HEPATIC

Protexin® VETERINARY

Smarter pet care, powered by biotics.

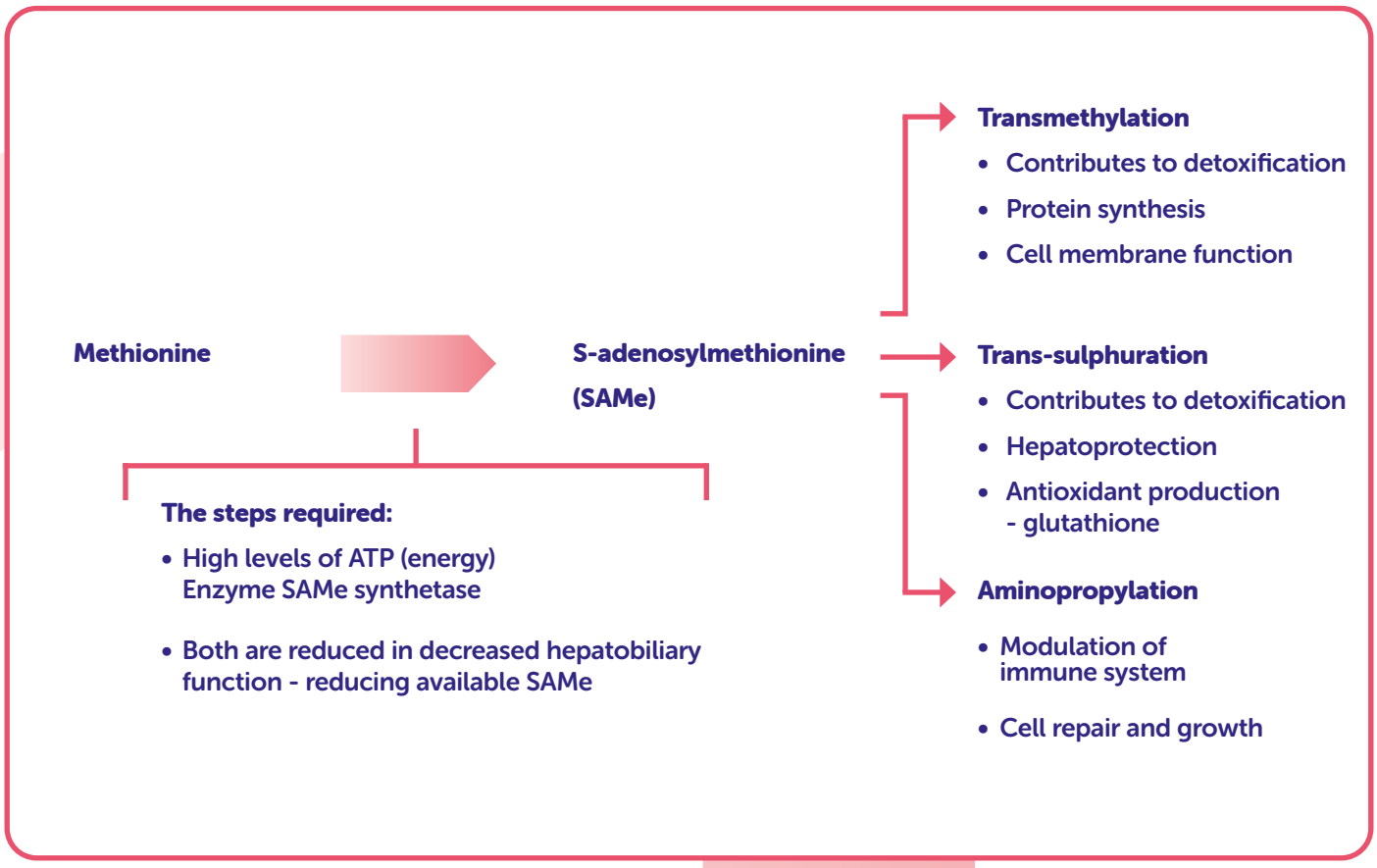
Denamarin Advanced for Dogs

High-level support for the liver and gut health.

