



VIVITONIN®

Leading the way to a healthier old age.

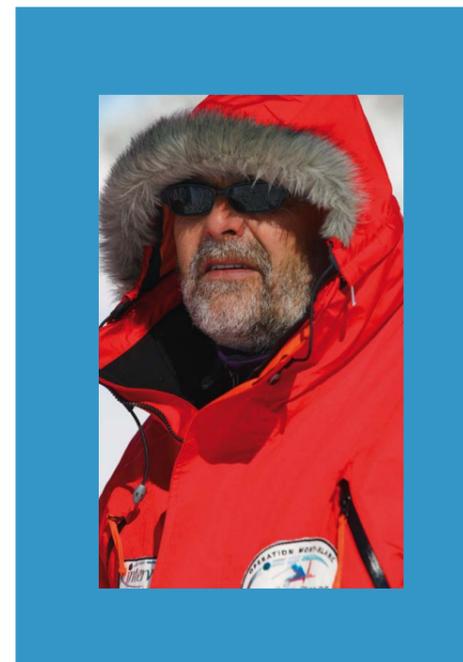
VIVITONIN® enhances the quality of life in ageing dogs. Not only does it increase oxygenation, but it also improves cardiovascular function and neurological performance. We have tested **VIVITONIN®** in a trial under some of the most extreme conditions imaginable. The oxidative stress that occurs under these conditions is the same process that is responsible for many of the signs of ageing seen in older dogs.

The dramatic results of this trial supports the existing clinical studies of this treatment in middle aged and older dogs.



“The Chiens des Cimes expedition allowed us to demonstrate the beneficial effects of Vivitonin in different areas: cardiovascular, cellular oxygenation, oxidative stress”

Prof. Dominique Grandjean, Head of the Breeding and Sports Medicine Unit (UMES) at the Ecole Nationale Vétérinaire d'Alfort and co-organiser of the expedition.



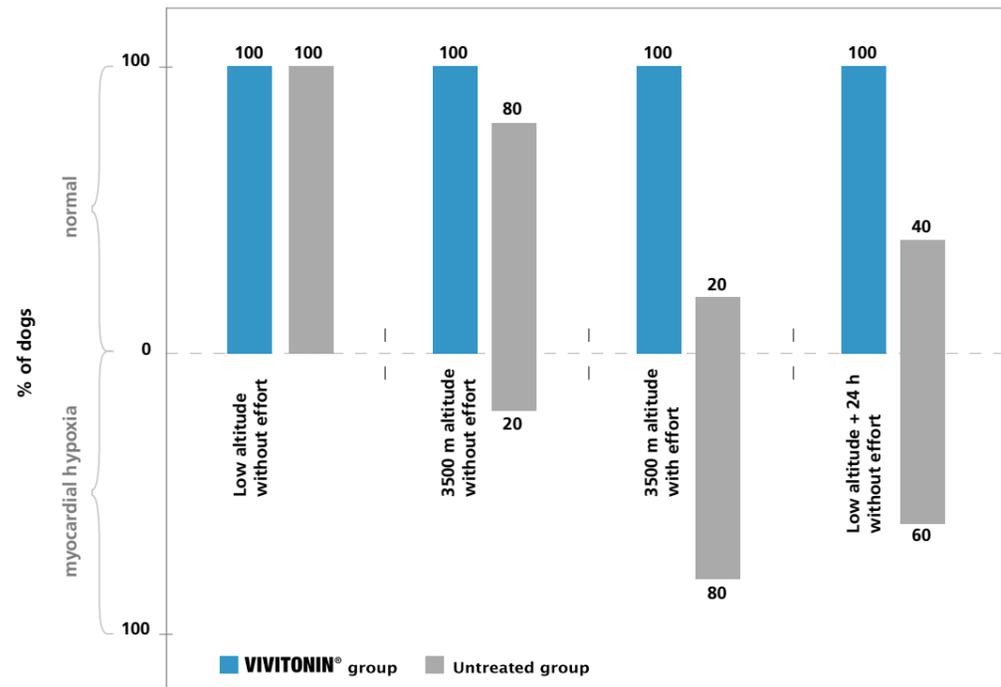
Proven in one of the world's toughest canine challenges

The 'Chiens des Cimes (Dogs of the Summits) - Mont Blanc' expedition 2004 was a world first, a study designed to investigate the physiological stresses experienced by search and rescue dogs, and to determine whether **VIVITONIN®** could reduce these.

