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MARIN® FOR DOGS

Nutramax Labs.

Sold Only Through Veterinarians

ACTIVE INGREDIENTS:

	Marin for Dogs <i>(for small to medium dogs)</i>	Marin for Dogs <i>(for large dogs)</i>
Vitamin E (As d- α tocopheryl acetate)	105 IU	300 IU
Silybin A+B	24 mg*	70 mg*
Zinc (As zinc gluconate)	17 mg	45 mg

OTHER INGREDIENTS:

Small to Medium Dogs: Natural liver flavor, microcrystalline cellulose, sucrose, dicalcium phosphate, natural chicken flavor, dried brewers yeast, phosphatidylcholine, silicon dioxide, and magnesium stearate.

Large Dogs: Microcrystalline cellulose, natural liver flavor, sucrose, natural chicken flavor, dried brewers yeast, phosphatidylcholine, silicon dioxide, and magnesium stearate.

*In a phosphatidylcholine complex to increase bioavailability.

Marin For Dogs is a combination of silybin in a phosphatidylcholine complex, vitamin E, and zinc for veterinary use only. It is available as a chewable tablet in two strengths for dogs: one for small to medium breeds and one for large breeds.

BACKGROUND

Silybin is the most biologically active component of an extract known as silymarin.¹ Silybin/silymarin has been shown to have beneficial effects on liver function.²⁻⁴ Vitamin E, a membrane-associated antioxidant, helps

protect the liver against oxidant injury.⁵ Zinc, an essential trace mineral and a component of approximately 200 enzymes, participates in many metabolic pathways, including protein and carbohydrate metabolism and hormone synthesis, in the liver and throughout the body.^{2,6,7}

PURPOSE

The combination of silybin, vitamin E, and zinc in Marin For Dogs provides a multi-faceted approach to liver support.

Silybin/silymarin has many different mechanisms of action. *In vitro* and *in vivo* studies have shown that it protects against oxidative stress;^{8,9} promotes hepatocyte protein synthesis,¹⁰ a mechanism for liver cell regeneration; inhibits leukotriene production,¹¹ which can be beneficial as production of leukotrienes is a component of the inflammatory response; stimulates biliary flow and production of hepatoprotective bile salts (e.g., beta-muricholate and ursodeoxycholate);¹² and increases levels of glutathione.¹³

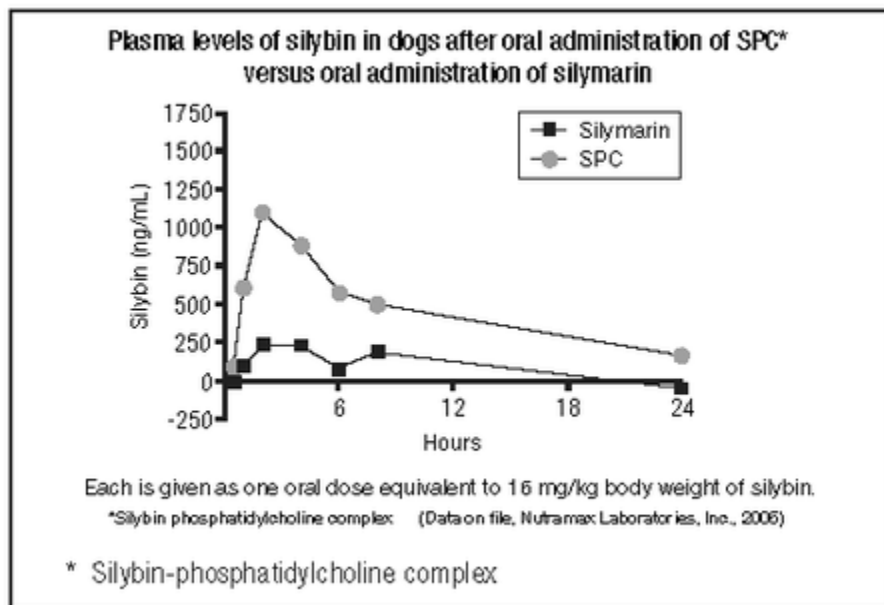
In a study, silybin was shown to be protective in acute *Amanita phalloides* mushroom poisoning in dogs, where one-third of the control dogs died, while all dogs in the silybin-group lived.³ Silybin-group dogs also had lower bilirubin, AST, ALT, and ALP levels and improved prothrombin times compared to control dogs.³ In another report, the liver enzymes improved in five out of six dogs with 30 days of silymarin administration.⁴

