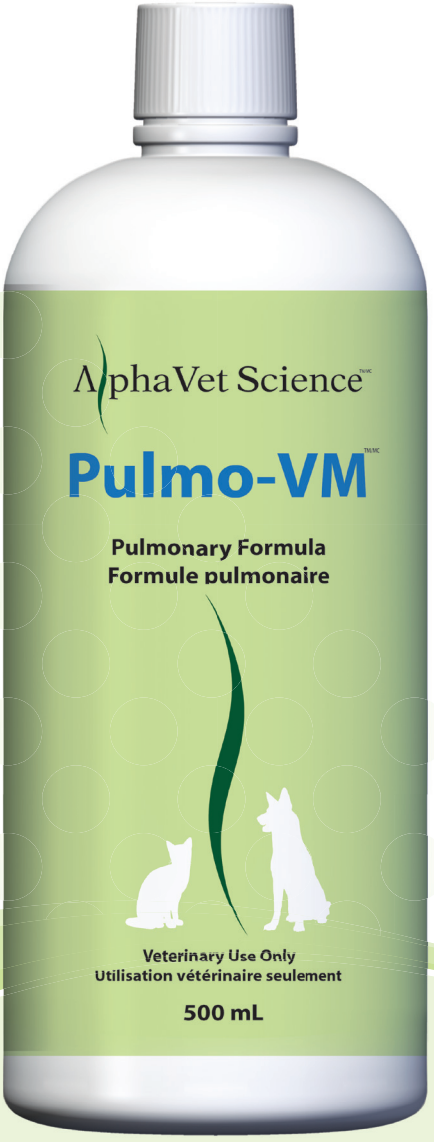
AlphaVet Science™/MC



Just Natural Science™

La science au naturel, simplement™

AlphaVet Science™

Pulmo-VM™

Pulmo-VM™ is a botanical formulation to augment pulmonary function through the clearance of bacterial and environmental contaminants.

INDICATIONS
- Supportive care in canine and feline respiratory diseases

INGREDIENTS ACTIONS
- Antibacterial
- Anti-inflammatory
- Antioxidant
- Antitussive
- Decongestant
- Detoxificant
- Expectorant

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.

PACKAGING 500 mL/bottle

Pulmo-VM™ FORMULA

1 teaspoon (5 mL) contains:

Japanese Honeysuckle Flower	(*Lonicera japonica*/Flos Lonicerae Japonicae)	175 mg
Rosemary Leaf	(*Rosmarinus officinalis*/Folium Rosmarini)	175 mg
Thunberg Fritillary Bulb	(*Fritillaria thunbergii*/Bulbus Fritillariae)	175 mg
Baikal Skullcap Root	(*Scutellaria baicalensis*/Radix Scutellariae)	100 mg
Chinese Senega Root	(*Polygala tenuifolia*/Radix Polygalae Tenuifoliae)	75 mg
Holy Basil Leaf	(*Ocimum sanctum*/Folium Ocimi Sancti)	50 mg
Monk Fruit	(*Siraitia grosvenorii*/Fructus Momordicae grosvenorii)	50 mg
Mullein Flower	(*Verbascum thapsus*/Flos Verbasci)	50 mg
White Mulberry Root Bark	(*Morus alba*/Cortex Mori Albae Radicis)	50 mg

NON-MEDICINAL INGREDIENTS

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

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

Lonicera japonica (Japanese Honeysuckle)

In traditional European herbal medicine, Flos Lonicerae Japonicae is used as a remedy for asthma and related respiratory disorders. Flos Lonicerae Japonicae has been known as an anti-inflammatory herb in traditional Chinese medicine and is used for upper respiratory tract infections. Luteolin, an active constituent of Flos Lonicerae Japonicae, has a spectrum of biological activities, especially with antioxidative and anti-inflammatory properties. It has been reported that luteolin has a potent antifibrotic activity; this effect was mediated, at least in part, by inhibition of lung inflammation and suppression of myofibroblast differentiation as well as epithelial-to-mesenchymal transition (Chen *et al.*, 2010). Other active constituents such as chlorogenic acid and isochlorogenic acid have demonstrated broad spectrum antibiotic actions (Chen & Chen, 2004).