The detailed results show that **VIVITONIN®** had an effect on all of the parameters studied. These results are not only relevant to working dogs; ageing pet dogs will also enjoy the benefits of improved oxygenation, cardiovascular and neurological performance.

Proven to prevent myocardial hypoxia

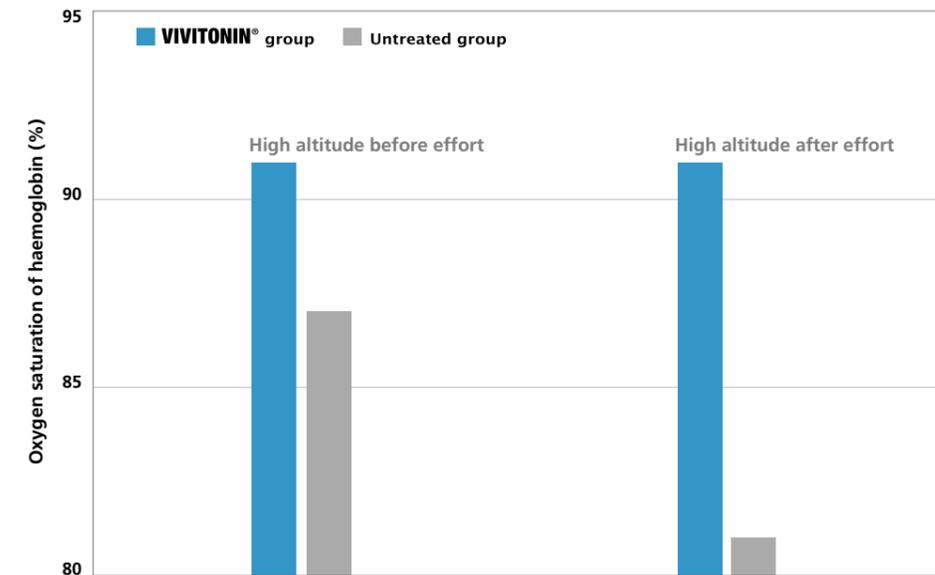
VIVITONIN® prevents ECG changes associated with myocardial hypoxia in dogs (as measured by ECG ST segment depression greater than -0.2 mV).



Proven to reduce oxidative stress

Oxidative stress harms the integrity of biological membranes, triggering further pro-oxidant reactions that exceed the antioxidant capabilities of affected organs or tissues - leading to further damage. VIVITONIN®'s vasodilatory and bronchodilatory effects help to improve oxygen delivery to tissues, combating these destructive processes.

VIVITONIN® treatment maintains oxygen saturation of haemoglobin, even during strenuous exercise at high altitude.



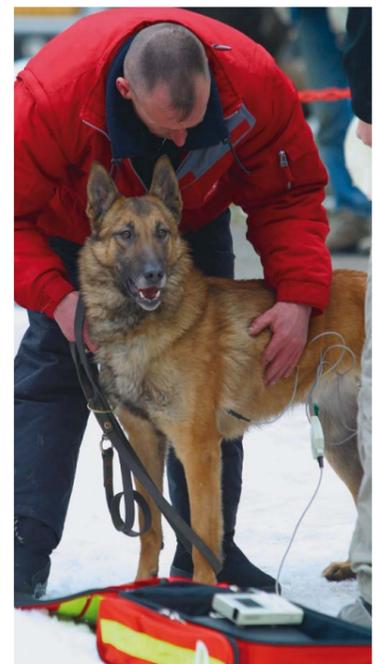
Chiens des Cimes and VIVITONIN®

In 2004, at an altitude of 3500 metres, with temperatures of -30°C and wind speeds of 50 km/h, search and rescue dogs and their handlers took part in a scientific study on Mont Blanc. The purpose of the study was to determine the effects of VIVITONIN® on the dogs' metabolic, cardiovascular and neurological performance whilst working in this extreme environment.

