

NEW &
IMPROVED

THE SIGN OF LIVER SUPPORT IS OBVIOUS...

Zentonil[®]



Zentonil[®]

Palatable & divisible tablet range of SAME for cats and dogs.

Vétoquinol



Signe de Passion

Introduction

The liver performs a central role in a diverse array of critical functions, including the synthesis and metabolism of various substances, immunity, storage of vitamins and detoxification.

Although the liver has a tremendous reserve capacity, it is critical to everyday life and so maintaining normal liver function is vital.



Oxidative stress

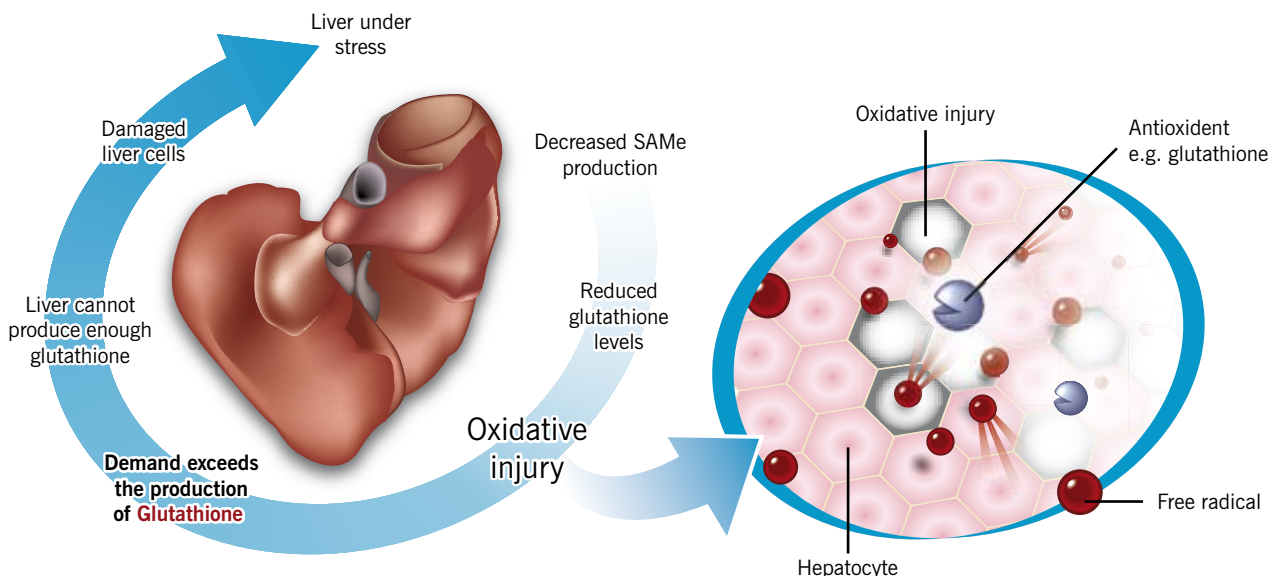
Whatever the underlying cause of the liver problem, the compromised liver undergoes oxidative stress due to the production of free radicals or Reactive Oxygen Species (ROS). ROS are unstable, high-energy molecules with a missing or unpaired electron. They cause damage when they remove electrons from other, nearby molecules.

The role of an antioxidant is to donate electrons to a ROS molecule and stabilise it. Oxidative stress occurs when the number of ROS exceeds the antioxidant capacity leading to damage.

Glutathione

The healthy liver produces an abundance of antioxidants to help preserve normal function. The major antioxidant is glutathione but unfortunately glutathione production is decreased in liver problems¹ when the need for production is even greater.

Diagram 1: The vicious circle

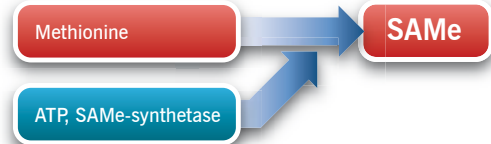


S-adenosylmethionine (SAmE)

SAmE is a nucleotide-like molecule that is synthesised by all living cells. It is derived from methionine and ATP and initiates 3 metabolic pathways, one of which is essential for glutathione production.

