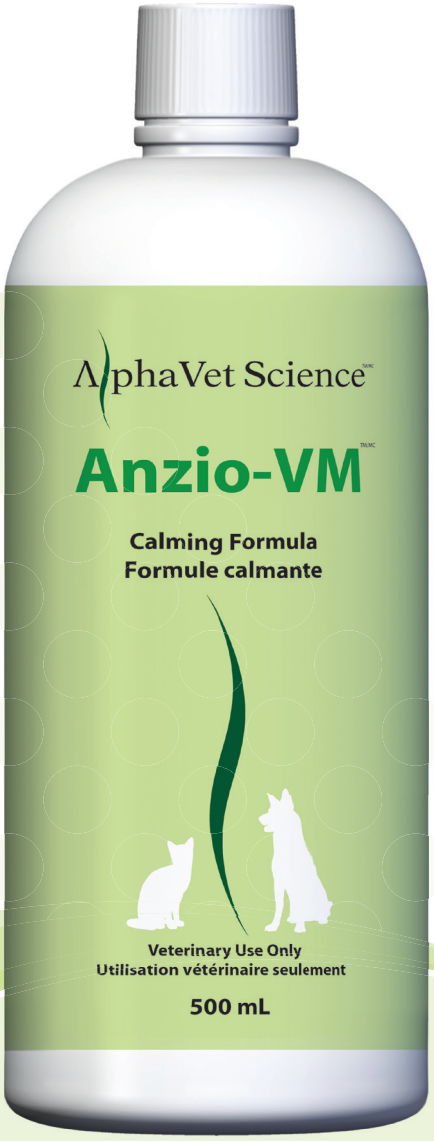
AlphaVet Science™/MC



Just Natural Science™

La science au naturel, simplement™

AlphaVet Science™

Anzio-VM™

Anzio-VM™ with its mild sedative actions supports the central nervous system in dogs and cats exhibiting anxiousness, nervousness, hyperactivity, discontentment or responding to environmentally-induced stress. Anzio-VM™ supports balanced behavior, promotes relaxation, and maintains calmness.

INDICATIONS
- Anxiety
- Depression
- Insomnia
- Irritability
- Restlessness
- Stress

INGREDIENTS ACTIONS
- Anxiolytic
- Calmative

PACKAGING 500 mL/bottle

ADMINISTRATION Oral

DOSAGE

1-10 lbs	2.5 mL (½ teaspoon) daily.
11-20 lbs	5 mL (1 teaspoon) daily.
21-50 lbs	7.5 mL (1½ teaspoons) daily.
51-100 lbs	10 mL (2 teaspoons) daily.
>100 lbs	15 mL (1 tablespoon) daily.

STORAGE Refrigerate after opening. Keep bottle cap tightly closed when not in use.

Anzio-VM™ FORMULA

1 teaspoon (5 mL) contains:

Fleece Flower Stem	(*Polygonum multiflorum*/Caulis Polygoni Multiflori)	375 mg
Chinese Arborvitae Seed	(*Platycladus orientalis*/Semen Platycladi)	350 mg
Chinese Jujube Seed	(*Ziziphus jujuba*/Semen Ziziphi Spinosae)	50 mg
Valerian Root	(*Valeriana officinalis*/Radix Valerianae)	50 mg
Passionflower Herb	(*Passiflora incarnata*/Herba Passiflorae)	50 mg
Silk Tree Bark	(*Albizia julibrissin*/Cortex Albiziae)	50 mg

NON-MEDICINAL INGREDIENTS

Stevia, Citric acid, Potassium sorbate, Purified water, Sodium benzoate.

Anzio-VM™ is manufactured under strict GMP standards and contains no dairy, yeast, corn, wheat or gluten. Does not contain animal by-products.

Polygonum multiflorum (Fleece Flower)

Caulis Polygoni Multiflori is beneficial in sleeping disorders such as insomnia, difficulty falling asleep or staying asleep (Chen & Chen, 2004). In an animal model study, the sedative effect of Caulis Polygoni Multiflori decoction (20 g/kg) was found to be comparable to diazepam [5 mg/kg] (Yang *et al.,* 1990). In traditional Chinese medicine Caulis Polygoni Multiflori is combined with Semen Ziziphi, Flos Albiziae, and Semen Platycladi to calm the Shen (Spirit). The term 'Shen' refers to the entire presentation of a being, including energy levels, the state of consciousness, and ability to think and reason (Chen & Chen, 2004).