In this randomised, controlled study, half of the dogs were administered VIVITONIN® before undergoing a range of intense physical tests. In order to provide a control situation, the tests were repeated at low altitude before and after the exercise tests on Mont Blanc.

After strenuous exercise, dogs treated with VIVITONIN® had significantly higher oxygen saturation levels of haemoglobin (90.6% ± 1.76 versus 81.4% ± 0.632)*

* Reference Grandjean and others (2005) Nouv Prat Vet 22, 6-65

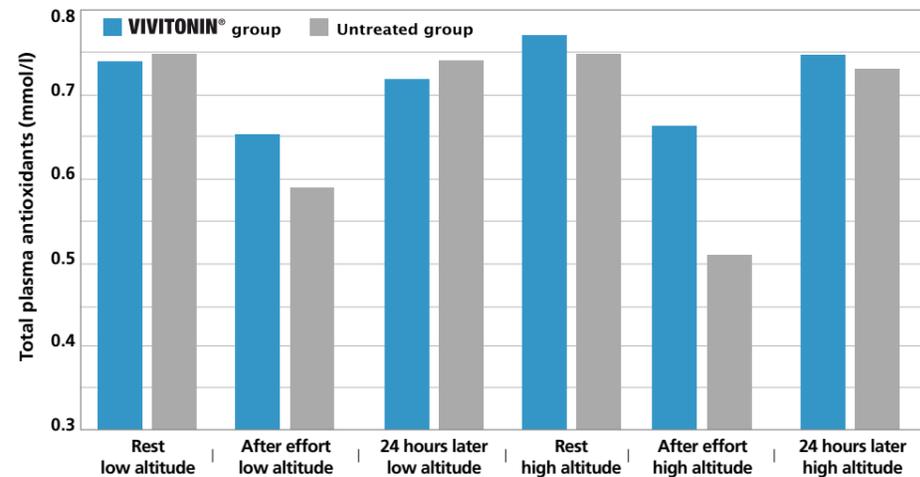


Proven to help ageing dogs

Cellular oxidative stress caused the physiological effects seen in the search and rescue dogs in this trial. This same process also causes many of the signs of ageing seen in older dogs, such as reduced alertness, lethargy and unwillingness to exercise. By improving circulation and oxygen delivery to organs and tissues, **VIVITONIN®** combats cellular oxidative stress, leading to:

- **Improved neurological function**
 - Improved cerebral blood flow
 - Adenosine potentiation
- **Improved cardiac function**
 - Improved myocardial blood supply
- **Improved respiratory function**
 - Bronchodilation
- **Improved skeletal muscular function**
 - Increased perfusion

VIVITONIN® treatment spares circulating antioxidants in dogs.



After strenuous exercise, total circulating antioxidants in plasma are spared in dogs treated with **VIVITONIN®**, limiting the impact of oxidative stress*

* Reference Grandjean and Renard (2005) Pract Vet Anim Comp 14, 3-6

VIVITONIN® (Propentofylline)

Propentofylline is an (alkyl)xanthine that has effects on cyclic adenosine monophosphate (cAMP), the endogenous adenosine system and phospholipase A2 and C. This results in significant effects:

Brain¹⁻⁵

- Potentiates the level of endogenous adenosine, an important protective agent in cerebral ischaemia and the prevention of neurodegeneration.
- Adenosine significantly increases cerebral blood flow and oxygen levels by arteriolar dilation.
- Reduces ischaemic nerve cell damage by reducing microglial cell proliferation.

