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DeerVelvet

Technical manual

New Zealand
Deer Products

Technical Manual
Version 6.3

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IMPORTANT NOTICE

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This information is intended as scientific information for the use of trade as a summary of research conducted on deer velvet. It is not intended as information for use by consumers and does not represent approved statements related to any product use.

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1 BACKGROUND

1.1 Introduction

This manual introduces deer velvet antler, the history of its use from ancient times to the present, its chemical composition and its health benefits and applications. It reviews and discusses the available literature on deer velvet. The purpose of the manual is to provide a link between the reported scientific information on velvet and information required by laypeople producing, selling or consuming velvet.

In discussing deer velvet antler, the terms 'velvet' and 'deer velvet' and 'velvet antler' are used synonymously.

1.2 Historical Perspective

For over 2,000 years, the velvet antler of male deer has been prized by the Chinese for its powerful health-promoting properties (Kong *et al.* 1985; Jette Undated). The first documented evidence of the use of velvet antler as a health tonic was found on a silk scroll recovered from a Han Tomb in Hunan Province in China. The scroll has been precisely dated at 168BC and contains a range of significant medical treatments and prescriptions using velvet antler. Since then, traditional and on-going Asian usage has focused on the promotion of well-being.

1.3 What is Velvet Antler?

Velvet antler can be defined as 'deer antlers during their phase of rapid growth', and it gets the name 'velvet' from its soft, velvet-like covering of hair. Velvet antler is considered by the Chinese to be one of the most powerful animal-based remedies in their Traditional Chinese Pharmacopoeia.

The annual growth cycle of antlers starts in spring with the rapid development of a soft cartilaginous core from each of the two bony protuberances, or 'pedicles', on the stag's skull. This core is covered with a layer of connective tissue, then skin with a dense covering of fine hair, and the whole antler is well supplied with blood vessels and nerves. Growth takes place very rapidly, at a rate of up to 2 cm per day. Velvet antler is very sensitive during this growth phase, and the male deer are protective of it and non-aggressive. As growth occurs, cartilage is gradually replaced by bone by a process of calcification. When growth is complete, the antler 'hardens' or calcifies completely, the blood vessels at the junction between the pedicle and the antler close off, and the skin, nerves and connective tissue dry, shrivel and flake off. The bony cores remain as hard antler ready for the 'rutting' season in autumn, when the stags are aggressive and combative as they compete for hinds. At the end of the rutting season, in early spring, the pedicle-antler junction weakens and the antlers are cast naturally.

Deer velvet is a unique structure, because it is the only organised mammalian tissue that completely regrows, and it does so every year. Moreover it grows extraordinarily rapidly, and the rapid growth is likely to be regulated by pharmacodynamic substances that are either unique or that can be found in other tissues but are at particularly high concentrations in deer velvet. In

Asia, the unique nature of deer velvet has no doubt contributed to its reputation as a powerful remedy.

1.4 A Renewable Resource

Because velvet antler regenerates completely each spring, it can be removed annually by a process called 'velvet removal'. Whether they are removed or are left to cast naturally, antlers are replaced the following spring by the same natural growth process, so deer velvet is a renewable resource.

1.5 New Zealand Environment

New Zealand is an island nation that has been relatively recently colonised. It has a temperate climate with few insect vectors of disease and, from the time livestock were first introduced, it has had efficient border controls to help prevent the introduction of new diseases. As a result, New Zealand livestock are free of many of the diseases that limit agricultural production and trade in other countries.

By and large, New Zealand's deer farms have good soil, a mild climate and a moderate rainfall, and deer farmers are relatively well-informed with an excellent supportive infrastructure of advisors. This environment promotes a high standard of deer farming and consistently high quality deer products.

1.6 Farming of New Zealand Velvet Antler

The farming of red deer, wapiti (elk) and red/wapiti hybrid stags for both velvet and venison has become an established industry in New Zealand (Drew 2008). All farmed deer in New Zealand are held extensively on pasture. Deer farms have specially designed yards and handling facilities for routine husbandry procedures, to ensure efficient, safe handling of deer and provide for the welfare needs of the animals.

