



**LIVER SUPPORT
WILL NEVER BE
THE SAME
SAMeLQ[®]**



LIVER SUPPORT SUPPLEMENT

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In all of the cases where I have switched from SAMe with milk thistle to SAMeLQ® (with licorice root extract), the patients have shown a significant improvement in hepatocellular and cholestatic enzymes.

CEVA SAMeLQ® TABLETS provide a comprehensive supplement for the support of the liver regardless of the underlying pathology. Its key ingredients include: Quercetin, N-Acetyl-L-Cysteine, L-Taurine, Glycyrrhizinate Ammonium (Licorice Root Extract), and B Vitamins (B3, B5, B6, B1, B2). As many patients with both acute and chronic liver injury end up on several medications, a single product that supports the liver in a multitude of ways is preferred by this author. Please note this product should be given to the dog/cat on an empty stomach to maximize absorption on the first pass into the liver. For patients that are difficult to medicate, it is okay to administer it in small amounts with less than 1 tablespoon of food, such as in a pill pocket, cream cheese, etc.

SAMeLQ® is my preferred product compared to other liver supportive nutraceuticals currently available to help support the liver. The product contains S-Adenosyl-L-Methionine (*SAMe*), which supports liver function and normal detoxification. It also contains Glycyrrhizinate Ammonium (*Licorice Root Extract*) which has been used for centuries to support both liver and kidney function and help maintain healthy liver cells. In addition, the product contains *N-Acetyl-L-Cysteine*, an antioxidant that helps decrease oxidative damage to the liver. Additional antioxidants in the product include: *quercetin*, *L-Taurine* and *zinc*. I personally have used this product in many of my cases needing liver support. In all of the cases where I have switched from SAMe with milk thistle to SAMeLQ® (with licorice root extract), the patients have shown a significant improvement in hepatocellular and cholestatic enzymes, as well as liver function as evidenced by improved bile acids. This product is my nutraceutical of choice for all of my liver cases.

Glycyrrhizinate Ammonium (Licorice Root Extract)

Licorice from the root of *Glycyrrhiza glabra* is one of the oldest and most well-used herbs in Eastern traditional medicine. In humans, it is used to treat tuberculosis, peptic ulcers and liver injury in a number of clinical disorders. The licorice plant is actually a shrub and a member of the pea family, native to areas of Asia and the Mediterranean. This plant has an extensive root system with the taproot or main root being harvested for use.

Glycyrrhiza is derived from the Greek root word “glykos”, which means sweet, and “rhiza”, which means root. The root is yellow on the inside due to a high content of flavonoids, which are potent antioxidants. Glycyrrhizin is the major active agent isolated from licorice that scavenges reactive oxygen species (ROS) and has an anti-inflammatory action. Specifically, it combats liver insult from a variety of mechanisms by the induction of heme oxygenase-1 and the down regulation of proinflammatory mediators (protective mechanism in CCl₄ injury).

Why are antioxidants important?

A by-product of cellular redox reactions, excessive free radicals cause oxidative damage to DNA, lipids and proteins. This oxidative damage is thought to be responsible for liver damage, cardiovascular diseases, neoplasia and neurodegenerative disease processes.

The constituents of licorice also have activity analogous to the mild effects of hydrocortisone. Additional factors in the inflammatory process inhibited by

glycyrrhizic acid include the formation of prostaglandin E2, cyclooxygenase activity, and platelet aggregation.

The antioxidant and liver protective properties of licorice and its constituents are significant as they inhibit the generation of reactive oxygen species by the neutrophils at the site of the inflammation.

A side effect most commonly reported with licorice therapy is hypertension which is due to the effect it has on the renin-angiotensin-aldosterone system (RAAS). Licorice saponins can potentiate aldosterone action as they bind to mineralocorticoid receptors in the kidney. This effect is known as "pseudo aldosteronism." These patients along with hypertension may experience hypokalemia, hypernatremia with subsequent edema. *Patients with hypertension should not use this product. If they do, they should use it with caution.* These side effects are related to the dose and duration of licorice intake and individual susceptibility. Patients with delayed gastric emptying are likely more susceptible to side effects due to enterohepatic circulation. Side effects are related to the dose and duration of the licorice intake as well as individual susceptibility. In man, pseudo aldosteronism or mineralocorticoid excess syndrome are seen over a wide range of doses from 1.5 g to 250 g daily. The concentration of the licorice in SAMeLQ[®] is unlikely to result in any side effects. If any side effects do occur, they are completely reversible with discontinuation of administration. In a patient who is hypertensive, and you are considering using it, make sure the hypertension is controlled prior to initiating therapy and check the blood pressure 1 week after starting treatment.