Heart^{6,7}

- Can assist cardiac circulation, primarily achieved by increasing coronary artery and myocardial blood flow.
- Studies have shown propentofylline increases coronary artery blood flow by up to 137%, blood flow to the myocardium by 41%, and decreases infarct size from 34.5% to 26.1% of left ventricular mass.

Circulation⁸

- Reduces blood viscosity by reducing platelet aggregation and improving erythrocyte flexibility.
- Produces vasodilation (including capillary beds), enabling increased blood flow.

Respiratory function

- Improved secondary to bronchodilation.

Muscle function⁶

- By improving the supply of blood, oxygen and nutrients to the microcirculation and terminal vascular beds, propentofylline has been shown to increase capillary density particularly in cardiac and skeletal muscle.

WHEN TO PRESCRIBE

After identifying any underlying medical conditions, prescribe **VIVITONIN®** when any of the disorders listed below, result in dullness, lethargy, poor overall demeanour, decreased willingness to exercise or poor exercise tolerance:

- Chronic, age-related circulatory problems
- Senility and behavioural changes
- Arrhythmia due to myocardial ischaemia
- Syncope
- Bronchial constriction
- Impaired circulation and tissue oxygenation, especially in the heart, brain and skeletal muscle.



Proven long-term

Middle aged and older dogs can benefit from regular treatment with **VIVITONIN®**. Administered orally twice daily on an empty stomach (at least 30 minutes before feeding), a positive response to treatment can be expected within 4 weeks, but may occur within 24 hours. **VIVITONIN®** can be continued lifelong in dogs where a positive response to treatment has been seen.

References

1. Rudolphi KA & Schubert P (1997) Modulation of neuronal and glial cell function by adenosine and neuroprotection in vascular dementia. *Behavioural Brain Research* 83: 123-128.
2. Foster AC *et al* (1995) Regulation of endogenous adenosine levels in the CNS: Potential for therapy in stroke, epilepsy and pain. *Purine and pyrimidine metabolism in man VIII*, Ed. Sahote A & Taylor M. Plenum Press, NY, 1995.
3. Park CK & Rudolphi K (1994) Anti-ischæmic effects of propentofylline (HWA 285) against focal cerebral infarction in rats. *Neurosci. Lett.* 178: 235-238.
4. Parkinson FE *et al* (1994) Propentofylline: a nucleoside transport inhibitor with neuroprotective effects in cerebral ischaemia. *General Pharmac.* 25: 1053-1058
5. Qui-Sheng Si *et al* (1996) Adenosine and propentofylline inhibit the proliferation of cultured microglial cells. *Experimental Neurology* 137: 345-349
6. Fielder VB & Komarek JV (1981) Effects of 1-(5'-oxohexyl)-3-methyl-7-propylxanthine (HWA 285) on viability of ischaemic jeopardised myocardium after acute coronary artery occlusion and reperfusion. *Arch. Int. Pharmacodyn.* 254: 70-84.
7. Hudlicka O *et al* (1981) The effect of a xanthine derivative, 1-(5'-oxohexyl)-3-methyl-7-propylxanthine (HWA 285), on heart performance and regional blood flow in dogs and rabbits. *Br. J. Pharmac.* 72: 723-730
8. Mubagwa K *et al* (1996) Role of adenosine in the heart and circulation. *Cardiovascular Research* 32: 797-813



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Indications for use:

VIVITONIN® is indicated for the alleviation of dullness, lethargy and improvement in overall demeanour in older dogs.

Contraindications:

DO NOT administer to pregnant bitches or breeding animals, as the compound has not been evaluated in these situations.

Registered pursuant to the ACVM Act 1997 No A5114. Prescription Animal Remedy (P.A.R) Class 1. For use only under the authority or prescription of a veterinarian. ®Registered Trademark. Schering-Plough Animal Health Ltd. 33 Whakatiki St, Upper Hutt. Phone 0800 800 543, www.intervet.co.nz. VIV-209-2010.