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DeerVelvet

Technical manual

New Zealand
Deer Products

14 BLOOD HEALTH

14.1 Health Benefits

Velvet antler is referred to frequently in Russian, Chinese and Korean literature as being useful as an anti-fatigue agent and for general weakness. One of the most common reasons for fatigue and weakness is anaemia. Research on laboratory animals has suggested that velvet antler is a haematinic and that it can aid recovery from anaemia. It is possible that it may have a supportive effect for red cell production in humans.

There are many possible specific causes of anaemia such as iron deficiency and chronic blood loss. In treating anaemia, the cause should be identified and the patient treated appropriately. But whatever the cause, haematinics such as vitamin B complex, iron and perhaps velvet antler may have a role to play in supporting recovery.

14.2 Suggested Physiological Rationale

The haematinic effect of velvet antler suggests that it contains an erythropoietin-type substance or substances, although this has not yet been proven.

14.3 Research Support

Song (1970) estimated erythropoietin activity in the blood of fasted and fed rabbits by measuring radioactive iron incorporation by red blood cells. Blood samples were obtained after 5 days of treatment with an alcohol extract of velvet antler. Each treated rabbit was injected with 2.5 ml/kg of a solution containing 40 mg/ml of extract. An equal number of control rabbits were injected with saline only.

In another part of the study, the effect of velvet antler extract on radioactive iron incorporation was measured in rabbits that had been made anaemic by the removal of 25 ml/kg of blood. The same measurements were carried out in fed and fasted rabbits. The results (Table 11) show that treatment with the extract in all cases significantly raised the radioactive iron uptake of the red blood cells. The improvement in radioactive iron uptake was similar for all treatment pairs, *i.e.* the effects of feed/starving and anaemic/normal haematocrit were not differently influenced by the velvet antler extract.

Table 11. Effect of velvet extract on iron uptake by red blood cells of either normal or anaemic rabbits

Data are mean uptakes of radioactive iron by normal rabbits and by rabbits made anaemic by bleeding (Song 1970) . SED = standard error of the difference.

	Normal Rabbits			Rabbits Made Anaemic		
	Control	Velvet Extract	SED	Control	Velvet Extract	SED
Fed	10.1	17.6	1.46	17.0	27.0	2.18
Starved	8.4	17.2	1.36	14.3	20.9	1.90

It can be concluded that a factor (or factors) in an alcohol extract of velvet antler strongly promoted iron uptake by red blood cells in healthy as well as anaemic animals. Moreover the results suggested that not only did velvet antler promote a return to normal, it raised red cell parameters above normal.

Bae (1976) fed velvet extract to male and female chickens for 8 weeks, and determined the effect on blood parameters in comparison to control animals not supplemented with velvet. Erythrocyte number was not consistently affected by velvet treatment, with male chickens showing no effect of supplementation, and only a single female treatment group exhibiting a significant increase in red blood cell count. Despite this, haematocrit (*i.e.* packed cell volume; PCV) and plasma haemoglobin were both significantly increased by velvet treatment in both male and female chickens.

Kim *et al.* (1979) studied the effects of velvet antler extracts from four species of deer (North American elk, reindeer, New Zealand red deer and Chinese sika deer) on the rate of recovery from anaemia in rabbits. Groups of five rabbits were made anaemic with a single injection of 20 mg/kg phenyl hydrazine. After 4 days, when the induced anaemia was most severe, the rabbits were treated with 250 mg/kg aqueous velvet antler extract. The rabbits were studied for a further 12 days. Haemoglobin concentrations, erythrocyte numbers and haematocrit were measured in blood samples taken every 2 days. The results are shown in Figure 7 - Figure 9 with blood values on day 4 as baseline values (100%). All rabbits had recovered by the end of the study. Compared with the control rabbits, which received no extract, the rabbits treated with the elk velvet antler extract showed a faster recovery than the others in terms of all three measurements. The rabbits treated with elk and New Zealand red deer extract also had higher haemoglobin concentrations and erythrocyte numbers than the controls. This point is further emphasised if the data are compared using day 0 as 100% (Figure 10 - Figure 12), thereby measuring overall changes from before the start of the study. In particular, the rabbits treated with New Zealand red deer velvet antler extract showed marked stimulation compared with control rabbits, and the haematocrit data appeared to show prolonged stimulation compared to controls.

