

# **Main Street Veterinary Services**

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# **Chinese Herbs For Liver Disease**

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Several compounds now commonly used were previously the province of holistic practitioners only, including milk thistle seed extracts, S-adenosyl methionine and bile salts. Despite the ready availability of these supportive

treatments, however, liver disease remains a frustration for many small animal clinicians. Ironically, although now frequently offered through mainstream pharmaceutical companies, milk thistle has been found to be of poor efficacy in liver disease, except where caused by toxicity.

In contrast, several Chinese herbal formulas are routinely and markedly effective for managing small animal liver disease. It used to be you had to be an expert in Chinese medicine to use them effectively, but there is now enough research on how these formulas probably work to allow us to prescribe them accurately using just our Western understanding of liver disease, together with laboratory profiles of our patients. This article focuses on Chinese herbal treatments for cholestatic, inflammatory, neoplastic and vascular disorders of the liver.

## **Sourcing formulas**

The formulas discussed below are widely available from a number of vendors. These notes pertain to formulas manufactured by the Natural Path Herb Company, but formulas with the same names from other companies, with the exception of Minor Bupleurum, will likely perform in a similar way. For a very low fee, you can see these formulas in action in an online presentation of this material through the College of Integrative Veterinary Therapies at civtedu.org.

# Administration by enema

While injectable forms of herbal medicine are not yet available, high quantities of the appropriate formula can be delivered to an acutely ill patient via retention enema. A patient's response to an herbal formula delivered by enema is rapid and dramatic, with liver enzyme

elevations subsiding and the patient stabilizing within a couple of days. Compounds in the formulas are absorbed across the large intestine mucosa into the portal circulation and from there move rapidly to the liver, bypassing any gastroparesis.

#### Method

- 9 grams (4.5 teaspoon) in divided doses TID
- Suspend each dose in a maximum of 10 to 15 ml of warm water
- Instil into the transverse colon using a small rubber French feeding tube
- Use only granular extracts or crushed tablets, never liquid extracts

# 1. Biliary tract inflammation

High ALP and no elevated post-prandial bile acids. Pathogenesis: cholestasis caused by steroid hepatopathy and biliary tract inflammation causes several secondary changes, including fibrosis and apoptosis of hepatocytes and cholangiocytes

Herbal treatment

Si Miao San (Four Marvels Powder)

Cang Zhu ~ Atractylodes rhizome Huai Niu Xi ~ Achryanthes root Yi Yi Ren ~ Coix seed Huang Bo ~ Phellodendron bark

### How it works:

- Anti-inflammatory and antioxidant
- Anti-microbial (important in cholangiohepatitis)
- Promotes bile synthesis and flow
- Inhibits nitric oxide synthase to limit acute inflammation

#### Dose:

- Dose of granular extract
- 1g (1/2 tsp) BID for 10kg animals
- 2g (1 tsp) BID for 20kg animals
- 3g (1½ tsp) BID for 30kg animals and higher
- Can be mixed in food or given in gel caps

# Management:

- May be used along with Ursodiol
- Additive or synergistic effect with other antibiotics
- No long term safety concerns
- Cease use if loose stools occur (due to promotion of peristalsis and reduction of mucosal blood flow)

# 2. Hepatocellular Adenocarcinoma

Both ALT and ALP markedly elevated, greater than five or six times normal. Acute abdominal pain is common and is often the first presenting sign. Often caused by chronic hepatitis, which leads to oxidative damage to liver DNA, potentially leading to tumor development. Surgical excision yields good survival, but may not be possible if the tumor has invaded the caudal vena cava.