Licorice root should also not be used at the same time as digoxin as it may increase the likelihood of cardiac arrhythmias. The use of licorice root and diuretics simultaneously may result in hypokalemia. In this instance, check the electrolytes prior to and one week after starting therapy.

The liver is made up of 60-65% hepatocytes, which have a crucial job in the metabolism of drugs, toxins and other exogenous chemicals. This makes it a target for toxic substances. The liver's

susceptibility to chemical injury by a variety of drugs is a function of its anatomical proximity to the bloodstream and gastrointestinal tract. In addition, the liver's ability to biotransform and concentrate xenobiotics. Reactive oxygen and nitrogen species (ROS/RON) are produced during this detoxification process, which leads to oxidative stress. Excessive production of free radicals as a by-product of cellular redox reactions causes oxidative damage to lipids, proteins and DNA. Imbalance in the system leads to increased levels of oxidants. This overwhelms the capacity of the antioxidant defense network, causing oxidative stress. Glycyrrhizin may provide maximum conjugation of free radicals, depriving them of their toxic abilities.

In summary, each component of SAMeLQ[®] has distinct features:

SAMe

- Supports liver function
- Supports normal detoxification
- Supports normal cleansing of the liver from impurities

N-Acetyl-L-Cysteine

- This antioxidant helps decrease oxidative damage
- Amino Acid
- Precursor to glutathione

Licorice Root Extract

- Helps maintain healthy liver cells
- Maintains liver & kidney function
- Promotes the body's innate resistance to pathogens

Antioxidants

- Quercetin, L-Taurine, B-Vitamins & other antioxidants help enhance immune response
- Assist the body by helping to remove damaging free radicals

The antioxidant and liver protective properties of licorice and its constituents are significant as they inhibit the generation of reactive oxygen species by the neutrophils at the site of the inflammation.

When compared to SAME products with milk thistle, SAME with licorice root demonstrates less apoptosis and greater antioxidant activity.

For liver support, antioxidants are key.

SAME (S-Adenosyl methionine) is formed from adenosine triphosphate and methionine, an amino acid present in food. It is converted in the liver to the antioxidant glutathione, and transmethylation helps stabilize cell membranes and promotes secretion of bile. It is converted into antioxidants, specifically methylthioadenosine, which has anti-inflammatory and analgesic properties. It is a sensitive molecule that degrades in heat and moisture. Storage conditions are important. It should be stored at room temperature (68-77° F), with no exposure to direct light.

Glycyrrhizate Ammonium (Licorice Root Extract) (In vitro study)

Liver Support

- Helps inhibit lipid peroxidation
- Less apoptosis with licorice root than silymarin (milk thistle)