Figure 7. Erythrocyte numbers (relative to day 4) in anaemic rabbits given velvet extracts from different species of deer

Data are from Kim *et al.* (1979).

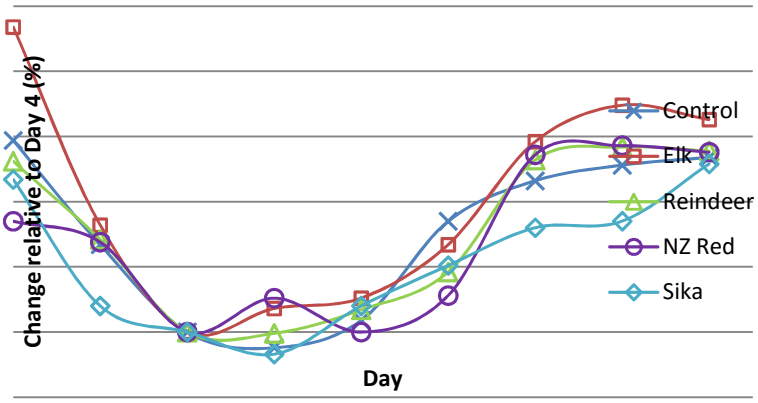


Figure 8. Haemoglobin levels (relative to day 4) in anaemic rabbits given velvet extracts from different species of deer

Data are from Kim *et al.* (1979).

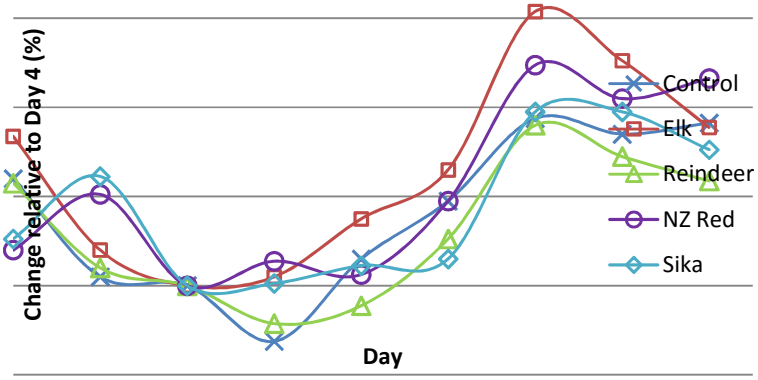


Figure 9. Haematocrit (relative to day 4) in anaemic rabbits given velvet extracts from different species of deer

Data are from Kim *et al.* (1979).

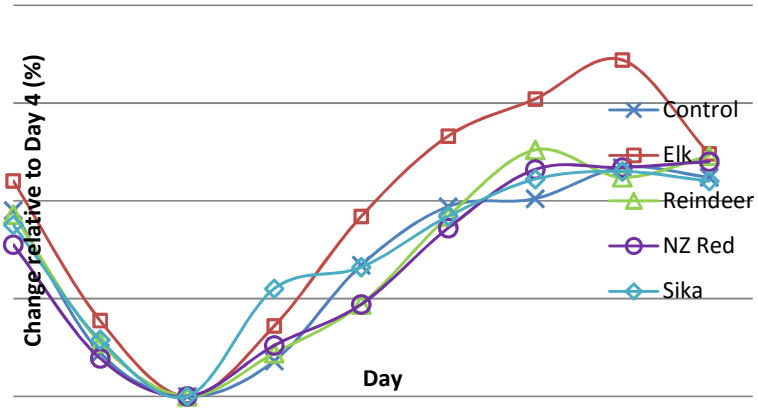


Figure 10. Erythrocyte numbers (relative to day 0) in anaemic rabbits given velvet extracts from different species of deer

Data are from Kim *et al.* (1979).