Deer velvet is removed when there is maximum soft tissue and minimal calcification of the bony core. For red deer this typically occurs 55–60 days after growth begins, and slightly later than this for the larger species of deer. The antlers are carefully cut off using a meat saw just above the junctions at the tops of the pedicles. A short portion of each antler is thus left in place. This hardens naturally and is cast as a hard 'button' in the following spring, at the time that the full antlers would have cast.

1.7 Welfare of the Deer during Velvet Removal

In New Zealand, velvet removal can only be carried out in accordance with a rigorous mandatory protocol that requires trained operators to use approved procedures designed to ensure the welfare of the stags. *It is important to note that pain control during velvet removal is ensured by use of local or general anaesthetic.* Velvet antler can be removed only by veterinarians or specially trained and registered farmers, and the farmers may remove velvet only from their own deer. New Zealand Government legislation called the Animal Welfare Act 1999 and the Code of Recommendations and Minimum Standards for the Welfare of Deer During the Removal of

Antlers 1992 set the standards. The National Velveting Standards Body (NVSB), which is jointly administered by Deer Industry New Zealand and the New Zealand Veterinary Association, has overall responsibility for managing and ensuring the integrity of the NVSB programme. The programme is endorsed by the National Animal Welfare Advisory Committee (NAWAC). NAWAC is a committee set up and administered by the New Zealand Government's MAF Biosecurity. NAWAC's functions include advising the Minister of Agriculture and Forestry on matters relating to animal welfare.

Stags that are kept for velvet production usually have a relatively long life, as they are often farmed for 10 years or more. Moreover they are farmed in extensive pastoral systems with few other interventions apart from routine health procedures. Thus they generally have a life of good quality. Velvet removal benefits the welfare of stags by reducing the risk of injury by fighting during the mating season.

1.8 Stringent Health Standards

Once removed, the velvet antler is frozen on farm and subsequently hygienically processed as required by the Ministry of Agriculture and Forestry (MAF) and the New Zealand Food Safety Authority. Processing is subject to inspection by MAF, and audits are performed at least every three months depending on the plant's performance. To assist with monitoring and to ensure traceability and compliance with the scheme, velvet is labelled immediately after removal using authorised unique identification labels.

1.9 Research

A great deal of relevant research has been carried out in the last 70 years to answer questions about the efficacy and safety of deer velvet. Mainly this has taken place in Asia, particularly in China, Korea, Hong Kong and Japan, and in the former USSR. In recent years an increasing amount of research has also been carried out in Western countries such as Australia, USA, Europe, Canada and New Zealand.

In general, the research tends to support the traditional view that deer velvet's effects on the human body are restorative, strengthening and protective. Accordingly, Russian scientists have termed velvet an 'adaptogen'. The findings supportive of velvet's purported enhancement of growth, wound healing and immune function, and its haematinic (anti-anaemia) and anti-ageing activities, are of particular interest. In some areas, for example its effects supporting the maintenance of normal blood pressure, the findings are equivocal. Furthermore, there is no evidence that deer velvet is an aphrodisiac in humans, and the results of a study by Conaglen *et al.* (2002; 2003) argue against it enhancing other aspects of sexual function too. Nor have anti-bacterial or anti-viral activities been proven, although evidence of anti-fungal activity has been provided.

An outline of much of the relevant research on deer velvet is presented below with summaries of the results. In the main, the papers reviewed are from reputable peer-reviewed scientific journals and, as a rule, more weight has been given to the more recent (post-1980) research than that done earlier.

1.10 Research in New Zealand

In New Zealand, most research relating to velvet antler composition and efficacy has been carried out by AgResearch and in particular by a team led by Dr J M Suttie.

All animal experimentation in New Zealand is carried out in accordance with the Animal Welfare Act 1999, under the supervision of Animal Ethics Committees to ensure high standards of animal welfare and minimise animal suffering.

AgResearch is a state-owned company dedicated to pastoral agricultural research, which was established in 1992 by combining research capabilities from the Ministry of Agriculture and Fisheries and the Department of Science and Industrial Research. The company has four major campuses throughout New Zealand and employs in excess of 1000 staff. Invermay, near Dunedin, is known principally as a Centre for Sheep and Deer research and this is where the internationally recognised Deer Science group is located.

