

# Herbal Monograph for *Xiao Chai Hu Tang*: Part Three

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*Editor's Note:* This is the third article in a four-part series on *xiao chai hu tang*. [Part two](#) appeared in the August 2007 issue. [Part one](#), with a complete list of references, appeared in the July 2007 issue.

1. Gastritis: Thirty-six patients with gastritis due to regurgitation of bile were treated with modified *xiao chai hu tang* for 30 days with marked results. Modifications of the herbs were as follows: *dan shen* (Radix et rhizoma salviae miltiorrhizae) was added for chronic gastritis with blood stagnation; *huang lian* (Rhizoma coptidis) for accumulation of heat; *zhi qiao* (Fructus aurantii) for abdominal distention and fullness; *san qi* (Radix et rhizoma notoginseng), *hai piao xiao* (Endoconcha sepiiae) and *bai fan* (Alumen) for ulceration. Most patients reported complete recovery or resolution of all symptoms. Endoscopy also confirmed varying degrees of recovery.<sup>46</sup>
2. Gastric pain: Modified *xiao chai hu tang* was used to treat 151 patients with stomach pain, with complete recovery reported in 84 patients, improvement in 49 patients, and no effect in 18 patients. Modifications included the addition of *wu mei* (Fructus mume), *dan shen* (Radix et rhizoma salviae miltiorrhizae), *wu ling zhi* (Faeces troglodyteris), *mu dan pi* (Cortex moutan) and others as deemed necessary.<sup>47</sup>
3. Gastric prolapse: Administration of modified *xiao chai hu tang* for one month in 60 patients with gastric prolapse was associated with complete recovery in 29 patients, marked improvement in 22 patients, and slight improvement in nine patients. The base formula contained *xiao chai hu tang* plus *mai ya* (Fructus hordei germinatus) and *ji nei jin* (Endothelium corneum gigeriae galli). *Xuan fu hua* (Flos inulae), and *zhe shi* (Haematitum) were added for belching, distention and pain. For epigastric pain, *dang shen* (Radix codonopsis) was removed, and *shi xiao san* (Sudden Smile Powder), and *da huang* (Radix et rhizoma rhei) were added. For individuals with emotional disturbance, *dang gui* (Radix angelicae sinensis), *bai shao* (Radix paeoniae alba), and dry-fried *xiang fu* (Rhizoma cyperi) were added. For feeling of coldness in the stomach region, *wu zhu yu* (Fructus evodiae) and *gao liang jiang* (Rhizoma alpiniae officinarum) were added. For dampness affecting the spleen, *cang zhu* (Rhizoma atractylodis), *zi su geng* (Caulis perillae), and *chen pi* (Pericarpium citri reticulatae) were added. For food stagnation, *sha ren* (Fructus amomi) and *jian shen qu* (Massa fermentata praeparata) were added. For yin deficiency, *shi hu* (Caulis dendrobii) and *sha shen* (Radix glehniae seu adenophorae) were added.<sup>48</sup>
4. Constipation: Modified *xiao chai hu tang* was used successfully to treat constipation in geriatric patients. Of 48 patients, 30 had complete recovery, 16 had marked improvement, and two had slight improvement. The base formula included *xiao chai hu tang* plus *tao ren* (Semen persicae), dry-fried *lai fu zi* (Semen raphani), and others. In addition, *bai jiang cao* (Herba cum radice patriniae) and *huang qin* (Radix scutellariae) were added for heat; *yan hu suo* (Rhizoma

corydalis) and *bai shao* (Radix paeoniae alba) were given in larger doses for severe abdominal pain; and *hou po* (Cortex magnoliae officinalis) and *da fu pi* (Pericarpium arecae) were given for a feeling of heaviness and distention in the abdomen.<sup>49</sup>