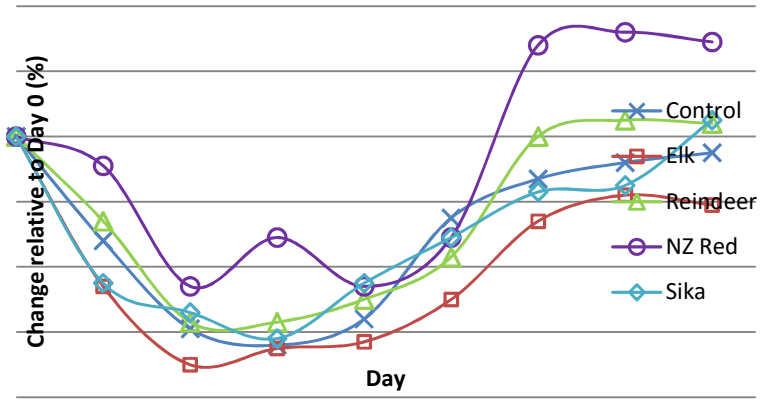


Figure 11. Haemoglobin levels (relative to day 0) in anaemic rabbits given velvet extracts from different species of deer

Data are from Kim *et al.* (1979).

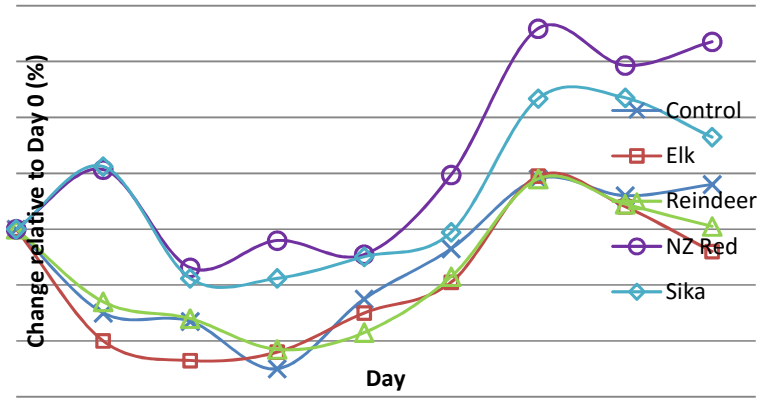
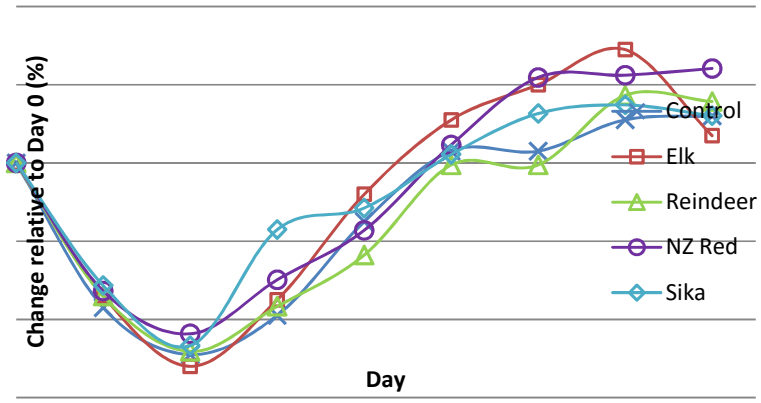


Figure 12. Haematocrit (relative to day 0) in anaemic rabbits given velvet extracts from different species of deer

Data are from Kim *et al.* (1979).



Similar to other studies, these data suggest that velvet antler extracts can aid recovery from anaemia in laboratory animals. Not only that, but velvet antler appears to be able to raise erythrocyte number, haemoglobin and haematocrit above the previous resting levels.