Velvet research at AgResearch has primarily been conducted under the leadership of **Dr Jimmy Suttie.** Dr Suttie obtained a First Class Honours BSc at Aberdeen University in 1977, then went on to study the growth and reproductive physiology of red deer stags, based at the Rowett Research Institute. This gained him a PhD from Aberdeen University in 1981. The same year, Dr Suttie accepted a post-doctoral position at Invermay studying the physiology of antler growth, and has been based at Invermay since that time. He is a world expert in antler physiology, antler composition and efficacy. Dr Suttie has presented invited papers at International Conferences in UK, Ireland, USA, China, Korea, Taiwan, Australia and Hungary. He is now General Manager of the Applied Biotechnologies group in AgResearch, and leads multiple teams engaged in research on animal genomics, reproduction, growth & development, and forage improvement and biotechnology, as well as Velvet Antler. Since 1989, the Velvet Antler group has focused on studies of the composition and efficacy of velvet antler.

1.11 Deer Industry New Zealand

Deer Industry New Zealand (DINZ) was established under the Deer Industry New Zealand Regulations 2004 (previously the Game Industry Board Regulations 1985) to promote and assist with the development of New Zealand's farmed deer industry. It does not trade but has a world-wide coordinating role through research and promotion of quality products developed from deer, especially velvet and venison. Its functions also include industry representation, quality assurance and market access, and it manages a training and certification programme for the removal of velvet.

This training and certification programme is administered by the National Velveting Standards Body (NVSB), and it is based on an animal welfare Code of Practice. The programme is approved under the 1994 Animal Remedies (Develveting) Regulations (see Section 1.7 above).

2 VELVET IN PERSPECTIVE

2.1 Relevance to Modern Lifestyles

Velvet antler has been extensively used in Asia and particularly China for over 2000 years, but its relevance to the lifestyle needs of the 21st century world is only now being explored. Currently there is considerable interest in velvet as a dietary supplement. This transcends the barriers that separate Eastern from Western medicine as consumers increasingly take a more holistic approach to health care and begin to explore tonics and remedies beyond the range traditionally available.

2.2 Health Benefits

Traditionally, Asians have considered deer velvet to be a 'tonic', producing effects consistent with restoration of normal body processes, strengthening of the body (by support for mental and physical performance) and protection of the body. In recent years, international research has tended to support some of these possibilities while others remain unproven.

2.3 Future Prospects for New Zealand Velvet Antler

Deer velvet antler is a product in transition from a medicine shrouded in mystery to a dietary supplement that is readily available off-the-shelf in many countries around the world. In New Zealand, where the standards of deer farming rank among the best in the world, deer velvet has great potential as a dietary supplement that can be used to complement conventional Western therapies.

3 DEER VELVET SAFETY INFORMATION

This section is a reproduction of a Sheet produced by Deer Industry New Zealand's (DINZ) advisors that considers the prudent use of deer velvet.

IMPORTANT NOTES

Although deer velvet may have many benefits for consumers, different people can be affected in different ways. There is a small chance that some consumers of deer velvet could experience adverse effects, some of which may be serious.

For this reason Deer Industry New Zealand has produced this Sheet which contains a summary of the possible adverse effects of deer velvet on which Deer Industry New Zealand believes it has reasonable information. This Sheet is intended to help consumers decide whether taking deer velvet is appropriate for them.

Deer velvet is available from many manufacturers in a number of different formulations. Therefore, this Sheet is not intended to apply to specific deer velvet products as the properties and effects of each deer velvet product may vary. Consumers should contact the manufacturers of any deer velvet product they intend to take for information on any risks associated with that particular product.

Before consumers use any form of deer velvet it is recommended that they consult their health professional. In particular, as with all dietary supplements, consumers should consult their health professional if they are:

- Taking any prescription medicines; or
- Receiving other medical treatment; or
- Pregnant or breastfeeding; or
- Under the age of 18.

Consumers must not rely on anything contained in or referred to in this Sheet in substitution for advice from their health professional.