TOXICOLOGY

Toxicity for Caulis Polygoni Multiflori has not been documented in dogs and cats when administered orally in therapeutic doses. No fatalities were reported when Caulis Polygoni Multiflori was given to mice at doses up to 1,000 g/kg of body weight. Intraperitoneal LD_{50} for Caulis Polygoni Multiflori is 169.4 g/kg of body weight in mice (Chen & Chen, 2004).

Equivalent toxic dose in 20 kg dog: 3,388 g IP of Caulis Polygoni Multiflori.
Equivalent toxic dose in 5 kg cat: 847 g IP of Caulis Polygoni Multiflori.

DRUG INTERACTIONS

Validated interactions studies do not exist for Caulis Polygoni Multiflori preparations. Clinical interactions with other drugs have not been reported. However, concomitant use of *Polygonum multiflorum* with anti-diabetic agents might increase the risk of hypoglycemia. Dosing adjustments for insulin or oral hypoglycaemic agents may be necessary. Theoretically, concomitant use of *Polygonum multiflorum* with other laxatives can increase the risk of fluid and electrolyte depletion (Brinker, 1998).

Platycladus orientalis (Chinese Arborvitae)

Semen Platycladi functions as a calmative. In traditional Chinese medicine, Semen Platycladi is used in insomnia, anxiety, palpitations, and forgetfulness caused by excessive worrying. In animal model experimental studies, Cacumen Platycladi decoction showed sedative action on the central nervous system as it prolonged phenobarbital-induced sleeping time, decreased motor activities, and prevented caffeine-induced seizures (Chen & Chen, 2004). The effects of Semen Platycladi are reinforced when combined with Semen Ziziphi Spinosae (Xie & Preast, 2010).

TOXICOLOGY

Platycladus orientalis

Toxicity for Cacumen Platycladi has not been documented in dogs and cats when administered orally in therapeutic doses. Ingestion of *Platycladus orientalis* has been associated with clinical signs of gastroenteritis and seizures in ruminants including bovine, caprine and ovine (Chizzola *et al.*, 2004). Intraperitoneal LD_{50} for Cacumen Platycladi is 15.2 g/kg of body weight in mice. No deaths were recorded among mice within 72 hours of being given 60 g/kg of body weight of a decoction of Cacumen Platycladi via intragastric administration (Li, 2002).

Equivalent toxic dose in 20 kg dog: 304 g IP of Cacumen Platycladi decoction.
Equivalent toxic dose in 5 kg cat: 76 g IP of Cacumen Platycladi decoction.

DRUG INTERACTIONS

Validated interactions studies do not exist for Cacumen Platycladi preparations. Clinical interactions with other drugs have not been reported.

Ziziphus jujuba [*Ziziphus spinosa*] (Chinese Jujube)

Semen Ziziphi Spinosae has been used extensively for the treatment of insomnia. In an animal study, spinosin a major constituent of Semen Ziziphi Spinosae, dose-dependently augmented pentobarbital induced sleep, reflected by increased sleep time and reduced sleep latency assessed with the loss-of-righting reflex (Wang *et al.,* 2008). Various tests on animals including dogs and cats were carried out to assess the sedative and hypnotic effects of Semen Ziziphi Spinosae and the results showed sedative effects and synergistic effects with other sedatives and hypnotics (Chang & But, 1987). It has also been found that Semen Ziziphi Spinosae possessed anxiolytic effects at a lower dose and sedative effects at a higher dose (Wen *et al.,* 2000). In a human study, Semen Ziziphi Spinosae showed a significant improvement in sleep quality and well-being without side effects (Bone, 2001).

TOXICOLOGY

Toxicity for Semen Ziziphi Spinosae has not been documented in dogs and cats when administered orally in therapeutic doses. In laboratory animals a single oral dose of 50 g/kg of body weight of Semen Ziziphi Spinosae did not produce any toxic symptoms, and a daily dose of 20 g/kg of body weight for 30 days had no toxic reactions (Dharmananda, 2001). Intraperitoneal LD_{50} of Semen Ziziphi Spinosae decoction is 14.3 ± 2.0 g/kg of body weight in mice (Chang & But, 1987).