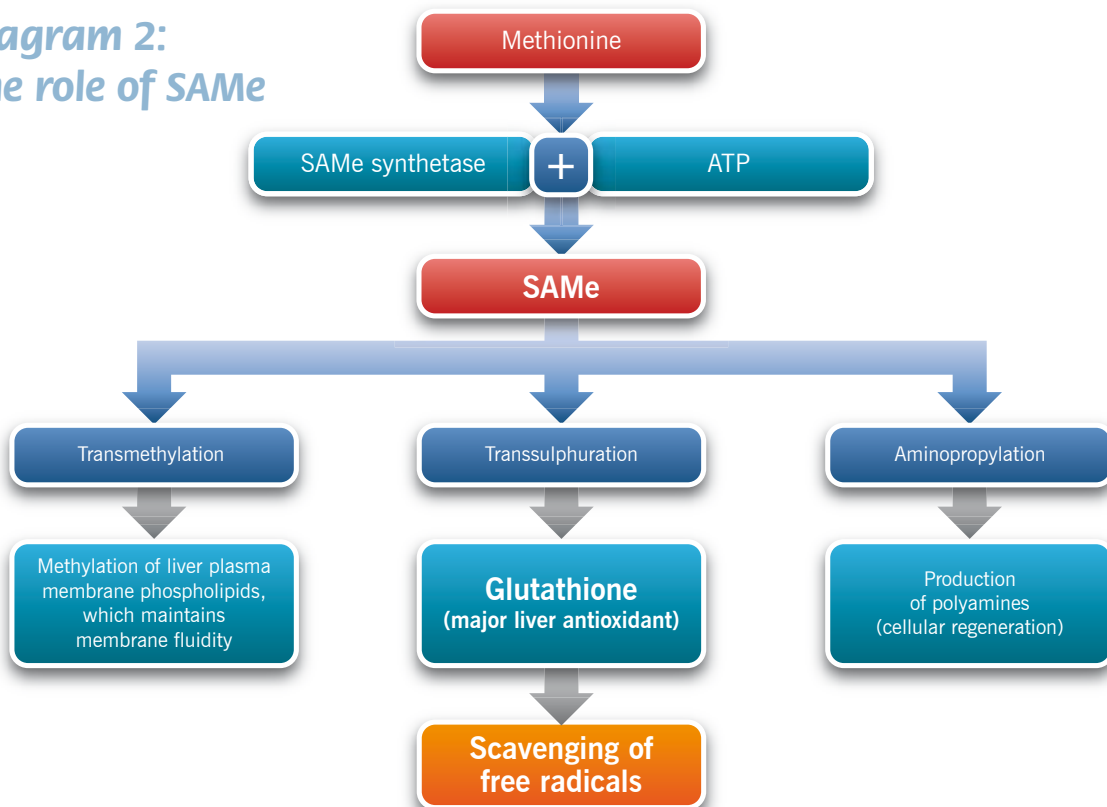
SAmE

- ▶ Increases hepatic glutathione concentrations⁴
- ▶ Helps maintain plasma membrane fluidity and function⁵
- ▶ Is involved in many biochemical pathways that can help maintain normal liver cell function (see diagram 2)



Methionine supplementation is not advised in liver problems as it is thought that the enzyme that converts methionine to SAmE is affected². Supplementation may therefore promote methionine toxicity³.

Diagram 2:
The role of SAmE



Silybin

Silybin is the most active component of milk thistle (silymarin)⁶ and it:

- ▶ Helps support glutathione synthesis⁵
- ▶ Has direct antioxidant activity⁷
- ▶ Helps maintain cell membrane structure⁷
- ▶ Helps maintain liver regeneration⁸

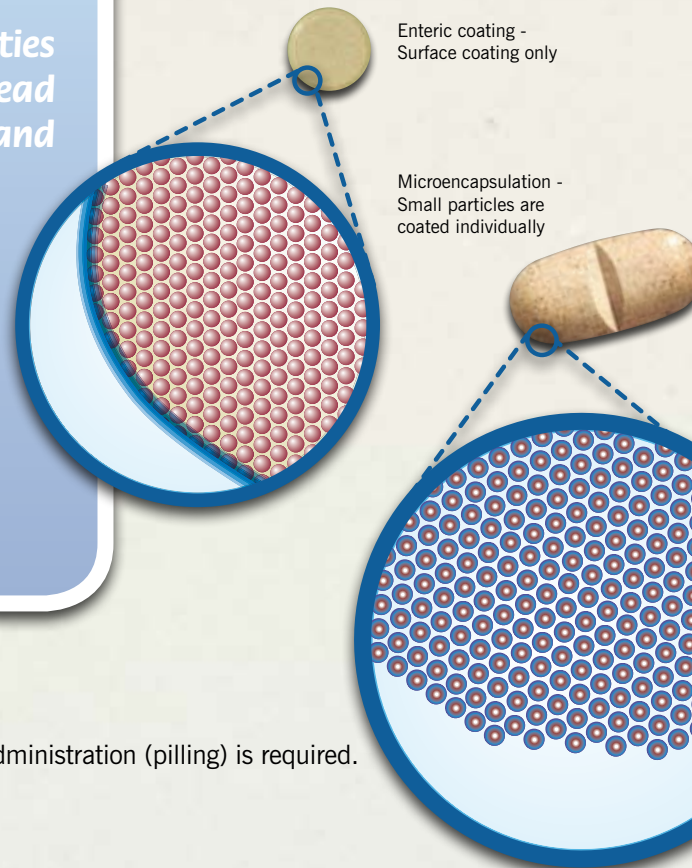
Vétoquinol
Signe de Passion

The Zentonil® Range

Vetoquinol have understood the difficulties associated with SAME administration that lead to decreased absorption and compliance and have provided the solutions.