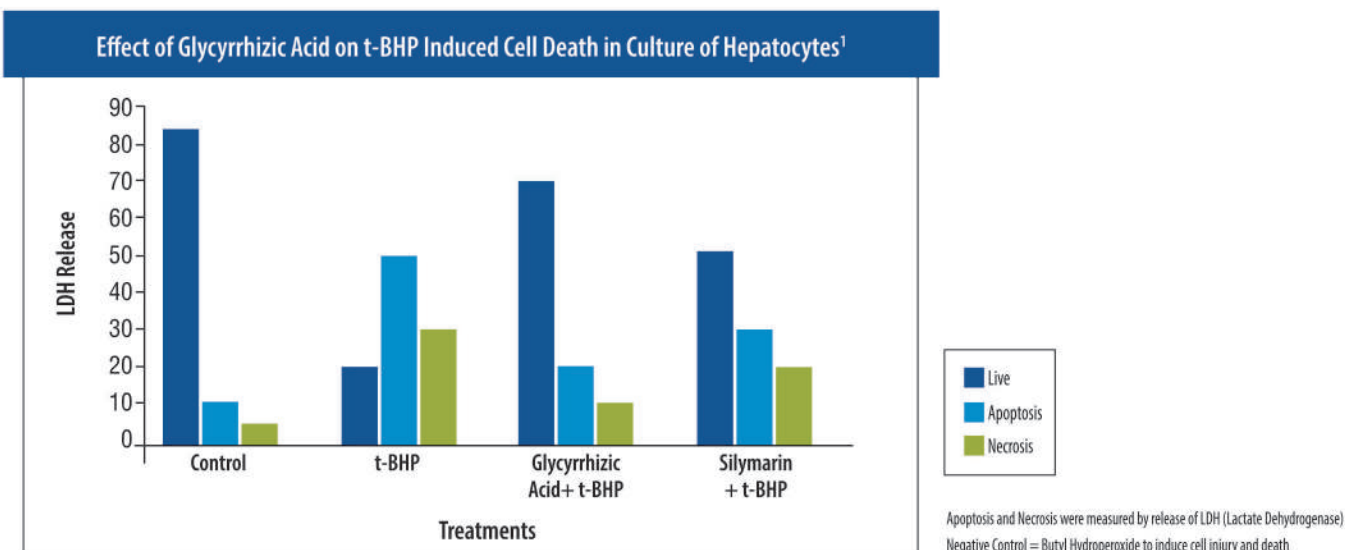
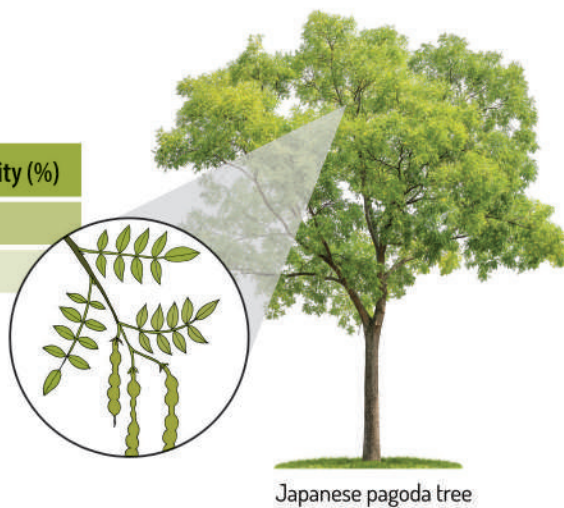


Figure 1—Tripathi, M., Singh B.K., Kakkar P. Glycyrrhizic acid modulates t-BHO induced apoptosis in primary rat hepatocytes. Food and Chemical Toxicology. 2009;47:339-347.

Quercetin is a plant extract from the Japanese pagoda tree. It is a flavonoid compound and a powerful antioxidant.

Compound	DPPH Scavenging Activity (%)	Superoxide Scavenging Activity (%)
Silybin	16.6%	38.2%
Quercetin	96.8%	93.8%

Figure 2—Wang F. et al. Preparation of C-23 esterified silybin derivatives and evaluation of their lipid peroxidation inhibitory and DNA protective properties. Bioorganic & Medicinal Chemistry. 2009;17:6830-6389. (DPPH, 1,1-diphenyl-2-picrylhydrazyl.)



Japanese pagoda tree

Table 5. Comparison of Liver Supplements

Ingredient/Feature	SAMeLQ® (Ceva)	Denamarin® (Nutramax)	Novifit® (Virbac)
SAMe	X	X	X
Licorice Root Extract	X		
Quercetin	X		
Milk Thistle Silybin/Silymarin		X	
N-Acetyl-L-Cysteine	X		
Zinc	X		
L-Taurine	X		
Chewable Tablet	X	X	
Enteric-Coated			X

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CASE EXAMPLES: SAMeLQ® IN ACTION

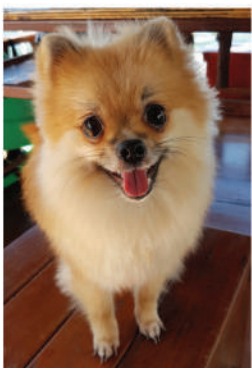


CASE: SHIVA, 4 years old, Doberman

Treatment: Initiated with Imuran® (azathioprine; 50 mg q24h), metronidazole 375 mg PO BID, Royal Canin® Veterinary Diet Hepatic Formula. SAMeLQ® was started after 3 months.