5. Acute tonsillitis: Use of modified *xiao chai hu tang* was found to have 94 percent effectiveness (102 of 108 patients) in treating acute tonsillitis. The herbal treatment used *xiao chai hu tang* plus *she gan* (Rhizoma belamcandae) and *xia ku cao* (Spica prunellae) as the base formula, with the addition of *ban lan gen* (Radix isatidis) for severe sore throat; *ma bo* (Lasiosphaera seu calvatia) and *pu gong ying* (Herba taraxaci) for abscesses; *sang bai pi* (Cortex mori) and *gua lou* (Fructus trichosanthis) for coughing with profuse sputum; charred *da huang* (Radix et rhizoma rhei) for constipation; *can sha* (Faeces bombycis) and *che qian zi* (Semen plantaginis) for loose stools; *xin yi hua* (Flos magnoliae) and *cang er zi* (Fructus xanthii) for profuse nasal discharge; and *shi gao* (Gypsum fibrosum) and *lu gen* (Rhizoma phragmitis) for thirst.<sup>50</sup>
6. Infectious parotitis: Modified *xiao chai hu tang* was effective in treating acute parotitis. The herbal treatment was based on *xiao chai hu tang*, with the addition of *xia ku cao* (Spica prunellae) and elimination of *ren shen* (Radix et rhizoma ginseng). *Jie geng* (Radix platycodonis) and *niu bang zi* (Fructus arctii) were added for early stages of infection; *jing jie* (Herba schizonepetae) and *fang feng* (Radix saposhnikoviae) for presence of exterior signs and symptoms; *jiang can* (Bombyx batryticatus) and *jin yin hua* (Flos lonicerae japonicae) for wind-heat and epidemic toxin; *huo xiang* (Herba agastaches) and *pei lan* (Herba eupatorii) for damp-heat in the interior; *da huang* (Radix et rhizoma rhei) for constipation; *ju he* (Semen citri reticulatae) for mastitis; and *li zhi he* (Semen litchi) for orchitis. Of 47 patients, 45 had complete recovery, and two had no improvement.<sup>51</sup>
7. Stomatitis: Complete recovery was reported in all 40 patients with stomatitis using *xiao chai hu tang* plus *huang lian* (Rhizoma coptidis) as a mouth gargle. The duration of treatment ranged from three to 15 doses of herbs.<sup>52</sup>
8. Allergic rhinitis: In one comparison study, patients with allergic rhinitis were treated with either herbs or drugs (antihistamines). In the herb group, *xiao chai hu tang* was used as the base formula, with the addition of *xin yi hua* (Flos magnoliae) and *ju hua* (Flos chrysanthemi) for severe nose itching and sneezing; *cang zhu* (Rhizoma atractylodis) and *sheng ma* (Rhizoma cimicifugae) for profuse nasal discharge; *bai zhi* (Radix angelicae dahuricae) and *bo he* (Herba menthae) for severe sinus swelling and congestion; *huang qin* (Radix scutellariae) and *chuan xiong* (Rhizoma chuanxiong) for severe inflammation; *tao ren* (Semen persicae) and *ge gen* (Radix puerariae lobatae) for nasal polyps; and other modifications as deemed necessary. The study reported 90.8 percent effectiveness for 65 patients in the herb group and 76.9 percent effectiveness for 65 patients in the drug (antihistamine) group.<sup>53</sup>
9. Meniere's syndrome: One study involving 268 patients with Meniere's syndrome reported marked improvement in most of the patients when they were treated with modified *xiao chai hu tang*. The herbal treatment contained *xiao chai hu tang* with *chuan xiong* (Rhizoma chuanxiong), *ju hua* (Flos chrysanthemi), and others as needed. The overall rate of effectiveness was 97 percent.<sup>54</sup>
10. Dizziness: Administration of *xiao chai hu tang* plus *fang feng* (Radix saposhnikoviae), *huo xiang* (Herba agastaches) and others, was effective within 24 hours in treating acute onset dizziness. Of 20 patients, 14 had complete recovery and six had slight to moderate improvement.<sup>55</sup>

11. Migraine: Administration of *xiao chai hu tang* plus *chuan xiong* (Rhizoma chuanxiong), *bai zhi* (Radix angelicae dahuricae) and *xi xin* (Radix et rhizoma asari), in 50 patients with migraine headache was associated with complete recovery in 32 patients, improvement in 15 patients, and no effect in three patients. The overall rate of effectiveness was 94 percent.<sup>56</sup>
  