Introducing the **first divisible & palatable** tablet range of SAME available in the UK & Ireland, with **proven bioavailability**.

Zentonil® contains a pure, stabilised salt of SAME in tablet form.



Problem:

SAMe should be given on an empty stomach⁵ and therefore manual administration (pilling) is required.

The solution is new Zentonil®:

Proven palatability⁹ makes administration without food, and therefore 'compliance', easier.

Problem:

Enteric coating is required as digestion by stomach acid may reduce bioavailability¹⁰. This means tablets cannot be split or chewed.

The solution is new Zentonil®:

Patent pending microencapsulation technique coats tiny particles of SAMe, **allowing tablets to be split and chewed** whilst protecting the SAMe molecules from the harmful effects of stomach acid.

Problem:

Inability to split tablets due to enteric coating:

- a) makes administration expensive for certain weights of animal
- b) leads to a wide variation in SAMe levels received between different weights of animal

The solution is new Zentonil®:

Divisible, scored tablets allowing **accurate tablet-to-weight administration** which limits costs.

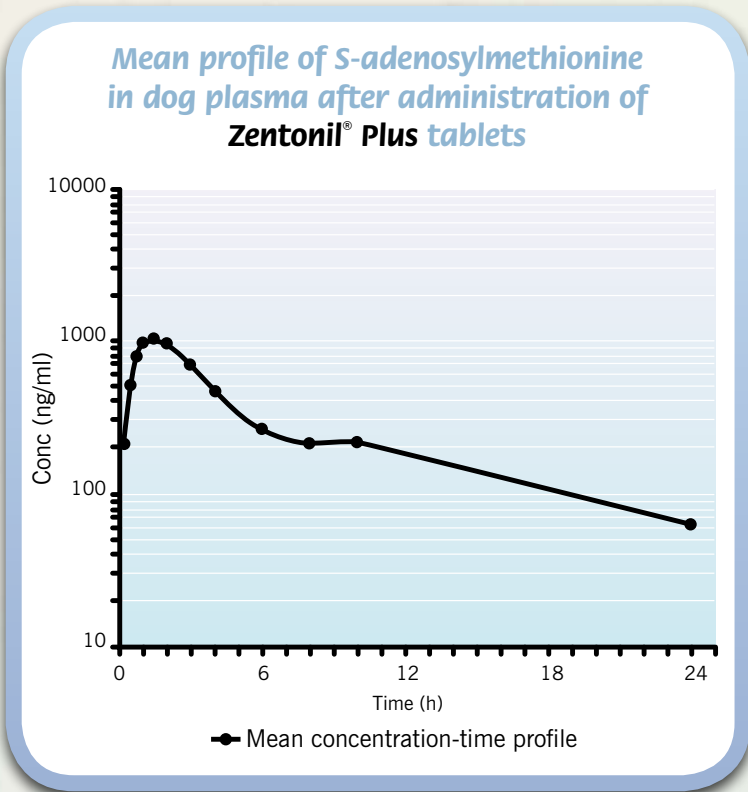
Problem:

Lack of data on bioavailability

**The solution is new Zentonil®:
Proven bioavailability¹¹**



*Mean profile of S-adenosylmethionine
in dog plasma after administration of
Zentonil® Plus tablets*



After oral administration of **Zentonil®**, SAME is available for use by the body within **10 minutes** of administration¹¹ and peak levels are achieved between 1 to 4 hours after administration. The bioavailability curves were constant between test subjects.

SAME should be given on an empty stomach for optimal effectiveness⁵. Feeding one hour after administration of **Zentonil®** allows optimal SAME absorption and the levels will be at their highest to support the liver through the time when digestion is occurring.

Zentonil® Plus

contains the single pure ingredient, SAME, in our divisible, palatable formulation.

Zentonil® Advanced

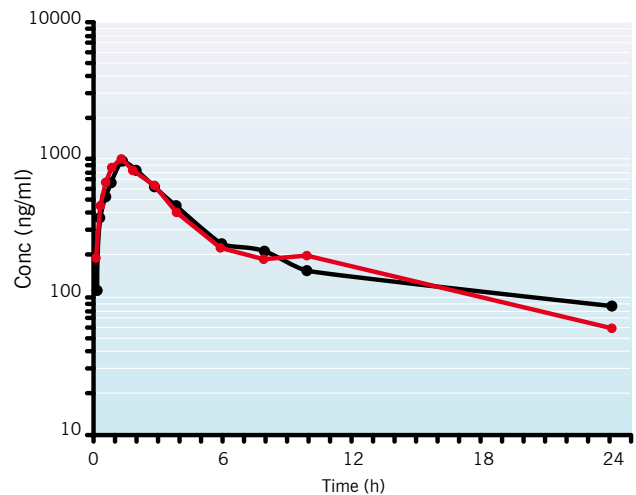
is a divisible, palatable formulation of SAME giving all the benefits of **Zentonil® Plus** with the additional benefits of silybin.