POSSIBLE ADVERSE EFFECTS

1. Many substances and foods in common use today are known to cause allergic responses, which in very rare cases can be severe and immediate. Deer velvet is no different in this respect and a small minority of persons will be allergic to deer velvet products. Therefore, deer velvet may be inappropriate for those with allergies. There are anecdotal accounts (meaning personal accounts which are not scientifically verified) of some people having an allergic response to deer velvet. However, Deer Industry New Zealand is not aware of any instances when a severe allergic response has occurred following consumption of deer velvet.

2. There is anecdotal evidence that, for some consumers, taking deer velvet:

   a. May cause bleeding noses.
   b. May cause a temporary increase in body temperature. Therefore, for example, it may be inappropriate for consumers to take deer velvet if they have a high temperature.
   c. May cause headaches.
   d. May cause diarrhoea.

   If a consumer experiences any of these problems, consumption of deer velvet should be reduced or stopped and if problems persist, medical advice sought.

TRADITIONAL MEDICINE

Deer Industry New Zealand is aware that practitioners of traditional oriental medicine may not recommend the use of deer velvet in certain circumstances. This Sheet does not provide information on such traditional medicinal practices. Please refer to a practitioner of traditional medicine if you are interested in this type of information.

FURTHER INFORMATION

If you would like further information on deer velvet, and the most up to date version of this Sheet, please refer to www.velvet.org.New Zeland or contact:

Deer Industry New Zealand
PO Box 10702
Wellington
NEW ZEALAND

4 TRADITIONAL USE

4.1 Early Recorded Use

The Ancient Chinese credited velvet with considerable health-giving properties. Plant and animal products have been used to benefit human health for thousands of years. Silk scrolls found in China and dating back 2,000 years describe the use of plants and animals, and it is likely that in even earlier times the shaman cultures of North Asia were familiar with medicinal plants and animals. Plant products have continued to be fairly widely used throughout the world, but generally the use of animal products has not been so common. In Europe, bee venom was used as a treatment for arthritis until relatively recently, and animal products such as chondroitin sulphate and shark cartilage have become widely used. The use of velvet antler has been greatest in China, and there are many references in Chinese literature to its beneficial effects. The best known text is the *Grand Materia Medica (Ben Cao Gang Mu)* written in 1596 by Li Shi-Zhen. This book lists 1,892 medicinal substances, and 444 of these, including velvet, are from animal sources.

4.2 Traditional Uses

The traditional uses of velvet antler are many and various, but they tend to fall into the general categories of support for:

- Body strengthening,
- Blood cell production,
- The immune system,
- Cardiovascular health and function.

4.3 Tonic Actions

Traditional Chinese Medicine (TCM) has always focused on promoting 'wellness' as a goal in itself. In both Chinese and Korean traditional usage, velvet antler is regarded as a promoter of health, in other words it is considered a 'tonic'. Similarly, in Russia velvet is regarded as an 'adaptogen', a natural product that is proposed to increase the body's resistance to stress, trauma, anxiety and fatigue. In general, conventional Western medicine does not recognise tonics/adaptogens as such. Nevertheless they may have a part to play in supportive therapy aimed at restoring health and strength. The mechanisms for any tonic activity of velvet antler are as yet poorly understood, but research such as that outlined below tends to support at least some of the claims that have been made over the centuries.

5 PROCESSING

5.1 Preservation

After velvet antler is removed from the stag (see Section 1.6 above) and frozen on farm, it must be processed to preserve it for human use. The traditional Chinese technique uses repeated dipping of the velvet in near-boiling water to cook each stick followed by oven-cooking and then cool air drying. In New Zealand, a technique has been developed that uses steam instead of hot water dipping to cook the velvet. Freeze-drying is also used to preserve velvet but without heat. Each processing method has its advantages and disadvantages, and the type of process used influences the composition of the end product and the purposes for which it is likely to be used.

Immediately after removal, New Zealand deer velvet is given a unique tag to ensure traceability and authenticity of source, and to demonstrate that its removal was carried out in compliance with the requirements of the National Velvet Standards Body Programme which ensures the welfare of the stag during its velvet removal.