TOXICOLOGY

Toxicity for Flos Lonicerae Japonicae has not been documented in dogs and cats when administered orally in therapeutic doses. The American Society for the Prevention of Cruelty to Animals does not consider the plant toxic to cats, dogs or horses (Whardon, 2011). Oral LD_{50} of Flos Lonicerae Japonicae is 53 g/kg of body weight in mice (Chen & Chen, 2004).

Equivalent toxic dose in 20 kg dog: 1,060 g PO of Flos Lonicerae Japonicae.
Equivalent toxic dose in 5 kg cat: 265 g PO of Flos Lonicerae Japonicae.

DRUG INTERACTIONS

Validated interactions studies do not exist for Flos Lonicerae Japonicae preparations. Clinical interactions with other drugs have not been reported. However, a case report of a human patient receiving an anticoagulant (warfarin) was associated with the development of easy bruising, epistaxis, bleeding gums, and elevated international normalized ratio (INR) with the ingestion of Flos Lonicerae Japonicae preparation (Barceloux, 2008).

Rosmarinus officinalis (Rosemary)

Rosmarinic acid, an active constituent of Folium Rosmarini increases the production of prostaglandin E_2 which is generally a bronchodilator, while reducing leukotrienes, which are bronchoconstrictors. This effect enhances the inhibition of the histamine constricting action on the bronchial smooth muscle and by its relaxant effect on the smooth muscle (al-Sereiti *et al.*, 1999). Oxidative damage to DNA, RNA, proteins and cell membranes occurs when the cellular concentration of reactive oxygen species exceeds the capacity of the cell to eliminate them. Folium Rosmarini is a source of some of the most potent herbal antioxidant phyto-chemicals known, which aids in scavenging reactive oxygen metabolites. The antioxidant activity of Folium Rosmarini extracts is mainly due to polyphenolic compounds such as rosmarinic acid, carnosic acid, carnosol, rosmadial and genkwanin (WHO, 2009). The effects of these constituents may contribute to membrane stabilization and hindrance of radical propagation, which may cooperate with the electron donor ability of Folium Rosmarini polyphenolic compounds in protecting the membranes against oxidative damage (Pérez *et al.*, 2010). The antioxidant effect of Folium Rosmarini against free radicals may have a role in the preventive use in bronchospasm diseases (al-Sereiti *et al.*, 1999).

TOXICOLOGY

Toxicity for Folium Rosmarini has not been documented in dogs and cats when administered orally in therapeutic doses. Oral LD_{50} of Folium Rosmarini essential oil is >2 g/kg of body weight in rats (de Faria *et al.*, 2011). Oral LD_{50} of rosmarinic acid is 5 mL/kg of body weight in rats (Newall *et al.*, 1996).

Equivalent toxic dose in 20 kg dog: >40 g PO of Folium Rosmarini essential oil.
Equivalent toxic dose in 5 kg cat: >10 g PO of Folium Rosmarini essential oil.

DRUG INTERACTIONS

Validated interactions studies do not exist for Folium Rosmarini preparations. However, dose dependent antagonistic interaction has been observed between essential oil of Folium Rosmarini and the antibiotic ciprofloxacin (van Vuuren *et al.*, 2009). Folium Rosmarini has shown antithrombotic activity *in vitro* and *in vivo* in mice and concurrent use with anticoagulants/antiplatelet drugs may increase the risk of bleeding (Yamamoto *et al.*, 2005; Naemura *et al.*, 2008).

