PAW HEPATOADVANCED®

ANTIOXIDANT SUPPORT FOR DOGS AND CATS WITH LIVER DISEASE

PAW HepatoAdvanced® is a convenient, chewable tablet containing a blend of bioavailable antioxidants, providing detoxification support in the management of canine and feline liver disease.

BENEFITS

- **Simple and convenient** dosing in the form of a tasty chewable tablet
- **Formulated with delayed release technology**, enabling steady metabolism by the liver and a prolonged duration of activity
- **Contains a unique and stable form of S-adenosylmethionine** (SAMe), a precursor to the potent antioxidant glutathione, which is hepatoprotective
- **Contains silybin in a phospholipid complex (Siliphos®)**, which has been shown to provide significantly enhanced bioavailability in dogs and cats compared to standardised milk thistle
- **Contains vitamin E** in its formulation, preventing the need for additional supplementation

Contains:

Active ingredients	Cat & Small Dog	Medium & Large Dog
S-Adenosyl-L-methionine disulfate p-toluenesulfonate (Equivalent to SAMe)	50 mg	310 mg
D-alpha tocopherol succinate (Vitamin E)	45 IU	200 IU
Silybin Phospholipids Equivalent to silybin phosphatidylcholine (Equivalent to silybin A+B)	13 mg	90 mg

Weight	Daily Dose
Cat & Small Dog Dosage	
1 - 2.4 kg	1 chewable tablet
2.5 - 9.9 kg	2 chewable tablets
10 - 14.9 kg	3 chewable tablets
Medium & Large Dog Dosage	
10 - 14.9 kg	½ chewable tablet
15 - 29.9 kg	1 chewable tablet
30 - 59.9 kg	2 chewable tablets*

*DO NOT exceed 2 chewable tablets per 24 hour period

For optimal absorption, administer HepatoAdvanced® (as per the dosing chart above), once a day on an empty stomach.

EDUCATION

Introducing glutathione

Glutathione (GSH) is the most abundant and important intracellular antioxidant in the body.[4] The liver is the major source of glutathione for the entire body, with 90% of the systemically distributed glutathione synthesised by hepatocytes.[5,6]

Glutathione is essential for a number of physiological functions including: the management of cell redox status, detoxification and conjugation reactions, normal enzyme functions, protein-structural configurations and gene expression.[7]

Putting the spotlight on antioxidant therapy

Therapeutic intervention with antioxidants is of vital importance in supporting acute and chronic liver disease, through the enhancement of natural hepatic defence mechanisms to inhibit inflammation and fibrosis, prevent apoptosis and protect against oxidative injury.[1, 2]

The essential roles of SAMe in health and disease

S-adenosylmethionine (SAMe) is an intermediary metabolite that is synthesised from the amino acid methionine and adenosine triphosphate (ATP) in all living cells.[7,8] Considering that SAMe is a glutathione precursor[9], it is of particular importance in hepatocytes.[7]

Severe liver injury can downregulate SAMe synthetase (the enzyme controlling methionine transformation into SAMe) and as such, SAMe can become a conditionally essential nutrient.[1, 7, 10]

SAMe supplementation replenishes hepatic glutathione concentrations and consequently decreases the production of reactive oxygen species in dogs.[10] Thus, it effectively protects against the risk of hepatotoxicity, particularly in necro-inflammatory and cholestatic diseases.[1, 3, 5]

Vitamin E: A powerful antioxidant

Vitamin E is a lipid-soluble vitamin and potent endogenous antioxidant that functions as a free radical scavenger to protect membrane phospholipids from peroxidative damage.[4, 13, 15, 16]

Considering that vitamin E plays a key role in the hepatic antioxidant network alongside glutathione, supplementation has been recommended in the nutritional management of hepatobiliary disorders likely to involve oxidative membrane injury.[1,11]

In addition, vitamin E aids in preserving the integrity of hepatocytes and reduces the activation of hepatic stellate cells, thus acting as an antifibrotic.[7, 17] Vitamin E acts to replenish hepatic glutathione levels, further reducing the impact of oxidative damage on hepatocytes.[17]

Silymarin: Antioxidant, anti-inflammatory and antifibrotic[1]

Silymarin is the major active ingredient of benefit in the milk thistle plant (*Silybum marianum*).[11]

Silymarin has a wide range of biological effects that are highly beneficial in the treatment of hepatobiliary disease, including antioxidant, anti-inflammatory, and antifibrotic properties. Primarily, silymarin acts as an antioxidant by reducing free radical production and lipid peroxidation. It also scavenges reactive oxygen species and aids in the replenishment of glutathione concentrations.[13, 14]

Warnings/safety

- For animal use only.
- For veterinary supply only.
- Use with caution in pregnant or lactating animals as safe use has not been established in this population.
- SAMe has a wide safety margin. Side effects or overdose effects are rare, but are limited to mild gastrointestinal signs, immediate post pill nausea and food refusal.
- Concomitant use of SAMe with tramadol, meperidine, dextromethorphan, pentazocine, MAOIs (selegiline), SSRIs (fluoxetine) and other anti-depressants (amitriptyline, clomipramine) may theoretically cause additive serotonergic effects. Use with caution simultaneously.
- Silymarin typically has no side effects, but consider drug interactions in polymedicated patients, such as the following: antiviral drugs, drugs affected by cytochrome P450 & CYP3A4 inhibition and drugs cleared via hepatic glucuronidation.
- There are no commonly noted toxic effects derived from vitamin E supplementation, although it may inhibit the absorption of other fat-soluble vitamins when administered at high doses. Therefore, it is recommended to not exceed a total daily dose of 400IU per dog. [4, 5, 10] Vitamin E is not recommended in liver disease patients with evidence of vitamin K deficiency.[10]

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