#### Herbal treatment

Ge Xia Zhu Yu Tang (Angelica and Corydalis)

Dang Gui ~ Chinese Angelica
Chuan Xiong ~ Ligusticum rhizome
Chi Shao Yao ~ Red Peony root
Zhi Ke ~ Bitter Orange peel
Gan Cao ~ Licourice root
Xiang Fu ~ Cyperus rhizome
Wu Yao ~ Lindera root
Mu Dan Pi ~ Peony Tree bark
Tao Ren ~ Persica seed
Hong Hua ~ Safflower flower
Yan Hu Suo ~ Corydalis rhizome

#### How it works:

- Actions contributed by several of its ingredients
- Reduction of nitric oxide synthase, resulting in reduced hepatic blood flow
- Inhibition of angiogenesis
- The net effect is a reduction of acute inflammation and the deprivation of blood supply to rapidly growing tumors
- Increases superoxide dismutase (SOD) levels, resulting in reduced free radical damage and lower ALT and AST levels
- Inhibits fibrosis and collagen synthesis
- Analgesic
- Antiproliferation and apoptosis inducing effects, particularly for hepatocellular carcinoma

#### Dose:

- Dose of granular extract
- 1g (1/2 tsp) BID for 10kg animals
- 2g (1 tsp) BID for 20kg animals
- 3g (1½ tsp) BID for 30kg animals and higher
- Can be mixed in food or given in gel caps

# 3. Chronic Hepatitis

Both ALT and ALP mildly to moderately elevated — usually up to three or four times normal, although some cases of extreme elevation will also respond. Pathogenesis: various etiologies cause the same ultimate pathophysiological and histological changes, including a progression to cirrhosis, which ends the patient's life.

Chinese herbs inhibit fibrosis and cirrhosis development, extending lifespan usually for years regardless of etiology.

Associated findings: by the time clinical signs appear, the animal already has a cirrhotic liver. Signs include loss of appetite, vomiting, weight loss, depression or lethargy, and increased thirst and urination. Laboratory changes occur before the patient becomes symptomatic.

Routine laboratory screening of patients will allow early detection and prevention of cirrhosis. Laboratory changes include elevated liver enzymes, and moderate to severe inflammation without evidence of tumor or infection. Additional genetic and copper metabolism testing is available for breeds prone to primary copper-associated hepatitis.

Note that the formula discussed below is not as effective for copper toxicosis. Use instead Angelica and Corydalis discussed above, either alone or in tandem with chelation.

Possible sequelae: hepatomegaly, jaundice, coagulation problems, ascites, weight loss, hepatic encephalopathy, hepatocellular adenocarcinoma. Prognosis is considered poor by the time clinical signs are obvious.

Herbal treatment

Rambling Ease Powder (Xiao Yao San; Bupleurum and Dang Gui Powder)

Chai Hu ~ Bupleurum
Dang Gui ~ Angelica sinensis
Bai Shao Yao ~ White Peony
Bo He ~ Mint
Bai Zhu ~ White Atractylodes
Fu Ling ~ Poria
Gan ~ Cao Licourice

# How it works:

- Reduces inflammation by safely increasing endothelial nitric oxide production
- This limits chemotaxis of neutrophils into the tissue, while increasing blood flow
- Increases superoxide dismutase (SOD) levels, resulting in reduced free radical damage and lower ALT and AST levels

- Inhibits fibrosis and collagen synthesis
- The net effect is a reduction of inflammation

#### Dose:

- Oral use is generally sufficient, since most cases are not emergencies
- Dose of granular extract
- 1g (1/2 tsp) BID for 10kg animals
- 2g (1 tsp) BID for 20kg animals
- 3g (1½ tsp) BID for 30kg animals and higher
- Can be mixed in food or given in gel caps

# Management:

- No herb/drug interactions are likely or expected
- If liver enzymes elevate significantly during use of this formula, then the patient has acute hepatic inflammation; use Ge Xia Zhu Yu Tang (Angelica and Corydalis) instead

# 4. Microvascular Portosystemic Shunt

Increased ALP with elevated post-prandial bile acids. Pathogenesis: probably most cases in dogs are due to intravascular inflammation, leading to increased blood pressure within the vessels, and secondary portal hypertension. Other causes include portal vein thrombosis, diffuse hepatic fibrosis and cirrhosis. In most dogs, the goal of therapy is to resolve the chronic intravascular inflammation.