Reactive oxygen species, antioxidants and the liver

Reactive oxygen species (ROS), including free radicals, are formed during normal liver metabolism but their production is increased during certain processes. [1,2] Antioxidants neutralise ROS to produce more stable compounds, thereby helping to keep ROS at healthy levels in the liver and other organs. [1,3,4]

The liver plays a vital role in regulating the body's endogenous antioxidant status and is the primary site for glutathione synthesis (up to 90%) which is the major intracellular antioxidant. [1,2,5] The liver converts the amino acid methionine into S-adenosylmethionine (SAMe) and then into glutathione via the trans-sulphuration pathway. [6-9] If this capability becomes compromised, the conversion of methionine into SAMe is reduced and consequently hepatic glutathione levels fall. [6-8,12]



SAMe and yeast

Due to the importance of SAMe in the glutathione pathway, it has commonly been supplemented to help support liver antioxidant levels. [9,11] Supplementation allows the utilisation of SAMe without requiring prior conversion from methionine. SAMe has been shown to not only maintain hepatic glutathione levels in cats and dogs but also support cell regeneration, influence membrane fluidity and support bile flow in cats. [10,11,13]

When supplementing SAMe it is important to note that there are two isomers of SAMe, R,S and S,S, with S,S being the bioactive form. [1,14,15] In synthetic manufacturing processes, the isomer ratios can vary greatly, with the bioactive S,S isomer potentially only making up 35% of the total SAMe content. [14,16,17]

Due to the instability of SAMe, manufacturing and storage are key in retaining its efficacy, with some SAMe products losing up to 50% of their activity while sitting on shelves. [9,15,18,19]

Grown under the correct conditions, a particular strain of the yeast *Saccharomyces cerevisiae* produces SAMe which it incorporates within its cellular structure. This SAMe comprises at least 90% S,S isomer, meaning it has a much higher percentage of the bioactive isomer than most synthetic SAMe.[15] The protection afforded by the intact cell wall of the yeast also promotes greater stability over time at ambient temperatures.[15] This helps to ensure that the SAMe being supplemented is efficacious. The combination of these features means that Denamarin Advanced is more stable and bioavailable. Consequently, lower amounts of SAMe reach the same area under the curve (AUC) as traditional SAMe compounds.[12]

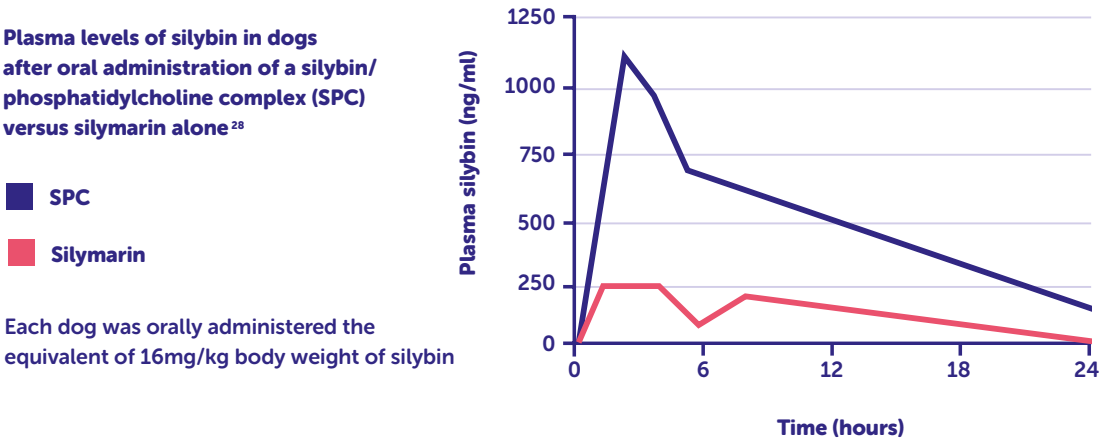
Silybin

Silybin is the most active flavanolignan isomer of the milk thistle extract silymarin. [20,21] Studies show silybin neutralises reactive oxygen species, [22,23] supports hepatocyte regeneration,[24] modulates immune pathways,[25] encourages normal biliary flow [26] and promotes healthy glutathione levels. [27]

Silybin complexed with phosphatidylcholine (as in Denamarin Advanced) has been shown to have increased bioavailability.