Erythrocyte numbers were also shown to be increased in rats with phenylhydrazine-induced anaemia following velvet extract treatment (Kim *et al.* 1982).

Yokozawa *et al.* (1994) investigated the effect of a hot water velvet extract, along with its ethanol-soluble and ethanol-insoluble fractions, on renal anaemia induced by feeding adenine to rats. Groups of rats were fed either 141 mg/rat/day of velvet extract, ethanol-soluble fraction or ethanol-insoluble fraction, or were given diets that were not supplemented with velvet (control and normal groups). After five days, 0.75% adenine was additionally given in the diets of all except the normal group of rats, and treatment continued for a further 25 days. After this period, significant reductions in blood indices such as red blood cell count, haemoglobin and haematocrit (Table 12) demonstrated the successful induction of anaemia in the adenine-treated animals . The ethanol-insoluble fraction of the water extract significantly inhibited the reductions in these parameters and also restrained significantly the weight loss exhibited by adenine-fed anaimals. Interestingly, the results for the group given the un-fractionated water extract were not intermediate between the groups fed the two fractions produced by its treatment with ethanol, as might be expected given that the components of the ethanol-insoluble fraction comprised 80% of the total water extract. Potentially this indicates an inhibitory interaction between the ethanol-soluble components and the ethanol-insoluble components of the water extract that prevented the latter exerting their affect in the un-fractionated extract.

Table 12. Blood indices in normal rats and rats with adenine-induced anaemia

Red blood cell (RBC) counts, haemoglobin levels and haematocrits in blood of normal rats, or rats with adenine-induced anaemia administered either a water soluble extract, its ethanol (EtOH) soluble or insoluble fractions, or else not supplemented with velvet (Control). Statistical significance: [a] $P<0.05$, [b] $P<0.001$ *vs* normal rats; [c] $P<0.05$, [d] $P<0.001$ *vs* adenine-fed control rats. Data are from Yokozawa *et al.* (1994).

Group	RBC ($x10^6/mm^3$)	Haemoglobin (g/dL)	Haematocrit (%)
Untreated rats			
Normal	7.67 ± 0.19	14.40 ± 0.28	45.51 ± 1.11
Adenine-fed rats			
Control	5.89 ± 0.18[b]	10.43 ± 0.61[a]	30.68 ± 1.62[b]
Water extract (total)	5.41 ± 0.19[b]	10.10 ± 0.28[a]	31.10 ± 1.15[b]
EtOH-soluble fraction	5.86 ± 0.15[b]	10.70 ± 0.21[a]	33.30 ± 1.08[b]
EtOH-insoluble fraction	6.74 ± 0.24[b,c]	11.82 ± 0.43[d]	36.58 ± 1.44[b,c]

Sim and Sunwoo (2001) also investigated the anti-anaemia effect of velvet supplementation in their experiment on the growth of rats subjected to immunisation stress (see page 41 for details of the experimental protocol). They found that the blood iron content and haematocrit (PCV) were both increased in the velvet treated rats. For the group fed the 3% velvet dose, the blood iron content was 457.3 ± 74.6 as compared to 336.4 ± 40.1 for the control animals. The haematocrit of the velvet group was 42.5 ± 0.09% compared to 40.4 ± 0.05% for the controls. Thus, these results are supportive of the earlier data obtained in rats, chickens and rabbits.

Li *et al.* (2004) compared the anti-anaemia activity of alcohol extracts of Chinese wapiti and New Zealand red deer velvet administered orally for 10 days to mice made anaemic by treatment with acetylphenylhydrazine. Treatment with New Zealand red deer velvet extract, but not Chinese velvet extract, significantly improved the survival rate of the anaemic mice at the end of the experiment (Table 13). In surviving mice, haematocrits were significantly elevated in groups fed extract of velvet from either country, as compared to controls. In contrast, only the groups given the New Zealand red deer velvet extract showed significant increases in red blood cell (RBC) count after 10 days, although the RBC counts of the Chinese velvet extract groups were significantly elevated at 5 days compared to control animals. There were also a number of significant differences between the Chinese velvet groups and New Zealand red deer velvet groups. This suggests there were differences in composition that affected extract efficacy, due either to deer species or specific antler processing methods used in each country.