Equivalent toxic dose in 20 kg dog: 286 g IP of Semen Ziziphi Spinosae decoction.
Equivalent toxic dose in 5 kg cat: 71.5 g IP of Semen Ziziphi Spinosae decoction.

DRUG INTERACTIONS

Validated interactions studies do not exist for Semen Ziziphi Spinosae preparations. Clinical interactions with other drugs have not been reported. However, Semen Ziziphi Spinosae has sedative and hypnotic effects. It potentiates the sedative effects of barbiturates (Chen & Chen, 2004).

Valeriana officinalis (Garden Valerian)

Clinical data indicates that Radix Valerianae is a mild sedative and sleep promoting agent. It is often used as a milder alternative or a possible substitute for stronger synthetic sedatives, such as benzodiazepines, in the treatment of states of nervous excitation and anxiety-induced sleep disturbances (WHO, 1999). The mechanism of action of Radix Valerianae in general and as a mild sedative in particular, remains unknown. Radix Valerianae extracts appear to have some affinity for the GABA (A) receptor, a class of receptors on which benzodiazepines are known to act (Holzl & Godau, 1989; Mennini, *et al.,* 1993). Aqueous extracts of the roots contain appreciable amounts of GABA that could directly cause sedation (Houghton, 1999). Valerenic acid in animals appears to inhibit the enzyme system responsible for the central catabolism of GABA, increasing GABA concentration and decreasing CNS activity, and direct binding of valerenic acid to GABA-receptors has been demonstrated (Benke *et al.,* 2009). Cats given 10 mg/kg of a Radix Valerianae extract by gastric lavage had a significant decrease in restless, fearful and aggressive behaviors (Von Eickstedt, 1969).

TOXICOLOGY

Toxicity for Radix Valerianae has not been documented in dogs and cats when administered orally in therapeutic doses. An unusual feature of *Valeriana officinalis* is that the essential oil of Radix Valerianae is a cat attractant similar to catnip. Radix Valerianae contains the cat attractant actinidine. Cats with implanted electrodes showed no changes in their EEGs following oral administration of 100 or 250 mg/kg of body weight of Radix Valerianae extract (EMEA, 2007).

In acute oral toxicity tests the LD_{50} of the sesquiterpene valeranone was greater than 3 g/kg of body weight in both rats and mice which corresponds to low toxicity. The LD_{50} of essential oil of Radix Valerianae is 1,500 mg in rats weighing 100 g. The LD_{50} of an ethanol Radix Valerianae extract made from the defatted herbal substance administered intraperitoneally to mice amounted to 3.3 g/kg of body weight, a value, which corresponds to a low toxicity. Valerenic acid caused inhibition of spontaneous motility after intraperitoneal administration to mice at a dose of 50 mg/kg of body weight; ataxia and temporary immobility at a dose of 100 mg/kg of body weight, muscle spasms at doses of 150-200 mg/kg of body weight; and severe convulsions and mortality at a dose of 400 mg/kg [6 of 7 animals *ad exitum* 24 hours after administration] (EMEA, 2007).

Equivalent toxic dose in 20 kg dog: 66 g IP of ethanol Radix Valerianae extract.
Equivalent toxic dose in 5 kg cat: 16.5 g IP of ethanol Radix Valerianae extract.

DRUG INTERACTIONS

Radix Valerianae lengthens the sedation time induced by barbiturates and may have synergistic effects with benzodiazepines (Carrasco *et al.,* 2009). Radix Valerianae may have an additive effect with haloperidol, causing hepatic damage (Dalla *et al.,* 2008). Radix Valerianae may interact with anaesthetics (Ang-Lee *et al.,* 2001).

Passiflora incarnata (Passionflower)

Herba Passiflorae has been approved by The German Commission E for the treatment of nervous unrest. In human studies Herba Passiflorae has been reported to reduce anxiety without inducing sedation (Moavafegh *et al.,* 2008). Based on pharmacological data, the experiences of traditional use and the use in combinations, Herba Passiflorae extracts are an important factor in the natural treatment of tenseness, restlessness and irritability with difficulty in falling asleep (Krenn *et al.,* 2002). In dogs, six months treatment with an extract containing Herba Passiflorae and Radix Valerianae had no toxic effects (Tabach *et al.,* 2009).