Associated findings: microcytosis, due to injury of erythrocytes in narrowed vasculature; mild non-regenerative anemia, which aggravates liver hypoxia and hypofunction; low BUN, creatinine, glucose, albumin and cholesterol, from reduced synthesis due to blood flow impairments; possible ALP, especially in young animals; serum bile acids not absorbed post-prandially due to shunting; liver often small in size, even in non-cirrhotic and idiopathic cases; fine needle aspirates and core biopsies often unrewarding

Possible sequelae: ascites, potential hepatic encephalopathy, GI ulceration (splanchnic vasculopathy), ammonium biurate urolithiasis

There is no specific conventional treatment for portal hypertension from microvascular injury.

# Herbal treatment

Rambling Ease Powder (Xiao Yao San; Bupleurum and Dang Gui Powder)

Chai Hu ~ Bupleurum

Dang Gui ~ Angelica sinensis

Bai Shao Yao ~ White Peony

Bo He ~ Mint

Bai Zhu ~ White Atractylodes

Fu Ling ~ Poria Gan Cao ~ Licourice

#### How it works:

- Reduces inflammation by increasing endothelial nitric oxide production
- This limits chemotaxis of neutrophils into the tissue, while increasing blood flow
- Stimulates bone marrow to correct anemia and further improve blood flow
- Increases superoxide dismutase (SOD) levels, resulting in reduced free radical damage and lower ALT and AST levels
- Inhibits fibrosis and collagen synthesis
- The net effect is a reduction of inflammation and improved liver perfusion, manifesting as a correction of laboratory abnormalities

#### Dose:

- Oral use is generally sufficient, since most cases are not emergencies
- Dose of granular extract
- 1g (1/2 tsp) BID for 10kg animals
- 2g (1 tsp) BID for 20kg animals
- 3g (1½ tsp) BID for 30kg animals and higher
- Can be mixed in food or given in gel caps

# Management:

• No herb/drug interactions anticipated

### 5. Autoimmune disease and septicemia

Liver enzyme elevations plus azotemia is a hallmark of systemic disease amenable to this formula. Pathogenesis: liver inflammation may be a source of immune complexes that promote glomerulonephritis; autoimmune tendencies can be enhanced in both tissues by immune system malfunction; deep-seated parasitic, bacterial and viral infections can promote inflammatory responses in multiple organ.

Conventional treatment includes ACE inhibitors, immune suppressive agents and antimicrobials, and anti-parasitic therapy for dirofilariasis.

#### Herbal treatment

Xiao Chai Hu Tang (Minor Bupleurum Combination)

Chai Hu ~ Bupleurum root
Ban Xia ~ Pinellia rhizome
Gan Cao ~ Licorice root
Sheng Jiang ~ Ginger rhizome
Da Zao ~ Jujube
Ren Shen ~ Ginseng root
Huang Qin ~ Scutellaria root

#### How it works:

- Much of the effect is contributed by Bupleurum, but adequate Ginseng levels seem necessary for proper effect in animals
- Preparations for human use lack this idealized ratio, and therefore are frequently less effective
- Reduces renal and glomerular inflammation
- Hepatoprotective
- Inhibit liver inflammation and fibrosis
- Antioxidant
- Enhances macrophage activity and pathogen clearance, but reduces T cell responses involved in hypersensitivity reactions
- Inhibits nitric oxide synthase in particular organs, including the liver and kidney
- Reduces acute inflammation
- Promotes resolution of inflammatory problems due to infectious agents, including liver abscesses

### Dose:

- Dose of granular extract
- 1g (1/2 tsp) BID for 10kg animals
- 2g (1 tsp) BID for 20kg animals
- 3g (1 ½ tsp) BID for 30kg animals and higher
- Can be mixed in food or given in gel caps

# Management:

• No herb drug interactions anticipated