Denamarin®

For Dogs and Cats

Raising liver support to a new level

nutramax® LABORATORIES VETERINARY SCIENCES, INC.

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Denamarin®

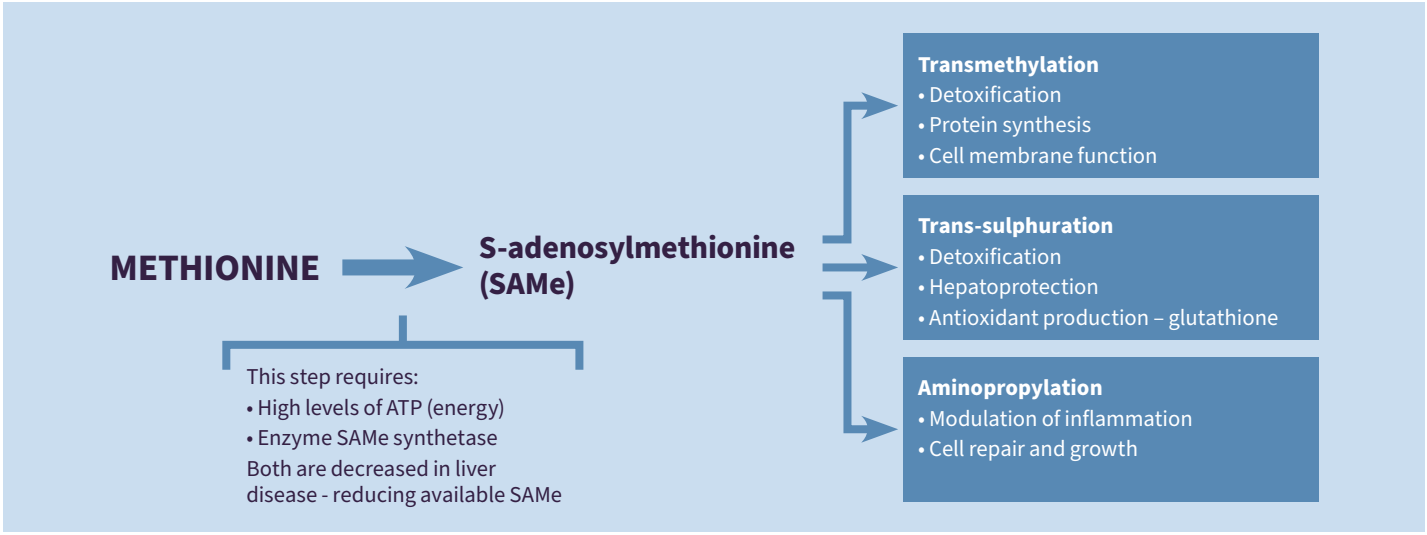


What is oxidative stress?

Reactive oxygen species (ROS), including free radicals, are a normal by-product of liver metabolism. The healthy liver utilises many different antioxidants, including glutathione, to minimise the damage that can be caused by ROS.

The redox state describes the summation of pro- and antioxidant molecules; oxidative stress occurs when an imbalance arises between levels of ROS and available antioxidants caused by:

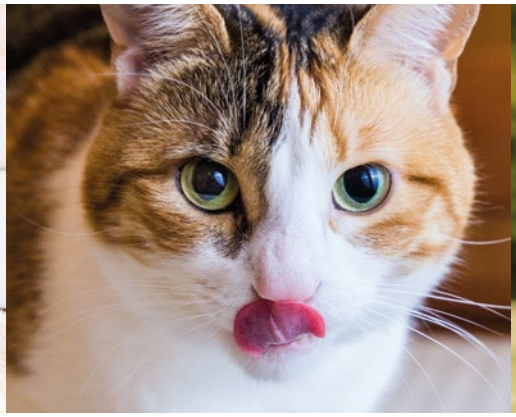
- A depletion of antioxidants, and/or
- An increase in ROS, which occurs in nearly all diseases of the liver and biliary tract[1].



Glutathione and SAMe

Glutathione is the most important antioxidant used by the liver to protect against oxidative stress. The healthy liver converts the amino acid, methionine, into S-adenosylmethionine (SAMe) and then into glutathione via the trans-sulphuration pathway. In liver disease this capability is compromised because the conversion of methionine into SAMe is reduced[1].

Denamarin®


Proven liver support – supplementing with SAMe and silybin

SAMe

Supplementation allows the continued utilisation of SAMe without requiring prior conversion from methionine. SAMe has been shown to:

- Increase hepatic glutathione levels in cats and dogs[2,3]
- Protect hepatocytes from toxins and death[4]
- Stimulate cell regeneration[1]
- Improve bile flow in cats[2].

Silybin

Silybin is the most active flavonolignan isomer of the milk thistle extract silymarin[5].
Studies show silybin:

- Protects against oxidative stress[6,7]
- Enhances hepatocyte regeneration[8]
- Has an anti-inflammatory effect via the inhibition of leukotriene production[9]
- Stimulates biliary flow[10]
- Increases glutathione levels[11].

Low glutathione concentrations are common in dogs and cats with decreased hepatobiliary function[12].