Table 6. Shiva after 2 months on SAMeLQ®

Normal Values	Pretreatment	Imuran®, hepatic diet x 3 mo	+ SAMeLQ® x 2 mo
ALP (20 - 150 U/L)	1389	967	60
ALT (10 - 118 U/L)	2351	905	167
GGT (0 - 7 U/L)	85	27	8
TBR (0.1 - 0.5 mg/dL)	1.2	0.4	0.4
BILE ACIDS (0 - 25 micromoles/L)	>300	120	27



CASE: TIRA, 8 years old, Pomeranian

Treatment: Cyclosporine microemulsion 30 mg PO BID (In a gel cap, on an empty stomach, one hour before or 2 hours after food.) Metronidazole 62.5 mg PO BID, Omeprazole 5 mg PO BID, Royal Canin® Veterinary Diet Hepatic Formula. SAMeLQ® started 3 months later.

Table 7. Tira after 2 months on SAMeLQ®

Normal Values	Pretreatment	Cyclosporine, hepatic diet x 3 mo	+ SAMeLQ® x 2 mo
ALP (20 - 150 U/L)	1242	151	140
ALT (10 - 118 U/L)	1575	142	59
GGT (0 - 7 U/L)	35	18	10
TBR (0.1 - 0.5 mg/dL)	0.6	0.4	0.3
BILE ACIDS (0 - 25 micromoles/L)	>140	>140	66



CASE: KODA, 8 years old, Labrador

Treatment: (for Chronic Hepatic Support)

Denamarin® 425 mg SAmE + 35 mg silybin 2 tablets once a day, Ursodiol 600mg q 24 hours, Metronidazole 375 mg PO BID, Omeprazole 5 mg PO BID, Royal Canin® Veterinary Diet Hepatic Formula. Switched from Denamarin® to SAMeLQ® after 1 year.

Table 8. Koda after 1 month on SAMeLQ®

Normal Values	Denamarin®, Ursodiol, hepatic diet x 12 mo	off Denamarin® + SAMeLQ® x 1 mo
ALP (20 - 150 U/L)	570	441
ALT (10 - 118 U/L)	205	155
GGT (0 - 7 U/L)	13	3
TBR (0.1 - 0.5 mg/dL)	0.5	0.5
BILE ACIDS (0 - 25 micromoles/L)	32	24



CASE: McCLAREN, 8 Years old, Shetland Sheepdog

Referred for evaluation of elevated hepatic enzymes.

Normal liver size on x-rays & US, hyperechoic liver on ultrasound; gall bladder sludge, low Vitamin B12 <150 ng/L = Distal small intestinal malabsorption (Range 500-908 ng/L), low Folic Acid 6.0 ug/L = Proximal small intestinal malabsorption (Range: 7.7-24.4 ug/L). Started SAMeLQ® after 3 months.

Table 9. McClaren after 3 months on SAMeLQ®

Normal Values	Pretreatment	+ B12, Folate Hydrolyzed Diet Metronidazole	+ SAMeLQ® x 3 mo
ALP (20 - 150 U/L)	852	745	160
ALT (10 - 118 U/L)	645	598	120
GGT (0 - 7 U/L)	12	10	7
TBR (0.1 - 0.5 mg/dL)	0.4	0.4	0.4
BILE ACIDS (0 - 25 micromoles/L)	27	20	18

SAMeLQ® SUMMARY

- **Unique Liver Support Formulation**
- **Antioxidants help enhance immune response and protect against free radicals**
- **SAmE to help promote liver metabolic activity**
- **Palatable, chewable tablet forms**

In summary, each component of SAMeLQ® has a variety of functions to help support normal liver function. The use of effective liver support nutraceuticals can be a beneficial addition to your liver support protocols.

The product is available in easy-to-use snap tablets and a palatable chewable tablet. Contact your Ceva representative for more information or visit www.SameLQ.com.

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