Vitamin E, a membrane-associated antioxidant, benefits liver function because oxidant injury to hepatocytes can affect liver health. Vitamin E has been shown to reduce the oxidative injury to the hepatocyte mitochondrial membranes caused by copper accumulation and hydrophobic bile salts (these bile salts build up in the liver when bile flow is impaired).⁵ Vitamin E supplementation may also be beneficial in dogs with copper accumulation as a study showed that these dogs have low hepatic levels of vitamin E.⁵ ALT, a marker of liver function, and GSH:GSSG ratio, a measure of oxidative status, were noted to improve in dogs with long-term liver compromise that were supplemented with vitamin E.¹⁴ Vitamin E has other actions separate from its antioxidant role that also help to support hepatic health.²

Zinc supplementation helps to support liver health in several ways. When the liver is compromised in dogs, especially long-term, hepatic zinc levels decrease; therefore, supplementing with zinc would be beneficial.^{2,5} Zinc's antioxidant and antifibrotic effects⁵ benefit the liver, and zinc is important to cell membrane function and immune responses.² It also is often recommended for its role via formation of metallothionein in binding metals, such as copper, which can accumulate excessively in the liver and cause damage.^{6,15} Breeds such as Bedlington Terriers, West Highland White Terriers, and Skye Terriers are known to be predisposed to excess copper accumulation,^{15,16} but copper may build up secondarily as well in the liver of any dog with long-term compromised liver function, which has affected biliary flow.¹⁵

PHARMACOKINETICS

Silybin has low bioavailability.¹⁷ Marin, therefore, has been specially formulated to address this issue. It contains silybin in a complex with soybean phosphatidylcholine, resulting in superior absorption and bioavailability compared to silymarin or silybin administration alone.¹⁷⁻¹⁹ A study in dogs showed plasma silybin levels more than four times higher with administration of a silybin-phosphatidylcholine complex (SPC) than obtained with administration of silymarin alone (see graph).²⁰ Studies in rats showed that administration of the silybin-phosphatidylcholine complex was capable of reaching effective intracellular levels in liver microsomes not achieved with silybin administration alone.⁸



Plasma levels in dogs after oral administration of silymarin versus SPC (silybinphosphatidylcholine complex). Each was given at the same amount based on silybin content (178 mg).²⁰

SAFETY

There are no known drug interactions or contraindications to the use of silymarin/silybin/silymarin in animals.^{21,22} While mild side effects, such as gastrointestinal upset, itching and headache, have been rarely reported in primates,^{6,21,23} no side effects have been noted in dogs.^{4,21,22,24} The specific silybin-phosphatidylcholine complex in Marin[®] has been evaluated in both acute and chronic use safety studies: an acute toxicity study in dogs using levels greater than 80x the amount in Marin revealed no adverse physiologic effects,²⁴ and a chronic toxicity study in monkeys who received greater than 80x the amount in Marin for 26 weeks showed no compound-related adverse effects.²³

Vitamin E is also well-tolerated in recommended amounts.⁵

Zinc is generally well-tolerated when administered in recommended amounts. Occasionally, vomiting or lack of appetite may be noted.^{2,6} To minimize any zinc sensitivity by some dogs, it is recommended to administer Marin for Dogs on a full stomach. Marin is formulated with the NRC-recommended daily intake of zinc for adult dogs.⁷

ADMINISTRATION

Marin For Dogs is formulated in a tasty chewable tablet that may be given as a treat or crumbled over the food. Tablets are scored for ease of administration. Recommended administration amounts are provided below.

DAILY ADMINISTRATION GUIDE*

Body Weight	Marin for Dogs (for small to medium dogs)	Marin for Dogs (for large dogs)
Less than 10 lbs	1/4 tablet	
11-19 lbs	1/2 tablet	
20-35 lbs	1 tablet	

36-54 lbs		1/2 tablet
55-99 lbs		1 tablet
Over 100 lbs		1 1/2 tablets

*Tablets should be given on a full stomach for dogs of all sizes.

STORAGE

Store in a cool dry place. Keep tablets in bottle until used.

Store in a cool, dry area out of direct sunlight.

Keep lid tightly secured to ensure freshness.

Keep bottle out of the reach of children.

This bottle contains (1) non-toxic desiccant to help preserve freshness and ensure the shelf life of the product.

References:

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02-1006-07

FOR SMALL TO MEDIUM DOGS	30 Chewable Tablets	00-1023-04
FOR LARGE DOGS	30 Chewable Tablets	00-1024-04

NAC No.: 12910073