Silybin in **Zentonil® Advanced** is complexed with phosphatidylcholine.

Oral bioavailability of silybin is very low but is significantly increased when complexed with phosphatidylcholine¹². By providing silybin in this form, bioavailability of silybin is up to 10 times higher than that achieved by giving silymarin¹³.

Whichever Zentonil® you choose, Vetoquinol's microencapsulation technique ensures optimal bioavailability of SAME¹¹.

Mean plasma SAME profiles after administration of **Zentonil® Plus** and **Zentonil® Advanced** tablets



Mean concentration-time profiles obtained after:
—●— **Zentonil® Plus** administration
—●— **Zentonil® Advanced** administration






















When should I use Zentonil®?

Zentonil® can be used in all cases when the liver is known or expected to require support in both dogs and cats.

Administration

Tablets should be given on an empty stomach⁵ at least one hour before or two hours after feeding for optimal effectiveness.

Specific recommendations (bodyweight) per day

| Bodyweight | Zentonil® Plus SAME | | Zentonil® Advanced SAME + Silybin | | |
|------------|---|---|---|---|---|
| | 200 | 400 | 100 | 200 | 400 |
| 2.5 kg | - | - |  | - | - |
| 5 kg |  | - |  |  | - |
| 10 kg |  |  |  |  |  |
| 15 kg |  | - | - |  | - |
| 20 kg |  |  | - |  |  |
| 30kg | - |  | - | - |  |
| 40 kg | - |  | - | - |  |

The tablets are scored for division into two parts but can be divided further if required.



Zentonil® Plus
200



Zentonil® Plus
400



Zentonil® Advanced
100



Zentonil® Advanced
200



Zentonil® Advanced
400





Pack sizes:

Zentoniil® Plus 200 contains 20 tablets, Zentoniil® Plus 400 contains 20 tablets, Zentoniil® Advanced 100 contains 22 tablets, Zentoniil®Advanced 200 contains 30 tablets and Zentoniil® Advanced 400 contains 30 tablets.

References:

1. Center SA: SAME an antioxidant and anti-inflammatory nutraceutical. Proc 18th ACVIM 550-552, 2000.
2. Ettinger, Feldman: Textbook of Veterinary Internal Medicine. Sixth Edition, Mosby Elsevier 393-406, 2007.
3. Toborek et al: Increased lipid peroxidation and antioxidant activity in methionine-induced hepatitis in rabbits. Nutrition 12:534-537, 1996.
4. Sartor L L et al: Rational pharmacologic therapy of hepatobiliary disease in dogs and cats. Compend Contin Educ Vet Pract 25: 432-447, 2003.
5. Flatland: Botanicals, vitamins and minerals in the liver: Therapeutic applications and potential toxicities. Compendium VetLearn 25(7):514-524, 2003.
6. Bonagura, Twedt: Kirk's Current Veterinary Therapy XIV. Saunders Elsevier 128:554-575, 2009.
7. Fraschini et al: Pharmacology of Silymarin. Clin Drug Invest 22(1):51-65, 2002.
8. Luper S: A review of plants used in the treatment of liver disease: part 1. Altern Med Rev 3 (6): 410-21, 1998.
9. Vetoquinol study number Zentpal0001.
10. Stramentinoli: Pharmacologic aspects of SAME: Pharmacokinetics and pharmacodynamics. The American Journal of Medicine 83 (5A) 35042, 1987.
11. Vetoquinol study number 208NP2F2.
12. Barzaghi et al: Pharmacokinetic studies on IdB 1016. A silybin-phosphatidylcholine complex, in healthy human subjects. Eur J Drug Metab Pharmacokin 15(4):333-338, 1990.
13. Morazzoni et al: Comparative pharmacokinetics of silipide and silymarin in rats. Eur J Drug Metab Pharmacokin 18(3):289-297, 1993.

Vétoquinol



Signe de Passion

För beställning av Zentoniil :

Birgitta Sjölin
Tel. 0705-32 94 64
birgitta@vetoquinol-scandinavia.com

Huvudkontor:
Box 9, 265 22 Åstorp
Tel. 042-676 03, Fax 042-676 04
info@vetoquinol-scandinavia.com
www.vetoquinol-scandinavia.com