

TECHNICAL REPORT for VETERINARIAN USE ONLY

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HEPATO-SUPPORT FORMULA

USE:

As a dietary supplement that nutritionally supports healthy hepatic function

Hepato Support can be used as a supplement in the following scenarios:

- 1) Provide nutritional support to enable healthy liver function
- 2) Provide nutraceutical and botanical protection from liver toxins
- 3) Support the liver's ability to regenerate and maintain homeostatic balance

INGREDIENT LIST (1 capsule contains):

Milk Thistle Extract: (<i>providing 80% of the active flavonoid Silymarin</i>)	100mg
Vitamin B1 (thiamine)	5mg
Vitamin B2 (riboflavin)	5mg
Vitamin B6. (pyridoxine)	5mg
Calcium pantothenate	10mg
Vitamin B12 (cyanocobalamin)	10mcg
Inositol	20mg
Choline	20mg
Methionine (pharmaceutical grade)	20mg
Alpha Lipoic Acid (thiotic acid)	5mg

INGREDIENT INFORMATION:

A) Milk Thistle Extract:

This herbal extract has a long history of safety and effectiveness for treating Amanita mushroom poisoning in Germany. In a 1984 study of Amanita poisoning in dogs, there was 0% mortality when the milk thistle extract was given much as 5-24 hours post-ingestion of the LD50 P.O. dosage of mushroom (85mg/kg). Untreated dogs had a mortality rate of 33%, which is consistent with other studies. (Vogel, 1984)

- a. Milk thistle extract has general hepatoprotective properties. In a Finnish hospital study in humans with elevated liver enzymes, mostly due to alcoholism, it was found that a dosage of 420 mg/day of Silymarin significantly reduced elevated liver enzymes values after 4 weeks. Histopathology of liver biopsy cores also demonstrated improvement in hepatic health. (Salmi, 1982)
- b. Studies have defined milk thistle's effectiveness in protecting the liver from a wide variety of insults, including: Acetaminophen, ethanol, carbon tetrachloride, and d-galactosamine, ischemic injury, radiation, iron toxicity, and viral hepatitis B. (Muriel, 1990, 1992), (Bosisio, 1992), (Halim, 1997), (Chrungoo, 1997), (Campos, 1989), (Wu, 1993), (Kropacova, 1998), (Pietrangelo, 1995), (McPartland, 1996)
- c. Milk thistle extract produces its beneficial effects on the liver by several mechanisms of action. Silymarin is a potent antioxidant, providing very strong protection from lipid peroxidation, as well as from aqueous free radical ion species. (Basaga, 1997)
- d. Milk thistle also enhances liver detoxification profiles by amplifying the phase two liver glucuronidation both by enhancing Phase II enzymes and inhibiting Phase I Cytochrome P450 activity (Amdur, 1991). Silymarin has been shown in animal studies to inhibit several specific induced P450 enzymes in mice. (Baer-Dubowska, 1998) The toxin from the Amanita mushroom, *Amanitin*, is activated by the P450 cytochrome system. This may explain milk thistles' effectiveness against this highly poisonous mushroom. Silymarin also inhibits the activity of beta-glucuronidase, which is used by a number of intestinal bacterial pathogens to breakdown glucuronidase-bound toxin, thus releasing the toxin back into the patient's system. (Kim, 1994) Milk thistle can reduce that re-intoxication effect due to its inhibition of beta-glucuronidase activity.
- e. Milk thistle enhances endogenous glutathione stores, thus protecting against depletion of this very important endogenous hepatic antioxidant. (Campos, 1989)
- f. Silymarin inhibits the formation of leukotrienes from hepatic PUFA's (polyunsaturated fatty acids) by inhibition of the enzyme lipoxygenase. (Fiebrich, 1979)

- g. Silymarin increases hepatocyte protein synthesis, which in turn promotes liver cell regeneration following injury or damage to the hepatocytes. (Sonnenbichler, 1986)
- h. Silymarin has reported anti-inflammatory effects due to its ability to stabilize mast cell membranes (Fantozzi, 1986)), neutrophil migration inhibition (De La Puerta, 1996), Kupffer cell inhibition (Dehmlow, 1996), and by the inhibition of both leukotriene synthesis and prostaglandin formation (Dehmlow, 1996)
- i. Silymarin has been demonstrated to reduce or reverse liver fibrosis in animal models. Progressive liver fibrosis without inflammation was induced in rats by complete ligation of the bile duct. Silymarin at a dose of 50mg/kg/day was found to reduce fibrosis by as much as 30-35% over the control group. A lower dosage of 25 mg/kg/day did not have a similar effect. (Boigk, 1997))

B) B-Vitamins

a. Vitamin B1 Thiamin

Found in highest concentrations in liver, heart and kidneys. Thiamin is enzymatically involved in the oxidative and non-oxidative decarboxylation of alpha keto-acids, as well as transketolation reactions. A non-enzymatic function is also ascribed to thiamin. Thiamin triphosphate concentrates in neurons and it is believed to affect chloride permeability in these cells. All of the B vitamins, including thiamine are essential for the liver to perform its multitude of metabolic functions. Supplementation with the B vitamins is recommended in general for small animal patients with hepatobiliary diseases. (SACN, 2000).