5.2 Processing Yields

A processed antler typically weighs 30–35% of its pre-drying weight, *i.e.* this is the dry matter content of fresh velvet. A typical red deer stag might grow 3–4 kg of velvet, although genetic improvement now sees good red deer stags producing antlers weighing over 8 kg. When the velvet is processed, the weight of the dried product is thus about 1–3 kg per stag.

5.3 Further Processing

A dried stick of velvet can be further processed in a number of ways. It can be finely sliced, often after soaking in alcohol, or it can be ground to a fine powder. The slices can be made into a broth with or without other herbs. The ground powder can be made into capsules or made into an extract using either water or alcohol, or a mixture. The extracts can be used as liquids or freeze- or spray-dried to powders. These powders can themselves be made into capsules or added to other products. The extracts can be further processed by using combinations of solvents with or without chromatographic separation.

5.4 Product Description

The term 'velvet antler' refers to the entire antler, not just the skin. Velvet products are made from the entire antler and contain all the bone and cartilage, blood, nerves and connective tissues that were in the original deer velvet.

Sliced velvet is traditionally-processed velvet antler that is soaked in alcohol and cut into slices 1mm thick or less. This is the form most commonly utilised in velvet-containing traditional medicines.

Dried velvet powder is velvet antler which has been either traditionally processed or freeze-dried and then ground to a powder.

Pantocrine is an extract of velvet made in Russia using a 1:1 ratio by volume of ethanol and acidified water, and is sold in liquid form.

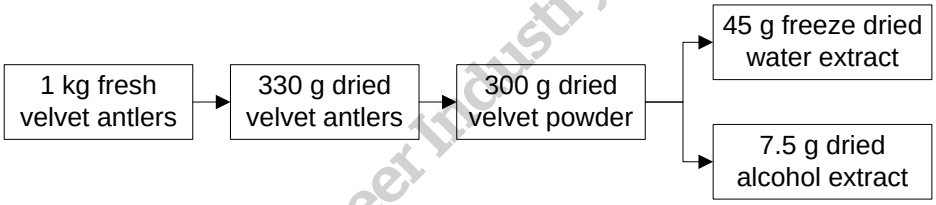
Water (aqueous) extract is an extract of antler velvet made using either hot or cold water at normal atmospheric pressure, or with hot water in a pressurised vessel. This extract can be prepared for use as a liquid or freeze dried to a powder.

Alcohol extract is an extract of velvet antler made using a mixture of ethanol and water. The ratios of these solvents can vary, unlike in Pantocrine. The alcohol extract will typically be used in the alcohol/water solution in which it was made and may be of variable concentration. The alcohol/water can be completely evaporated to give antler grease, or the mixture can be freeze-dried to a powder once the alcohol has been removed.

Organic extract is an extract made from velvet using a non-ethanol solvent, for example methanol or chloroform. Use of these types of solvents is not common for preparing commercial extracts, because of their toxicity.

5.5 Extraction Yields

The following are indicative estimates of yields at different stages of velvet processing:



6 COMPOSITION AND ACTIVE SUBSTANCES

6.1 Overview

Velvet antlers take about 120 days to complete their development, and as they mature their composition varies. The data presented here relates to velvet removed mid-way through this growth period, at the time when most velvet is removed for commercial purposes. Some specific activities that have been ascribed to individual substances isolated from velvet are noted throughout the following discussion of velvet composition, and are discussed in more detail in subsequent sections on health benefits.

6.2 Basic Composition of Velvet Antler

At AgResearch, the velvet antlers from 17 mature red deer stags were processed and analysed using standard laboratory procedures (Fennessy *et al.* 1992; Suttie *et al.* 1993a; Suttie *et al.* 1994). For analysis, the antlers were separated into four major portions (tip, upper, mid and base) (Figure 1), which had markedly different chemical compositions. The mineral and crude lipid analysis is shown in Table 1. Broadly, lipid and protein (calculated as nitrogen% x 6.25) decreased from the tip to the base while the ash and calcium concentrations increased. Similar results have also been reported for velvet from Canada (Sunwoo *et al.* 1995), Korea (Jeon *et al.* 2004) and China (Chen *et al.* 1998b; Wang *et al.* 2008). This reflects the fact that degree of mineralisation of the initial cartilage matrix progressively increases towards the base of the velvet antler.