Table 13. Effects of velvet antler extracts on the survival rate of anaemic mice

Anaemia was induced in all groups of mice by administration of acetylphenylhydrazine. Alcohol extracts of either Chinese wapiti velvet or New Zealand red deer velvet were orally administered for 10 days to groups at the indicated doses. Each group contained 17 mice at the start of the experiment. Statistical significance: * P<0.05 *vs* the control group. Data are from Li *et al.* (Li *et al.* 2004).

Group	Dose (mg/kg)	Animals Surviving	Survival Rate (%)
Control	0	11	64.7
Chinese wapiti extract	200	12	70.1
	600	13	76.5
New Zealand red deer extract	200	16	94.1*
	600	14	82.4

18 SUPPORT FOR MEMORY FUNCTION

18.1 Health Benefits

In the Chinese Herbal Medicine Materia Medica, Li Shi-Zhen in 1596 listed 'improving vision and hearing' as properties of velvet, and for centuries in China there has been and still is a widespread belief that velvet antler supports mental capacity. It is not uncommon for students in China to take velvet antler while studying for examinations. Similar use is made of velvet in Russia.

18.2 Suggested Physiological Rationale

If velvet antler does support memory and mental capacity, as some evidence suggests, the rationale is currently not clear.

18.3 Research Support

Brechman (Undated, ~1971) quoted some results of Taneyeva , who studied the effect of Pantocrine (alcohol velvet antler extract) on the mental capacity of humans. She asked people to make specific editorial corrections to a text before and after consuming a control solution of alcohol or one of two doses of alcohol velvet antler extract. The data in Table 15 show the average increase in the number of corrected signs and the decrease in the percentage of errors from the first to the second test after consuming the control or velvet antler extract solutions.

Table 15. Effect of Pantocrine on text correction results

Specific editorial corrections made to a text before and after consuming a control solution of alcohol or of one of two doses of alcohol velvet antler extract. Data are from Taneyeva AI (1969), as quoted by Brechman (Undated, ~1971). *Significantly different to the control group ($P < 0.05$).

Preparation	Dose (ml)	No of subjects	Average increase in the number of corrections	Average decrease in percentage of errors
Control (50% alcohol)	10	9	90 ± 13	0.2 ± 0.05
Pantocrine	10	11	132 ± 17*	1.0 ± 0.36*
Pantocrine	20	11	141 ± 16*	0.8 ± 0.26*

In all groups the level of performance from the first to the second test improved, and there was a significant increase in the number of corrected signs for both of the groups treated with velvet antler extract. Similarly the percent of errors decreased for all groups from the first test to the second, but the decrease was greater for the velvet treated subjects than the controls.

In a more recent double-blind, placebo-controlled study in female Russian university students aged between 18 and 19 (Kaigorodova *et al.* 2004), Pantocrine was shown to significantly increase a measure of exactness (precision) compared to the control treatment and also enhance (non-

significantly) the volume and speed of work completed. Indicators of memory function were also increased in the Pantocrine group as compared to the control.

A study in rats has shown that velvet extract can reduce the learning and memory impairments induced by the administration of scopolamine (Lee *et al.* 2009). Tacrine was used as a positive control in the experiment. Amnesia induced by intra-peritoneal administration of scopolamine (2 mg/kg) was ameliorated by oral administration of either deer velvet extract (200 mg/kg) or tacrine (10 mg/kg), as shown by Morris water maze tests. Both treatments prevented the increased activity of acetylcholinesterase in the brain caused by scopolamine, and also normalised the brain acetylcholine contents of treated rats back up to the level of control animals that were not given scopolamine. MAO-B activity was also reduced by velvet or tacrine treatment compared to the scopolamine-control treatment, although not significantly. The results suggest that velvet extract could be an effective agent for the prevention of the cognitive impairment induced by cholinergic dysfunction.