12. Angina: *Xiao chai hu tang* demonstrated good results in treating 41 patients with angina. While 35 had resolution of symptoms, they showed varying degrees of improvement based on ECG reports. The herbal treatment used *xiao chai hu tang* plus *dang gui* (Radix angelicae sinensis), *chuan xiong* (Rhizoma chuanxiong), and *fu zi* (Radix aconiti lateralis praeparata) as the base formula. Larger doses of certain herbs were used, depending on the differential diagnosis of the condition: *ren shen* (Radix et rhizoma ginseng) for severe *qi* deficiency; *fu zi* (Radix aconiti lateralis praeparata) for severe *yang* deficiency; *chai hu* (Radix bupleuri), *dang gui* (Radix angelicae sinensis), and *chuan xiong* (Rhizoma chuanxiong) for *qi* and blood stagnation; and *ban xia* (Rhizoma pinelliae) and *sheng jiang* (Rhizoma zingiberis recens) for phlegm stagnation.<sup>57</sup>
  
13. Depression: One study reported 78.8 percent effectiveness using modified *xiao chai hu tang* to treat depression. Modifications to the formula included the addition of *zeng ye tang* (Increase the Fluids Decoction) for *yin*-deficient heat; *xiang fu* (Rhizoma cyperi), *yu jin* (Radix curcumae) and *zhi qiao* (Fructus aurantii) for liver *qi* stagnation; and *hou po* (Cortex magnoliae officinalis), *bai zhu* (Rhizoma atractylodis macrocephalae) and *fu ling* (Poria) for damp and phlegm in the spleen. Of 90 patients, the study reported complete recovery in 64 patients and improvement in seven patients. Poor results were noted in 19 patients, who were then treated with drugs.<sup>58</sup>
  
14. Chronic fatigue syndrome: Modified *xiao chai hu tang* was used to treat 36 patients with chronic fatigue syndrome characterized by low-grade fever, chills, depression, muscle aches and pains in the entire body, lack of energy, bitter taste in the mouth, poor appetite, etc. The herbal treatment used *xiao chai hu tang* plus *ban lan gen* (Radix isatidis) and *gui zhi* (Ramulus cinnamomi) as the base formula, with more herbs added when necessary. Herbs were given for 10 days per course of treatment, for 1-4 courses. The study reported complete recovery in 26 patients and improvement in 10 others.<sup>59</sup>
  
15. Morning sickness: One study reported 88 percent effectiveness using *xiao chai hu tang* to treat nausea and vomiting during pregnancy. Of 320 patients, the study reported complete relief in 180 patients, improvement in 100 patients and no effect in 40 patients.<sup>60</sup>
  
16. Postpartum infection: Use of modified *xiao chai hu tang* had 96.6 percent effectiveness in treating 178 patients with postpartum viral infection (common cold or influenza). The herbal treatment contained *xiao chai hu tang* plus *huang qi* (Radix astragali), *yi mu cao* (Herba leonuri) and *dang gui* (Radix angelicae sinensis) as the base formula. Modifications were made as needed. For dry mouth and stuffy or runny nose, *sheng jiang* (Rhizoma zingiberis recens) was removed, and *sang ye* (Folium Mori), *ju hua* (Flos chrysanthemi), *bo he* (Herba menthae), and *lu gen* (Rhizoma phragmitis) were added. For nasal obstruction, *zi su ye* (Folium perillae) was added. For high fever without perspiration, *qing hao* (Herba artemisiae annuae) was added. For thick sticky sputum, *zhi mu* (Rhizoma anemarrhenae) and *zhe bei mu* (Bulbus fritillariae thunbergii) were added. For white, foamy sputum, *chen pi* (Pericarpium citri reticulatae) and *fu ling* (Poria) were added. For sore throat, *ban lan gen* (Radix isatidis), *she gan* (Rhizoma belamcandae), and *ma bo* (Lasiosphaera seu calvatia) were added. For red tongue body with little tongue coating, *yu zhu* (Rhizoma polygonati odorati) was added. After 1-2 packs of herbal treatment, the study reported complete recovery in 154 patients, improvement in 18 patients and no effect in six patients.<sup>61</sup>