Fritillaria thunbergii (Thunberg Fritillary)

Bulbus Fritillariae is an important traditional Chinese herbal medicine commonly used as an antitussive and expectorant (Li *et al.*, 2003). The major alkaloids of Bulbus Fritillariae are peimine (verticine) and peiminine (verticinone) have exhibited antitussive effects and smooth muscle relaxation (Zhang *et al.*, 2008). Peiminine may exert its antitussive effect via both the peripheral (modulated by ATP-sensitive K+ channels) and central mechanisms [modulated by the opioid receptor] (Xu *et al.*, 2007). Bulbus Fritillariae has exhibited antiasthmatic properties through inhibitory effects on airway inflammation by suppression of Th2 cytokines (IL-4, IL-5 and IL-13), IgE, histamine production, reduction of eosinophilic accumulation and increase of interferon-gamma production (Yeum *et al.*, 2007).

TOXICOLOGY

Toxicity for Bulbus Fritillariae has not been documented in dogs and cats when administered orally in therapeutic doses. Intravenous LD_{50} of peiminine an isolate of Bulbus Fritillariae is 8-10 mg/kg of body weight in cats and 10-12 mg/kg of body weight in rabbits (Chen & Chen, 2004).

Equivalent toxic dose in 20 kg dog: 160-200 mg IV of peiminine, an isolate of Bulbus Fritillariae.
Equivalent toxic dose in 5 kg cat: 40-50 mg IV of peiminine, an isolate of Bulbus Fritillariae.

DRUG INTERACTIONS

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

Scutellaria baicalensis (Baikal Skullcap)

Several studies evaluating the antimicrobial effects of Radix Scutellariae have been performed and have been shown to be beneficial in treating upper respiratory infections. *In vitro* testing of Radix Scutellariae preparation on selected oral bacteria demonstrated bacteriostatic and bactericidal effects (Tsao *et al.*, 1982). Baicalin, an active constituent of Radix Scutellariae was found to be synergistic with beta-lactam antibiotics against certain resistant strains (Liu *et al.*, 2000). The anti-inflammatory effects of Radix Scutellariae have been well documented and the activity of the flavonoids such as wogonin, baicalein, and baicalin, were found to have an effect similar to prednisolone (Chung *et al.*, 1995).

TOXICOLOGY

Scutellaria baicalensis

Toxicity for Radix Scutellariae has not been documented in dogs and cats when administered orally in therapeutic doses. In experimental studies, long term intravenous administration of wogonin, an active constituent of Radix Scutellariae, had no toxicity in dogs (Peng *et al.*, 2009). Oral LD_{50} of wogonin is 3.9 g/kg of body weight in mice (Hui *et al.*, 2002). Intraperitoneal LD_{50} of baicalein an isolate of Radix Scutellariae is 3,081 mg/kg of body weight (Chen & Chen, 2004).

Equivalent toxic dose in 20 kg dog: 78 g PO of wogonin, an active constituent of Radix Scutellariae.
Equivalent toxic dose in 5 kg cat: 19.5 g PO of wogonin, an active constituent of Radix Scutellariae.

DRUG INTERACTIONS

Baicalin, an active constituent of Radix Scutellariae, can decrease the blood level of statin drugs (Fan *et al.*, 2008). Baicalin acts synergistically with oxytetracycline and tetracycline, enhancing its antimicrobial activity against *Staphylococcus aureus*, including methicillin and tetracycline-resistant strains (Novy *et al.*, 2011). Baicalin exhibits synergism with beta-lactam antibiotics, such as ampicillin, amoxicillin, methicillin, and cefotaxime (Liu *et al.*, 2000). Wogonin an active constituent of Radix Scutellariae inhibits CYP1A2 and CYP2C19, and can affect the intracellular concentration of drugs metabolized by these enzymes (Li *et al.*, 2011). Radix Scutellariae decreases the bioavailability of cyclosporine (Lai *et al.*, 2004).