Some minerals showed interesting trends. Selenium was concentrated at the velvet antler tip, and levels of iron were highest in the upper and tip portions reflecting the relatively high blood content in these sections.

Practitioners of Traditional Chinese Medicine use velvet from different sites for different purposes, and the upper parts of the velvet are more prized for their health benefits. Most biologically active components of velvet are likely to be organic molecules, including peptides/proteins, lipids and carbohydrates. The finding that the upper part of the velvet is where the highest proportions of these molecules are found tallies with the supposed greater health benefits of these parts.

Comparative studies have shown some differences in basic composition of velvet from difference species. A detailed comparison was made of New Zealand red deer velvet with that of New Zealand wapiti, New Zealand fallow, Russian, Chinese wapiti (malu), Chinese sika (meihualu), Australian rusa and reindeer (Fennessy *et al.* 1992; Suttie *et al.* 1993a; Suttie *et al.* 1994). Stage of antler development was also examined in the study, by analysis of antlers removed from 2 year old red deer stags 43 – 67 days after casting of the previous antler. Chinese sika were comparable with top grade New Zealand red deer, and New Zealand wapiti and New Zealand fallow are also of high quality (low mineralisation, high lipid content). Overall, the Chinese wapiti velvet also did not substantially differ in composition from that of New Zealand red deer, but individual antlers showed marked variability. Levels of ash were higher and lipids lower in tips and beams in reindeer velvet compared with red deer but appropriate statistical analysis were not possible

owing to the fact that only pieces rather than whole antlers were available for analysis. The Russian velvet had lower lipid content than red deer velvet, and also tended to be more mineralised. However, since significant correlations were found between the composition of antlers and their stages of development at time of removal, it was concluded that this may have been a major determining factor leading to some of the observed differences between the velvet from the various deer species. In terms of a "market place comparison", though, New Zealand red deer velvet was demonstrated to be at least as high in quality as its competitors, and probably superior to Russian top grade product which is harvested at a more advanced stage of maturity. The latter view is supported by comparative data reported for New Zealand and Russian velvet by Lunitsin *et al.* (2004).

Ahn *et al.* (1994) compared velvet from sika deer, Formosan deer (a subspecies of sika) and red deer. The sika deer velvet was more mineralised and contained less protein than velvet of the other two species (particularly the red deer velvet) but, despite this, had a higher content of crude lipid. However, the results need to be viewed with some caution given that the relative stages of development of the antlers is not apparent from the publication, if it was known.

The pattern of ash content showed some unexpected complexity when narrow discs or slices cut from the main beams of antlers from two New Zealand red deer were analysed (Figure 2) (Haines *et al.* 2001b; Haines *et al.* 2001a). Ash content was very low at the tip, but rose very rapidly and peaked just a few centimetres down the main beam. It then decreased in the region of the trez tine before gradually increasing towards the base. In one antler, the decrease in ash content from its peak value was quite marked, while in another from a different stag there were much less pronounced changes. These data demonstrate that, while overall ash content of antlers removed at the same stage of development is similar, the pattern of that ash content can vary significantly between individual antlers.

Figure 1. Antler sections used for analysis of composition in New Zealand studies

