CLINICAL NOTES:
Novel Ideas for the Supplementation Treatment of Liver Disease in Dogs & Cats

A common dilemma faced by the astute practitioner involves the artful treatment of waxing and waning insidious liver disease, often presenting long before, or not even associated with, fulminant liver failure. Ideally, any treatment plan should deliver evidence-based bioavailable, nontoxic therapy that has clinical relevance in the dog or cat. However, data from prospective, randomized, placebo-controlled clinical trials involving large numbers of patients are not always available for drug and supplement combinations that are currently used for chronic liver disease in humans and animals.

Much of our understanding of supplemental (complementary or “alternative”) treatment in chronic small animal hepatic disease is taken from human medicine, anecdotal experience, and case reports. The disparity between what is currently practiced and what is supported by modern evidence is slowly evolving into a non-biased acknowledgement of ancient concepts and a call for more research. An example of this is a recent review on the use of milk thistle for liver disease in the conventional Journal of Veterinary Internal Medicine.

KEY POINTS
- Many supplemental compounds derived from ancient herbal medicine can be used to support the healing liver.
- SAMe and silymarin are evidence-based supplements used for thousands of years to treat liver disease.
- Quercetin is a potent free radical scavenger that can prevent oxidative damage in hepatocytes.
- N-acetylcysteine is an amino-acid derived compound that is known to support the endogenous hepatic antioxidant glutathione.
- Glycyrrhizin contributes to a reduced incidence of hepatic injury in toxicity studies.

ANTIOXIDANT THERAPY
Oxidative stress plays a major role in the pathogenesis of liver disease. The most comprehensively described antioxidants in veterinary medicine are SAMe, or S-adenosylmethionine, and silymarin. SAMe is of critical importance in generating the body’s own glutathione, which is responsible for detoxifying reactive oxygen species in dogs and cats.

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TREATMENT GOALS
In general, “conventional” treatment strategies address the underlying cause of disease, reduce and/or prevent further inflammation, reduce and/or prevent storage or accumulation (eg, copper or fat), reduce and prevent oxidative damage, reduce fibrosis, and also emphasize adequate nutrition. Complementary approaches tend to emphasize the overall energy level and comfort of the patient as well as addressing side effects of conventional therapies.

Supplements, such as herbal medications, vitamins, amino acids, and bioflavonoids, are commonly used to improve the clinical outcome of a liver disease patient or to reduce the theoretical potential hepatotoxicity of medications (eg, NSAIDs, steroids, antibiotics, antifungals). Traditionally, these agents have included vitamins B1, B12, E, and K1, taurine and carnitine (particularly for cats), ursodeoxycholic acid, SAMe, and silymarin. New products of interest also may combine SAMe and silymarin with lesser known but potent substances like quercetin, N-acetylcysteine, and glycyrrhizin.

Comprehensive Supplementation Therapy May Include:
- Silymarin, SAMe, quercetin, N-acetylcysteine, glycyrrhizin
- Taurine and carnitine in cats
- Ursodeoxycholic acid
- Zinc
- Vitamins B1 [thiamine] and B12 [cobalamin]
- Vitamins E and K1
- Chinese herbal medicine

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Acetaminophen has been combined with infusions of N-acetylcysteine are the intoxication. For example, intravenous infusions of N-acetylcysteine are the standard therapy for paracetamol (acetaminophen) intoxication. Oral N-acetylcysteine has been combined with selenium in rats to explore the synergism of these antioxidants. Further studies are necessary to determine if all dietary antioxidants can be delivered together effectively.

**ANTIINFLAMMATORY THERAPY**

Glycyrrhizin, an extract of the plant Glycyrrhiza glabra (licorice root), has long been used in Japan and some European countries as an oral and intravenous anti-inflammatory, immunomodulatory, and hepatoprotective agent. Early studies showed that animals treated with glycyrrhizin had a reduced incidence of hepatic injury. Inhibition of free radical generation and lipid peroxidation, decreased depletion of glutathione concentration, and inhibition of apoptosis of hepatocytes have been shown in various experimental models of hepatocyte injury in mice. The absorption of glycyrrhizin is not clearly defined in animals but the wealth of information in laboratory studies and thousands of years of anecdotal accounts of its use in humans for liver disease indicate that it has promise, and further studies are warranted.

**IN CONCLUSION**

As new products for liver disease evolve, it will be important to critically evaluate clinical data for a given product, its medical grade and route of administration, and whether each compound in it is bioavailable and subsequently clinically relevant in pets. It is also important to carefully consider which supplements may be indicated based upon the species, pathophysiology of disease, and condition of the pet as supplements are not indicated if the pet isn't eating. Thousands of years of herbal and nutritional therapy have opened the gate for western researchers to discover new modalities and therapeutic compounds, inviting future research to help elucidate our understanding of how these compounds work when treating liver disease.

**REFERENCES**


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