Polygala tenuifolia (Chinese Senega)

Radix Polygalae Tenuifoliae is used as an expectorant for symptomatic treatment of coughs due to bronchitis, emphysema and catarrh of the upper respiratory tract (Martindale, 1996; WHO, 2004). The expectorant activity of Radix Polygalae Tenuifoliae is due to the saponins which produce local irritation of the mucous membranes of the throat and respiratory tract. This irritation stimulates an increase in bronchial secretions, thereby diluting the mucus, reducing its viscosity by reducing the surface tension, and facilitating expectoration (WHO, 2004). In intragastric administration of Radix Polygalae Tenuifoliae in cats, the output of respiratory tract fluid increased by up to 173% within three to four hours (Kalra *et al.*, 2011). It has been suggested that Radix Polygalae Tenuifoliae acts as an expectorant by way of a reflex from the stomach. Oral administration of Radix Polygalae Tenuifoliae syrup to dogs increased the output of respiratory fluid within 5 minutes (Misawa & Yanaura, 1980).

TOXICOLOGY

Polygala tenuifolia

Toxicity for Radix Polygalae Tenuifoliae has not been documented in dogs and cats when administered orally in therapeutic doses. Oral LD_{50} of Radix Polygalae Tenuifoliae saponin is 3.95 g/kg of body weight in mice (Yao *et al.*, 2010).

Equivalent toxic dose in 20 kg dog: 79 g PO of Radix Polygalae Tenuifoliae saponins.
Equivalent toxic dose in 5 kg cat: 19.75 g PO of Radix Polygalae Tenuifoliae saponins.

DRUG INTERACTIONS

Validated interactions studies do not exist for Radix Polygalae Tenuifoliae preparations. Clinical interactions with other drugs have not been reported. However, Radix Polygalae Tenuifoliae exhibits diuretic effects and concurrent use with diuretic drugs may lead to increased elimination of water and/or electrolytes (Chen & Chen, 2004).

Ocimum sanctum (Holy Basil)

In several ancient systems of medicine including Ayurveda, Greek, Roman, Siddha and Unani, Folium Ocimi Sancti has a vast number of therapeutic applications including asthma and bronchitis (Gupta *et al.*, 2002). In a study without controls, oral administration of an aqueous extract of dried Folium Ocimi Sancti to 20 human patients with asthma increased lung vital capacity and relieved laboured breathing (Sharma, 1983). Dietary supplementation with Folium Ocimi Sancti oil protects against bacterial colonization of the lungs (Saini *et al.*, 2009).

TOXICOLOGY

Toxicity for Folium Ocimi Sancti has not been documented in dogs and cats when administered orally in therapeutic doses. The LD_{50} for fixed oil of Folium Ocimi Sancti was calculated at 42.5 mL/kg of body weight and long-term use of oil at 3 mL/kg of body weight does not produce any adverse effects in rats (Singh *et al.*, 2007). The LD_{50} of ethanol extract of Folium Ocimi Sancti in adult mice was found to 4.5 g/kg of body weight oral and 3.2 g/kg of body weight intraperitoneal (Rahman *et al.*, 2011).

Equivalent toxic dose in 20 kg dog: 90 g PO of Folium Ocimi Sancti ethanol extract.
Equivalent toxic dose in 5 kg cat: 22.5 g PO of Folium Ocimi Sancti ethanol extract.

DRUG INTERACTIONS

Validated interactions studies do not exist for Folium Ocimi Sancti preparations. Clinical interactions with other drugs have not been reported.

Siraitia grosvenorii [Momordica grosvenori] (Monk Fruit)

In traditional Chinese medicine Fructus Momordicae grosvenorii is used as an expectorant and antitussive, to treat lung congestion, cough and other respiratory ailments. These therapeutic benefits are attributed to the unique component of Fructus Momordicae grosvenorii which are the triterpene glycosides, most importantly mogroside-5 (Dharmananda, 2004). Mogroside-5 has also been reported to be an antioxidant agent that can scavenge reactive oxygen species and prevent DNA damage (Zhang *et al.*, 2011).

TOXICOLOGY

Toxicity for Fructus Momordicae grosvenorii has not been documented in dogs and cats when administered orally in therapeutic doses. Oral LD_{50} of Fructus Momordicae grosvenorii is >10 g/kg of body weight in mice (Nabors, 2011).

Equivalent toxic dose in 20 kg dog: >200 g PO of Fructus Momordicae grosvenorii.
Equivalent toxic dose in 5 kg cat: >50 g PO of Fructus Momordicae grosvenorii.