The synergistic effect of the two main active ingredients in Denamarin

SAMe

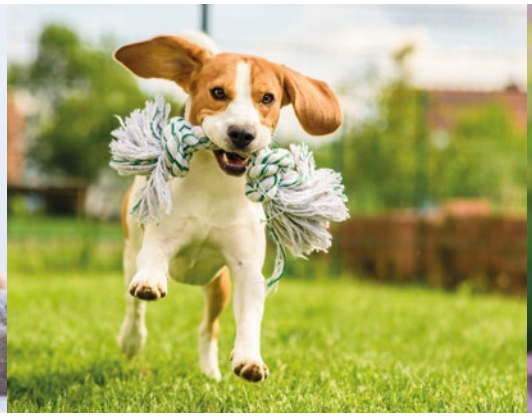
- Essential for three important biochemical pathways
- Maintains cell membrane function and fluidity
- Stimulates cell replication and repair
- Enhances detoxification

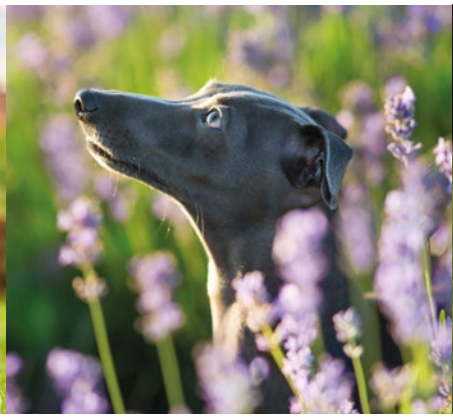
- Increases glutathione levels - the primary antioxidant
- Hepatoprotective
- Promotes protein synthesis
- Improves bile flow

SILYBIN

- Anti-fibrotic
- Anti-inflammatory (inhibits leukotriene production)
- Direct antioxidant
- Inhibits toxin membrane binding

Raising liver support to a new level

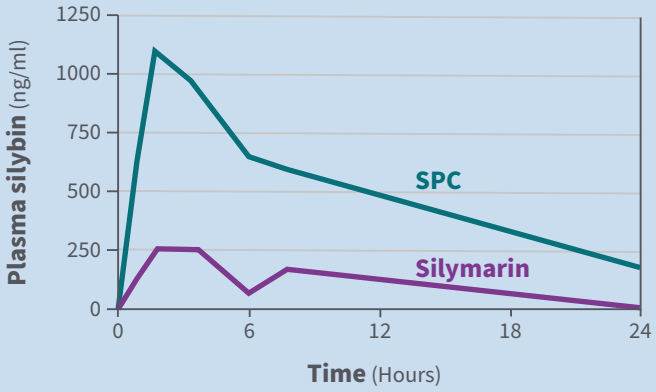




Denamarin provides multifaceted support for the liver through its US-patented combination of SAMe and silybin:

- Stabilised S,S-SAMe isomer, the biologically active form which is predominantly synthesised in cells[13]
- Silybin complexed with phosphatidylcholine which has been shown to increase bioavailability; studies show that peak plasma silybin levels are more than four times higher with a silybin/phosphatidylcholine complex (SPC) than silymarin alone[14,15].

Plasma levels of silybin in dogs after oral administration of a silybin/phosphatidylcholine complex (SPC) versus silymarin alone[15]



Each given as one oral dose equivalent to 16mg/kg body weight of silybin.

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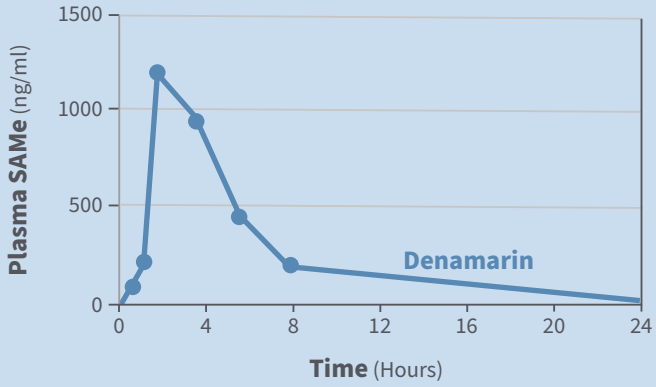
Proven safety

- Wide safety margin - the ingredients within Denamarin possess exceptionally wide margins of safety, supported by oral acute toxicity studies[16]
- High quality assurance, guaranteed to meet label claims.

Bioavailability of SAMe – The mean (fasted) plasma SAMe concentration time-course after administering Denamarin[17]



Protective coating

A proprietary protective coating is crucial to:

- Protect SAMe from moisture and to increase SAMe bioavailability[1]
- Prevent degradation of the S,S-SAMe isomer to the inactive R,S-SAMe isomer[13].

Directions for use

Denamarin tablets are coated to protect them from being oxidised. They must therefore be fed whole (do not split or crumble the tablets).

Tablets should be given on an empty stomach at least one hour before a meal for optimum absorption (an overnight fast is preferred). If necessary, the tablets can be disguised in a small amount of food for easier administration, however this may impact the product's bioavailability.

The number of tablets administered may be gradually reduced, or increased as necessary.

	Tablets per day		
Weight of pet (kg)	**Cat and Small Dog** (90mg SAMe)	**Medium Dog** (225mg SAMe)	**Large Dog** (425mg SAMe)
Up to 5kg	1 tablet		
5-15kg		1 tablet	
15-30kg			1 tablet
30-55kg			2 tablets
Over 55kg			3 tablets

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Suite 1 Ground Floor, 10A Julius Ave, North Ryde, Sydney, NSW 2113, Australia
Telephone: **+61 2 8879 4888** Email: **anz@protexin.com**
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