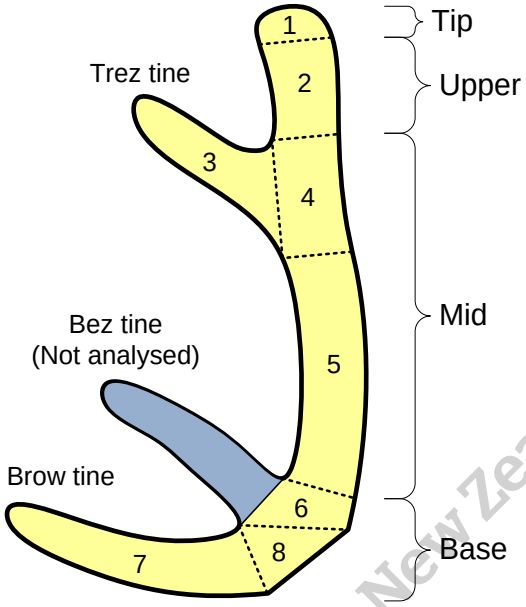


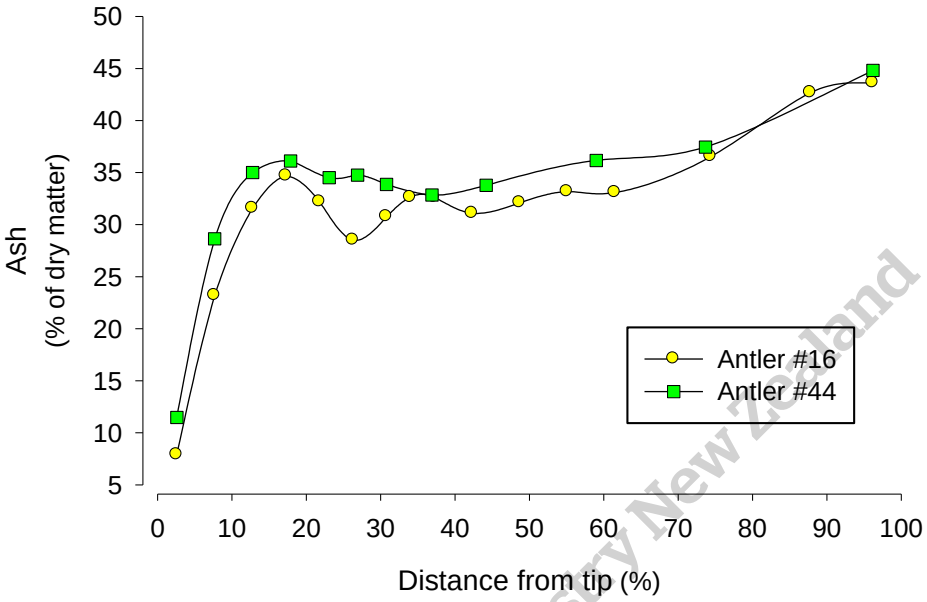
Table 1. Composition of adult New Zealand red deer velvet antler

Data are mean values (n=17) with the standard deviation for the components in each of the four main sections of the antler and the combined total (Suttie *et al.* 1994).

	Antler Section				
	Tip	**Upper**	**Mid**	**Base**	**Combined**
% of antler dry weight	2.7	35.3	29.8	32.5	100
Components (% Dry Matter ± Standard Deviation)					
Ash	6.6 ± 0.75	28.4 ± 2.4	37.8 ± 2.6	38.8 ± 2.2	34.0 ± 2.0
Calcium (Ca)	0.29 ± 0.22	9.3 ± 1.0	13.5 ± 1.2	14.7 ± 1.8	12.1 ± 1.1
Lipid	5.6 ± 1.3	2.7 ± 0.69	2.0 ± 0.47	2.6 ± 0.65	2.5 ± 0.56
Magnesium (Mg)	0.05 ± 0.01	0.21 ± 0.02	0.27 0.02	0.28 ± 0.02	0.25 ± 0.02
Nitrogen (N)	12.2 ± 0.6	9.1 ± 0.5	8.1 ± 0.6	7.6 ± 0.6	8.4 ± 0.51
Phosphorus (P)	0.64 ± 0.11	5.0 ± 0.75	6.3 ± 0.51	6.5 ± 0.36	5.8 ± 0.32
Potassium (K)	0.91 ± 0.12	0.59 ± 0.06	0.33 ± 0.06	0.29 ± 0.04	0.42 ± 0.43
Sodium (Na)	1.09 ± 0.15	0.90 ± 0.08	0.80 ± 0.04	0.77 ± 0.05	0.83 ± 0.04
Sulphur (S)	0.85 ± 0.11	0.54 ± 0.03	0.35 ± 0.03	0.34 ± 0.04	0.43 ± 0.03
Trace mineral components (mg per kg Dry Matter ± Standard Deviation)					
Cobalt (Co)	0.05 ± 0.05	0.04 ± 0.06	0.03 ± 0.03	0.03 ± 0.03	0.04 ± 0.03
Copper (Cu)	5.2 ± 1.1	5.1 ± 0.7	5.6 ± 0.8	5.3 ± 0.8	5.3 ± 0.5
Iron (Fe)	462 ± 227	472 ± 92	288 ± 100	179 ± 53	319 ± 69
Manganese (Mn)	2.6 ± 1.4	3.2 ± 0.8	3.4 ± 0.6	3.5 ± 0.8	3.4 ± 0.4
Selenium (Se)	0.35 ± 0.12	0.25 ± 0.09	0.14 ± 0.06	0.13 ± 0.05	0.18 ± 0.07
Zinc (Zn)	46 ± 7.9	72 ± 9.1	67 ± 10.1	68 ± 12.0	69 ± 9.2