b. Vitamin B2: Riboflavin

Riboflavin and its related metabolites are found as coenzymes in over 50 enzymatic processes in mammalian species. Concentrations in the liver of folate, riboflavin, nicotinamide, pantothenic acid, pyridoxine and Vitamin B12 have been found to be decreased in human patients with cirrhosis of the liver. (Levy, 1982)

c. Vitamin B5: Pantothenic acid (Calcium pantothenate)

Supplies both the macromineral calcium as well as the B vitamin pantothenate (B5). Vitamin B5 is utilized in the manufacture of coenzyme A (CoA) and acyl carrier protein (ACP) of which both are compounds that have essential roles in the utilization of fats and carbohydrates for energy production. Cats and dogs with pantothenic acid deficiency will have fatty livers and demonstrate poor appetites, and weight loss. (Baker, 1986)

d. Vitamin B6: Pyridoxine

The active forms of this vitamin are involved primarily in amino acid metabolism. It is also involved in the utilization of glycogen stores and the metabolism of lipids.

Vitamin B6 plays an important role in the multiplication of all cells, with particular benefit to mucous membranes, skin, red blood cells and the immune system. (SACN, 2000)

e. Inositol:

This member of the B-vitamins functions closely with choline. It is a primary component of cell membranes and although not an essential nutrient has been found in humans to be effective when used in liver disorders. Both inositol and choline provide a lipotropic effect as a result of their role in transporting fat from the liver. (Murray, 1996)

f. Choline:

Choline, unlike other B-vitamins is synthesized in the liver, and is an essential nutrient for all animals. It is the principal component of lecithin and is found bound to phospholipids as phosphatidylcholine. It has the following functions: 1) It is a structural component of all cell membranes; 2) It is a lipotropic agent (see inositol); 3) It is a precursor in the formation of the neurotransmitter acetylcholine; it along with methionine is the source of methyl groups, which are used by the body for transmethylation reactions. (SACN, 2000) Choline deficiency creates fatty liver, along with depressed growth hemorrhagic renal degeneration and thymic atrophy in dogs. (Baker, 1986) Phosphatidylcholine supplementation along with protein supplementation in primate models protects against alcohol-induced liver damage. (Rogers, 1979) A Danish study in humans found that phosphatidylcholine supplementation to patients with non viral hepatitis B chronic active hepatitis along with their normal immunosuppressive medications significantly improved liver biopsy results. (Jenkins, 1982)

g. Vitamin B12: Cyanocobalamin

First extracted from liver tissue in 1948, vitamin B12 was found to be the 'extrinsic' factor of food that treats pernicious anemia. Since then, Vitamin B12 has also been found to be essential for the normal functioning of all cells, but especially those of the gastrointestinal system, bone marrow and nervous tissue. With methionine, folic acid and choline, cobalamin participates in the transfer of methyl groups during the synthesis of the nucleic acids, purines and pyrimidine intermediate species. (Mahan, 1996).

C) Alpha Lipoic Acid (*Thiotic acid*)

This very potent anti-oxidant has been found to be synthesized by mammalian systems. It is unique as an antioxidant due to its ability to work in both its reduced and oxidized forms in both water and fat soluble tissues. Alpha lipoic acid is also very

readily absorbed from oral dosages. Alpha lipoic acid possesses other properties distinct from its potent effectiveness as an antioxidant. It has been shown to be a very potent heavy metal chelation agent.

Clinically, alpha lipoic acid is useful in the management of cataracts (Maitra, 1995), glaucoma (Filina, 1995), protection from free radical damage following ischemia-reperfusion injuries such as with myocardial infarction or CVA (Panigrahi, 1996), Amanita mushroom poisoning (Bartter, 1980), as well as for diabetic neuropathies (Nagamatsu, 1995). Alpha lipoic acid has been found to increase intracellular glutathione stores (Busse, 1992).

D) Methionine:

An alternate source of methyl groups to choline. Has been shown to reverse nutritional choline deficiency. (Zapsalis, 1985 #30) This is the most stable form of methionine and substitutes equivalently for pure methionine. (Zapsalis, 1985 #31)

HEPATO SUPPORT USE:

HEPATO SUPPORT for Dogs and Cats has been designed as a supportive clinical tool to be used as an adjunctive therapy:

1. *Liver toxins (Phenobarbital, corticosteroids, chemotherapeutics, pesticides, etc.)*
2. *Liver disease Acute:*
3. *Cholangiohepatitis, cholecystitis*
4. *Liver disease Chronic:*
5. *Hepatic lipodosis, Liver cirrhosis, neoplasia, hyperadrenocorticism*
6. *Concurrently with pharmaceutical therapies such as: Advantage™, Program™, Frontline™, Revolution™, Interceptor™, Heartguard™ (especially if animal is already sensitive).*

RECOMMENDED DOSAGES:

DOGS: One capsule twice daily for each 10-20 kg body weight.
Once capsule daily for dogs under 10kg body weight.
Dosage may be increased 2-3X for serious conditions, with no risk of toxicity, but with increased efficacy.

CATS: One capsule daily or ½ capsule twice day with meals

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