DRUG INTERACTIONS

Validated interactions studies do not exist for Fructus Momordicae grosvenorii preparations. Clinical interactions with other drugs have not been reported.

Verbascum thapsus (Mullein)

From antiquity *Verbascum thapsus* has been used as a medicinal herb, it contains diverse polysaccharides, iroid glycosides, flavonoids, saponins, volatile oils and phenylentanoids. Verbascoside has anti-inflammatory properties since it reduces the production of superoxide radicals and consequently reduces the activity of inducible nitric oxide synthase [iNOS] (Speranza *et al.*, 2010). Flos Verbasci has been used for the treatment of inflammatory diseases, asthma, spasmodic coughs, and other pulmonary problems. Aqueous extracts of Flos Verbasci has exhibited antibacterial activity against *Klebsiella pneumonia, Staphylococcus aureus, Staphylococcus epidermidis*, and *Escherichia coli* (Turker & Camper, 2002).

TOXICOLOGY

Toxicity for Flos Verbasci has not been documented in dogs and cats when administered orally in therapeutic doses. Oral LD_{50} of ethanol extract of *Verbascum thapsus* is >400 mg/kg in rats (Murti *et al.*, 2011).

Equivalent toxic dose in 20 kg dog: >8000 mg PO of ethanol extract of *Verbascum thapsus*.
Equivalent toxic dose in 5 kg cat: >2000 mg PO of ethanol extract of *Verbascum thapsus*.

DRUG INTERACTIONS

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

Morus alba (White Mulberry)

Pharmacological studies on Cortex Mori Albae Radicis showed cathartic, analgesic, diuretic, antitussive, antiedema, sedative, anticonvulsant, and hypotensive actions in animals including dogs (Yamatake *et al.*, 1976). Cortex Mori Albae Radicis was shown to inhibit the inflammatory process in lung tissue through suppression of the IkappaB signaling pathway and may prove helpful in the management of asthma, various allergic disorders, sepsis, or any other condition associated with pulmonary inflammation (Lee *et al.*, 2009). Cortex Mori Albae Radicis has demonstrated antioxidant activity (Chang *et al.*, 2011) and immunomodulating effects (Kim *et al.*, 2000). Kuwanon G isolated from Cortex Mori Albae Radicis has exhibited antibacterial activity against *Streptococcus sobrinus, Streptococcus sanguis*, and *Porpyromonas gingivalis* by condensation of the cytoplasm and inducing morphological damage to the cell wall (Park *et al.*, 2003).

TOXICOLOGY

Toxicity for Cortex Mori Albae Radicis has not been documented in dogs and cats when administered orally in therapeutic doses. Oral LD_{50} of Cortex Mori Albae Radicis is 10 g/kg of body weight in mice and intraperitoneal LD_{50} is 5 g/kg of body weight (Chen & Chen, 2004).

Equivalent toxic dose in 20 kg dog: 200 g PO of Cortex Mori Albae Radicis.
Equivalent toxic dose in 5 kg cat: 50 g PO of Cortex Mori Albae Radicis.

DRUG INTERACTIONS

Validated interactions studies do not exist for Cortex Mori Albae Radicis 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.
- Not to be used in high doses with anticoagulant drugs.
- Not to be used one week prior to surgery.
- Consult your veterinarian for potential drug interactions.
- Off-label use of this product in ruminants is not recommended.
- Administer during or after the animal has eaten to reduce incidence of gastrointestinal upset.
- Oral use only.
- 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.

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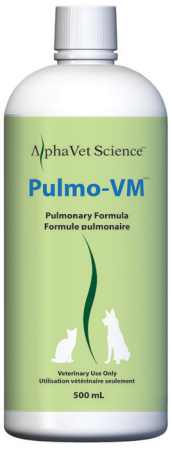
CONTRAINDICATIONS

- Contraindicated in pregnant and nursing dogs and cats.
- Contraindicated with cyclosporine.

AlphaVet Science™

Pulmo-VM™



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