Adjunct Therapy for Liver Disease

Silymarin, a standardized extract of milk thistle fruits and seeds, contains at least 7 flavonolignans; silibin is considered the primary active ingredient.

The primary phase metabolite, silibinin glucuronide, is metabolized and secreted in bile wherein concentrations are 100x concentrations in serum. Silibinin is water insoluble and not readily absorbed by intestines; however, milk thistle extracts can be combined with solubilizing substances to improve oral bioavailability. The mechanism of action is understood as an antioxidant free radical scavenging and an inhibition of lipid peroxidation in hepatocytes, peripheral blood, and several other body tissues, making it useful as a protectant for the liver. The multiple cellular effects of silibinin include various inhibitions of inflammatory mediators. In humans with nonalcoholic fatty liver disease, silibinin can decrease C-reactive protein, inflammatory cytokines, and indices of hepatic fibrosis.

Silibinin is considered a safe drug, with no deaths or life-threatening symptoms reported in humans. In veterinary medicine, applications include administration in toxicity cases, hepatic disease (eg, hepatitis, cirrhosis), or fatty liver disease. Not to be considered a sole treatment, silibinin is a useful adjunct to acute and chronic disease affecting liver function. There is limited evidence regarding silibinin pharmacokinetics in domestic small animals and large animal herbivores, so its use warrants further investigation.

Commentary

Silymarin and its major constituent silibinin have been used for the treatment of liver disease for thousands of years. In addition, it is undergoing research as a promising therapy in cancer with solubilizing substances to improve oral bioavailability. The mechanism of action is understood as an antioxidant free radical scavenging and an inhibition of lipid peroxidation in hepatocytes, peripheral blood, and several other body tissues, making it useful as a protectant for the liver. The multiple cellular effects of silibinin include various inhibitions of inflammatory mediators. In humans with nonalcoholic fatty liver disease, silibinin can decrease C-reactive protein, inflammatory cytokines, and indices of hepatic fibrosis.

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Global Commentary

Treatment of inflammatory liver disease can be a challenge. The basis of therapy lies in immunomodulation, usually with corticosteroids; however, recent evidence suggests that cyclosporine may be more effective. Ursodeoxycholic acid, a synthetic bile salt, is also useful in treating many liver diseases. Because most liver damage is associated with oxidative damage within the hepatocyte, adjunctive use of antioxidants has long been recommended. This includes S-adenosylmethionine (SAMe) and vitamin E. This research suggested that the silibin in milk thistle, a folk remedy to treat liver disease in humans, has strong antioxidant properties. As the authors suggested, however, controlled studies of its efficacy in veterinary medicine are lacking and sorely needed.—Colin F. Burrows, BVetMed, PhD, Hon FRCVS, DACVIM

Source


Nah/ATO-GCS/5 07/08

Brief Summary: For full product information see product insert.

Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Description: ATOPICA (cyclosporine capsules, USP) MODIFIED is an oral form of cyclosporine that immediately forms a microemulsion in an aqueous environment.

Indications and Usage: ATOPICA is indicated for the control of atopic dermatitis in dogs weighing at least 4 lbs body weight.

Dosage and Administration: The initial daily dose of ATOPICA is 5 mg/kg/day (0.3-0.7 mg/kg/dog) as a single daily dose for 10 days. Following this initial treatment period, the dose of ATOPICA may be tapered by decreasing the frequency of dosing to every other day or two times a week, until a minimum frequency is reached which will maintain the desired therapeutic effect. ATOPICA should be given at least one hour before or two hours after a meal. If a dose is missed, the next dose should be administered (without doubling) as soon as possible, but dosing should be no more than once daily. See Product Insert for dosing chart.

Contraindications: ATOPICA is contraindicated for use in dogs with a history of neoplasia.

WARNINGS: ATOPICA (cyclosporine) is a potent systemic immunosuppressant that may increase the susceptibility to infection and the development of neoplasia.

Human Warnings: Not for human use. Keep this and all drugs out of reach of children.

Precautions: Gastrointestinal problems and gingival hyperplasia may occur at the initial recommended dose. ATOPICA should be used with caution with drugs that affect the P-450 enzyme system, such as ketoconazole, may lead to increased plasma levels of cyclosporine.

The safety and effectiveness of ATOPICA has not been established in dogs less than six months of age or less than 4 lbs body weight. ATOPICA is not for use in breeding dogs, pregnant or lactating bitches.

Since the effect of cyclosporine use on dogs with compromised renal function has not been studied, ATOPICA should be used with caution in dogs with renal insufficiency.

There have been reports of convulsions in human adult and pediatric patients receiving cyclosporine, particularly in combination with high dose methyldopadrenaline.

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