17. Postpartum fever: Modified *xiao chai hu tang* effectively reduced body temperature within an average of 10 hours in all 60 postpartum women with fever. The herbal treatment contained *xiao chai hu tang* plus *dang gui* (Radix angelicae sinensis), *yi mu cao* (Herba leonuri) and others, as the base formula. In addition, *jin yin hua* (Flos lonicerae japonicae) and *jing jie* (Herba schizonepetae) were added for sore throat; *tao ren* (Semen persicae) and *hong hua* (Flos carthami) for lower abdominal pain with spotting; and *pu gong ying* (Herba taraxaci) and dry-fried *chuan shan jia* (Squama manis) for breast distention and pain.<sup>62</sup>
18. Dysmenorrhea: Administration of *xiao chai hu tang* was associated with 96.5 percent effectiveness in relieving primary dysmenorrhea. The treatment protocol was to take the herbs starting the first day of the period for 10 days, for three months per course of treatment. Of 57 patients, the study reported complete recovery in 28 patients, significant improvement in 22 patients, slight improvement in 5 patients, and no effect in two patients.<sup>63</sup>
19. Premenstrual syndrome (PMS): Use of modified *xiao chai hu tang* had 93.41 percent effectiveness in treating 167 women with PMS (complete relief in 77 patients, significant improvement in 57 patients, and moderate improvement in 22 patients). Modifications to the formula were made based on the condition of the patient. For breast distention and hypochondriac pain, *chuan lian zi* (Fructus toosendan), *xia ku cao* (Spica prunellae), and *bai shao* (Radix paeoniae alba) were added. For edema, *fu ling* (Poria), *ze xie* (Rhizoma alismatis), and *che qian zi* (Semen plantaginis) were added. For irritability, restlessness, and elevated body temperature, *ren shen* (Radix et rhizoma ginseng) and *ban xia* (Rhizoma pinelliae) were removed, and *mu dan pi* (Cortex moutan), *zhi zi* (Fructus gardeniae) and *di huang* (Radix rehmanniae) were added. For diarrhea, dry-fried *bai zhu* (Rhizoma atractylodis macrocephalae) and *yi yi ren* (Semen coicis) were added. For palpitations and insomnia, *yuan zhi* (Radix polygalae), *dang gui* (Radix angelicae sinensis) and dry-fried *suan zao ren* (Semen ziziphi spinosae) were added. For nausea and vomiting, *gan cao* (Radix et rhizoma glycyrrhizae) and *da zao* (Fructus jujubae) were removed, and *zhu ru* (Caulis bambusae in taenia), and *zi su geng* (Caulis perillae) were added. For dizziness and headache, *ju hua* (Flos chrysanthemi) and *chuan xiong* (Rhizoma chuanxiong) were added.<sup>64</sup>

#### Herb-Drug Interaction

- Interferon: Increased risk of acute pneumonitis may be associated with the use of interferon, *xiao chai hu tang* or both in combination. Among patients with chronic hepatitis or liver cirrhosis, the frequency of drug-induced pneumonitis was 0.5 percent in those given only interferon-alpha, 0.7 percent in those given only *xiao chai hu tang*, and 4.0 percent in those given both interferon-alpha and *xiao chai hu tang*.<sup>65</sup> Many theories have been proposed on the mechanism of this interaction. One theory stated that the herbs have not been shown to injure the lung tissues, but may overstimulate the neutrophils to release granulocytes, elastase and oxygen radicals, which subsequently damage lung tissue. The fibroblasts that repair the damaged tissue may increase the risk of pulmonary fibrosis.<sup>66</sup> Another theory stated that acute pneumonitis was associated with concurrent use of interferon and *xiao chai hu tang* may be due to allergic-immunological mechanisms.<sup>67</sup>
- Interleukin 2: Concurrent use of *xiao chai hu tang* and interleukin 2 showed a synergistic anti-tumor effect against murine renal cell carcinoma cell line in mice. The treatment protocol was to administer *xiao chai hu tang* at 2.5 g/kg daily over 30 days, and interleukin 2 at 10(4) U/subject by subcutaneous injection every other day for a total of 8 doses. The combination of these two

substances inhibited growth of the tumor and prolonged survival significantly as compared with the untreated mice.<sup>68</sup>