Wang (1996) considered that the active ingredient for memory enhancement was a phospholipid. He purified an antler-specific phospholipid and showed that it alone, rather than an extract, appeared to improve the memory of mice trained to respond to a specific stimulus.

Some research has examined the potential neurogenic effects of velvet. Chinese scientists (Huo 1997; Huo *et al.* 1997) demonstrated that aqueous extract of freeze dried sika deer velvet was able to stimulate the nerve fibre growth of the dorsal root ganglia of chicken embryo. It also enhanced the differentiation of rat adrenal pheochromocytoma (PC-12) cells in similar fashion to nerve growth factor (NGF). Interestingly, the velvet extract was inactive if prepared from traditionally dried antlers, showing the active component(s) was heat sensitive (consistent with it being a polypeptide growth factor). Yan *et al.* (2007) isolated a novel 14-amino acid polypeptide from sika deer velvet that stimulated the proliferation of another neuronal cell line (HT-22), derived from mouse hippocampus.

Lu *et al.* (2005) have investigated the neurogenic effects of the velvet polypeptides isolated in the laboratory of Wang Ben Xiang (discussed on pages 57-58 in Section13). Neural stem cells derived from E12-14 rat brain were isolated, cultured, and expanded for 7 days until neural stem cell aggregations and neurospheres were generated. The neurospheres were cultured with different concentrations of velvet polypeptides followed by immunocytochemistry to detect the differentiation of neural stem cells. It was found that the velvet polypeptides markedly promoted differentiation of neural stem cells, and most neural stem cells were induced to differentiate towards the direction of neurons at certain concentrations. The authors concluded that stem cells can be successfully induced into neurons by velvet *in vitro*, which could provide a basis for regeneration of the nervous system.

15 BLOOD PRESSURE AND CARDIOVASCULAR HEALTH

15.1 Health Benefits

The Chinese Herbal Medicine Materia Medica states that velvet antler supports cardiac output, but Russian and Korean research evidence on this is equivocal, so any effect of velvet antler on cardiac output in humans has not yet adequately been proven.

It is important that the use of any product having an effect on health does not mask symptoms that would indicate a serious underlying disease. If velvet antler does have an effect on cardiac output or on blood pressure, it should not be taken without medical supervision by anyone with a heart abnormality or abnormal blood pressure. It may be that the use of velvet antler to normalise blood pressure could prevent or delay the diagnosis of an underlying cardiovascular abnormality.

15.2 Suggested Physiological Rationale

A substance or substances in velvet antler may have a supportive effect on the maintenance of normal blood pressure by acting on peripheral blood vessels via the parasympathetic nervous system in a manner similar to a cholinergic substance. Some research also suggests an inhibitory effect on angiotensin I-converting enzyme (ACE), which is an enzyme that is implicated in hypertension.

15.3 Research Support

Most of the studies of the effect of velvet on hypertension were carried out pre-1980 and in general they do not stand up to scientific scrutiny for a variety of reasons such as lack of controls.

For example, Al Bov (1969) studied 32 patients with high blood pressure related to early onset menopause or obesity. They were treated with Pantocrine (alcohol velvet antler extract) either orally or by injection for 20 or 30 days respectively. In 26 of the patients this was associated with a reduction in blood pressure and the patients reported an improvement in condition. Those reporting no improvement had had high blood pressure for an extended period of 9 to 10 years. Al Bov also reported the effects of alcohol velvet antler extract on 13 patients with hypertension caused by disorders of heart muscle activity. The patients were given an injection of velvet antler extract daily for 20 days and were examined 10 days after the final treatment. Eleven (84%) showed an improvement. In both studies, the dose levels were 2 ml/day by injection or 4.5 ml orally. There were no control patients in these studies, nor in studies by Tevi (1969). He also studied the acute hypotensive effect of alcohol velvet antler extract. He suggested that Pantocrine acted on the peripheral vascular system through the parasympathetic nervous system and that velvet antler extract counteracted the effect of previously administered adrenalin. The author concluded that velvet antler extract acted in a manner similar to a cholinergic substance.