Studies show that peak plasma silybin levels are more than four times higher with a silybin/phosphatidylcholine complex (SPC) than silymarin alone. [28]

Plasma levels of silybin in dogs after oral administration of a silybin/phosphatidylcholine complex (SPC) versus silymarin alone [28]



Each dog was orally administered the equivalent of 16mg/kg body weight of silybin

The gut–liver axis

The gut–liver axis is an intricate bidirectional relationship where the gastrointestinal microbiome and the liver interact in multiple ways, each of which can affect the health of the other. This can be via metabolic, immune, neuroendocrine and microbial interactions. [29-32] Some specific examples of their interactions are nutrient absorption, bile acid utilisation and breakdown and enterohepatic circulation of drugs and toxins. [30]

Blood from the gastrointestinal tract passes through the portal vein meaning that the metabolites from the microbiota have the potential to activate the immune system in the liver. [31] The microbiome also influences gut barrier integrity, which is important in avoiding translocation of microorganisms and metabolites not only to the liver but through the circulatory system to other organs. [29-32]

Petbiotix®

Our Petbiotix have been expertly developed to support a healthy microbiome. The microbiome is essential for the normal functioning of the gastrointestinal tract and for the gut's interaction with the rest of the body. Our Petbiotix help support the natural balance in the animal's gut and keeps them at their best.

Prebiotics

Prebiotics selectively feed beneficial bacteria, supporting a diverse and healthy microbiome.

Postbiotics

Postbiotics are inactivated microorganisms which remain bioactive in the gut, providing health benefits.

Saccharomyces cerevisiae

The *Saccharomyces cerevisiae* which provides the SAMe in Denamarin Advanced is an inactivated yeast and therefore acts as a postbiotic, performing multiple functions. As well as containing SAMe, it also contains the prebiotics mannan-oligosaccharide (MOS) and beta-glucan, which are both derived from the cell wall of *S. cerevisiae* and have been shown to have immunomodulatory properties in dogs. [33-40]

Mannan-oligosaccharide (MOS)

Mannan-oligosaccharide (MOS) is a prebiotic which, as well as being fermented by the microbiota to produce short-chain fatty acids, is able to bind to fimbriae on certain bacteria, including *E. coli* and *Salmonella* spp., thereby reducing their adhesive properties. [41,42]

Beta-glucans

Beta-glucans, specifically those with 1,3/1,6 linkage in their chemical structure, have been shown to stimulate the innate immune system in dogs. Some immune cells, such as macrophages, have dectin-1 receptors that recognise and may respond to beta-1,3/1,6-glucans resulting in the observed stimulation of the innate immune system.[36,37]

Denamarin Advanced for Dogs

Available as chewable tablets, Denamarin Advanced provides multi-faceted high-level nutritional support for the liver due to its combination of high SAMe yeast and silybin.

Instructions for use

The tablets should be given on an empty stomach. However, if necessary, they can be given with a small amount of food or a treat.

Denamarin Advanced for Dogs is available for dogs in two weight categories: under 10kg and over 10kg.

Give tablets in the quantities shown in the table below.

Denamarin Advanced for Dogs is not suitable for cats.

Weight	Tablets per day
Dogs under 10kg	
<1.5kg	½
1.5-4.5kg	1
4.5-10kg	2
Dogs over 10kg	
10-14kg	1
14-21kg	1 ½
21-28kg	2
28-35kg	2 ½
35-42kg	3
42-49kg	3 ½

Add half a tablet for every additional 7kg over 49kg.

Ingredients

Each tablet of Denamarin Advanced for Dogs contains:

SAMe found in inactivated yeast (*Saccharomyces cerevisiae*) per tablet
For dogs under 10kg: 59mg*
For dogs over 10kg: 161mg*

Silybin per tablet
For dogs under 10kg: 12mg
For dogs over 10kg: 32mg

*More bioavailable than original Denamarin.

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GASTROINTESTINAL | DERMATOLOGY | URINARY | CALMING | HEPATIC | JOINT

For information on our full range of products for dogs, cats and rabbits, please visit our website.

For references please visit protexinvet.com/den-refs or scan

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