: Chelsea Green Publishing, 2011.

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