TOXICOLOGY

Toxicity for Herba Passiflorae has not been documented in dogs and cats when administered orally in therapeutic doses. No side effects are known in humans when Herba Passiflorae is taken with recommended dosages (Blumenthal, 2000). In toxicity studies, the LD_{50} of Herba Passiflorae was calculated to be: Extracts: oral: >15 g/kg of body weight (mice and rats); intraperitoneal: 3,510 mg/kg of body weight (rats), 3,140 mg/kg of body weight (mice); subcutaneous: >10 g/kg of body weight (rats), 8,300 mg/kg of body weight [mice] (EMEA, 2008).

Equivalent toxic dose in 20 kg dog: 300 g PO of Herba Passiflorae extract.
Equivalent toxic dose in 5 kg cat: 75 g PO of Herba Passiflorae extract.

DRUG INTERACTIONS

Herba Passiflorae may potentiate the effects of pentobarbital (Speroni *et al.,* 1996). Herba Passiflorae may increase the sedative effects of benzodiazepines by increasing the binding activity of benzodiazepines to GABA receptors (Carrasco *et al.,* 2009).

Albizia julibrissin (Silk Tree)

Traditionally known in China as the "herb of happiness," *Albizia julibrissin* is one of the most valued Chinese botanicals for supporting a healthy mood. *Albizia julibrissin*, also known as mimosa, has been traditionally used for centuries to elevate the mood, promote mental and emotional calmness, and support a peaceful night's sleep. Studies show that Cortex Albiziae extract has anxiolytic properties acting via the serotonergic nervous system (Kim *et al.*, 2004). Animal model studies showed that the antidepressant effects of Cortex Albiziae extract are equal to that of imipramine, and that it acts via the 5-HT1A receptor system (Kim *et al.*, 2007). Cortex Albiziae exhibits a synergism with Radix Polygoni Multiflori and this combination is commonly used in treating insomnia in Asian countries (Chen *et al.*, 2009).

TOXICOLOGY

Toxicity for Cortex Albiziae has not been documented in dogs and cats when administered orally in therapeutic doses. The LD_{50} value for Cortex Albiziae has not been determined.

NOTE: Anzio-VM ™ contains Cortex Albiziae (bark) which is non-toxic to animals. However, Semen Albiziae (bean) contains a neurotoxic alkaloid which is a pyridoxine antagonist, causing nervous symptoms. Poisoning occurs when trees with green or mature pods are made avaiable to cattle, sheep or dogs. The lethal dose is about 1.5 percent of an animal's body weight in green or brown legumes containing seeds. Signs of poisoning occur 12 to 24 hours after intake of the legumes and include: exaggerated response to stimuli; muscular twitching; labored respiration; salivation; convulsive seizures; death (AgriLIFE).

DRUG INTERACTIONS

Validated interactions studies do not exist for Cortex Albiziae preparations. Clinical interactions with other drugs have not been reported.

PRECAUTIONS

- An examination from a veterinarian is recommended prior to using this product.
- Safe use in pregnant animals or animals intended for breeding has not been proven.
- If animal's condition worsens or does not improve, stop product administration and consult your veterinarian.
- May increase the effects of other sedatives.
- Not be used one week before surgery because Radix Valerianae may interact with anaesthesia.
- Not to be used before urine test.
- Consult your veterinarian for potential drug interactions.
- Off-label use of this product in ruminants is not recommended.
- Oral use only.
- Administer during or after the animal has eaten to reduce incidence of gastrointestinal upset.
- Shake well before use.

WARNINGS

- To be used in dogs and cats only.
- Keep out of reach of children and animals.
- In case of accidental overdose, contact a health professional immediately.

ADVERSE REACTIONS

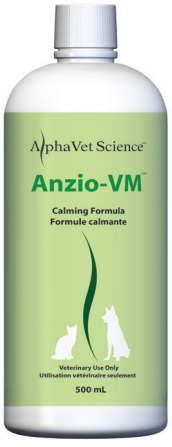
- Mild gastrointestinal discomfort may occur which is dose dependent.

CONTRAINDICATIONS

- Contraindicated in pregnant and nursing dogs and cats.
- Contraindicated with sedatives.
- Contraindicated in cases of acute and chronic diarrhoea.

AlphaVet Science™

Anzio-VM™



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