- Lamivudine (Epivir; 3TC): One study reported synergistic antiviral effect when *xiao chai hu tang* is combined with antiviral drugs such as zidovudine (AZT), lamivudine (3TC) or AZT plus 3TC. Used alone, *xiao chai hu tang* moderately inhibited HIV-1 replication at a concentration of 25 mcg/mL. Used together, *xiao chai hu tang* enhanced the anti-HIV-1 activity of 3TC. The researchers suggested that the combination of *xiao chai hu tang* and 3TC has potential as a chemotherapeutic modality for HIV-1 infection.<sup>69</sup>
- 5-fluorouracil (5-FU): The combination of 5-FU and *xiao chai hu tang* had a synergistic effect for treatment of cancer in mice by increasing the life span by 56 percent and alleviating side effects of 5-FU.<sup>70</sup>
- Drug-induced liver damage: Administration of *xiao chai hu tang* has been shown to have beneficial effects in preventing and/or treating damage induced by drugs, such as halothane, danazol, D-galactosamine and carbon tetrachloride.<sup>71,72,73,74</sup>
- Liver enzyme inhibition: The effect of *xiao chai hu tang* on cytochrome P450 enzymes was evaluated in 26 healthy subjects. Use of this herbal formula (2.5g twice daily for 5 days) was associated with a decreased mean activity of CYP1A2 by 16 percent on both day 1 and day 5 compared with the baseline (P=0.001).<sup>75</sup> In another study on the metabolic activity of different cytochrome P450 (CYP) isoforms, *xiao chai hu tang* was reported to be a competitive inhibitor of CYP2C9, but not CYP2D6. The study concluded that because of this inhibitory effect on liver metabolism, care should be taken with concurrent use of *xiao chai hu tang* and drugs.<sup>76</sup>
- Pentobarbital: Administration of *xiao chai hu tang* was associated with significantly shortened pentobarbital-induced sleeping time in mice. The mechanism of this interaction was attributed to the up-regulation of the mRNA expression of CYP2B, CYP3A1, CYP2E1 and CYP4A1.<sup>77</sup>
- Carbamazepine: Administration of one dose of *xiao chai hu tang* was associated with decreased peak concentration, and the time needed to reach the peak concentration, of carbamazepine in rats. However, 2-week repeated treatments of *xiao chai hu tang* did not affect plasma concentration-time profile or any pharmacokinetic parameter of carbamazepine, an indication that *xiao chai hu tang* did not affect the liver metabolism of carbamazepine. The study attributed the mechanism of this interaction to decreased gastrointestinal absorption of carbamazepine due to delayed gastric emptying.<sup>78</sup>
- Tolbutamide: *Xiao chai hu tang* demonstrably reduced the bioavailability of tolbutamide after oral administration in rats. The formula was found to accelerate the initial absorption rate, reduce the area under the plasma concentration-time curve, and decrease the overall bioavailability of tolbutamide.<sup>79</sup> The mechanism of this interaction was attributed to the inhibitory effect of *xiao chai hu tang* on the function of gastric emptying, thereby decreasing gastrointestinal absorption of tolbutamide.<sup>80</sup>
- Ofloxacin: In an open, random-crossover investigation study with seven volunteers, a single dose of ofloxacin and a one-week dose of *xiao chai hu tang* were given concurrently. Using high-performance liquid chromatography to evaluate the bioavailability of ofloxacin, it was determined that there is no significant effect on the rate or extent of bioavailability of ofloxacin

when given concurrently with *xiao chai hu tang*.<sup>81</sup>

SEPTEMBER 2007