Tsujibo *et al.* (1987) determined that lysophosphatidyl choline was responsible for at least part of the purported hypotensive activity of velvet. More recently, Wang (1996) provided further evidence supporting this finding.

In studies of cardiac function, Clifford *et al.* (1979) measured the effect of alcohol velvet antler extract on cardiac output, stroke volume, heart rate, arterial pressure and central venous pressure in anaesthetised dogs. They found significant increases in stroke volume compared with untreated dogs, but no other consistent significant changes were observed.

Sano *et al.* (1972) found that Pantocrine reduced heart rate in isolated guinea pig atria. Reshetrikova (1954) found that administering Pantocrine was associated with improved operation of the heart in sick children, but his trials were not controlled so cause and effect cannot be assumed.

A double-blind, placebo-controlled study conducted by Kaigorodova *et al.* (2004) provided data on the effects of Pantocrine and two other adaptogens (honey-enriched bee pollen and Siberian ginseng) on the cardio-vascular system (CVS) of healthy young females. Female students, aged 18-19 years, were given either 2 ml of adaptogen or placebo (weak tea containing alcohol) twice daily for three periods of two months each over the course of a year . Cardiac rhythm reaction analysis was performed using an automated system ("ORTO-420") at the beginning of the study and at the end of each treatment period. A significantly higher proportion of the Pantocrine-treated group showed an improvement of CVS responses as compared to the control group that received placebo . Of the individual measures examined, the greatest improvement as a result of Pantocrine treatment was seen in the cardiac output of blood volume. The authors concluded that Pantocrine significantly stimulated an increase in reserve capacity of the CVS, and warranted further studies in male and female subjects.

Table 14. Effect of Pantocrine on responses of the CVS

The effect of Pantocrine on the direction of cardiovascular system responses, based on ORTO-test results. The data are the percentages of each treatment group showing improved or decreased responses, or no change, and are reproduced in part from Kaigorodova *et al.* (2004). *Significantly different to the control group ($P < 0.05$).

Response of the CVS	Pantocrine	Control
Improvement	58.3*	11.1
No change	25.0*	55.6
Decrease	16.7*	33.3

ACE inhibitors are commonly used clinically to treat hypertension. However most synthetic ACE inhibitors have damaging side effects, and significant efforts have been going into the search for ACE inhibitors derived from natural sources such as food. Recently Karawita *et al.* (2005) demonstrated that enzyme hydrolysates of velvet exhibit ACE-inhibitory activity. In particular, a pepsin digest of velvet, and its low molecular weight (< 10 kDa) fractions, were found to show strong activity. In addition, the inhibitory activity of the pepsin digest was retained after further

digestion with other enzymes, although it was slightly reduced. This result is significant, given that resistance to degradation by gastrointestinal proteases is important for anti-hypertensive effects of orally administered ACE-inhibitory peptides. The authors concluded that antler is a potential candidate for the treatment of hypertension, although more research is required to identify the compound(s) responsible for the antihypertensive effects.

A water extract of velvet, and a 70% ethanol-soluble fraction of the extract, have been shown to have affects *in vitro* on the amplitude and rate of beating of cultured myocardial cells (Huang *et al.* 1990; Huang *et al.* 1991). Of most interest, pre-treatment with the ethanol-soluble fraction afforded significant protection against the reductions in the percentage of beating cells and the beating rate caused by treatment with the powerful cytotoxic chemotherapy drug doxorubicin (Adriamycin). Lactate dehydrogenase leakage from doxorubicin-administered myocardial cells was also significantly diminished by the pre-treatment with this fraction, though ATP content in the cells was not appreciably recovered. Since the toxicity of doxorubicin has been attributed to the action of free radical species, the authors concluded that velvet extract may confer a tonic effect on stressed organs including the heart via an antioxidant activity.