Figure 2. The patterns of ash content of two individual New Zealand red deer velvet antlers

The ash contents of narrow discs cut from the main beams of two representative New Zealand red antlers are plotted against their positions, as percentages of their distances from the tips of the antlers to the bases (Haines *et al.* 2001b; Haines *et al.* 2001a).



6.3 Proteins

Protein molecular weight profile

The molecular weights of the proteins in velvet antler were estimated by an analytical technique called gel filtration chromatography (GFC) (Haines unpublished data). The profile of these protein molecular weights was found to be particularly sensitive to antler processing method (Figure 3). Freeze-dried velvet was found to contain mainly proteins of moderate to high molecular weight (over 20,000 Daltons), many of which appeared to be derived from blood. In contrast, velvet antlers processed using traditional methods contained a lower proportion of these serum proteins. In the latter, a number of low molecular weight peptides, probably resulting from break-down of the larger proteins, were evident in the protein profiles.

The protein profiles were also different for different sections of the antler (Figure 4). The proportion of blood-derived proteins was highest in the mid section, consistent with pooling of blood in this region. Overall, the protein profile of the base section was very similar to the mid section, although the size of the haemoglobin peak (the large peak at about 30,000 Daltons) was reduced. In contrast, the profile of the antler tip contained a much higher proportion of polypeptides with molecular weights around 5,000 Daltons.

Figure 3. Protein profiles of velvet antlers dried using different processing methods

The protein profiles of samples of velvet dried using different processing techniques were determined by GFC on a Superose 12 column (Pharmacia), and have been overlaid on the same vertical scale. The approximate molecular weight scale depicted by the labelled arrows was based on calibration of the column using a mixture of proteins of known molecular weights.

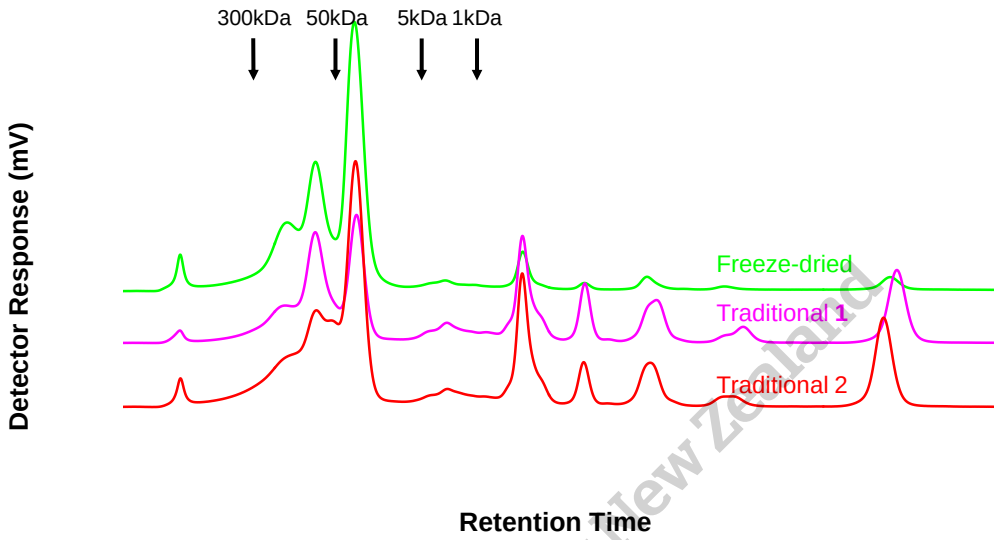
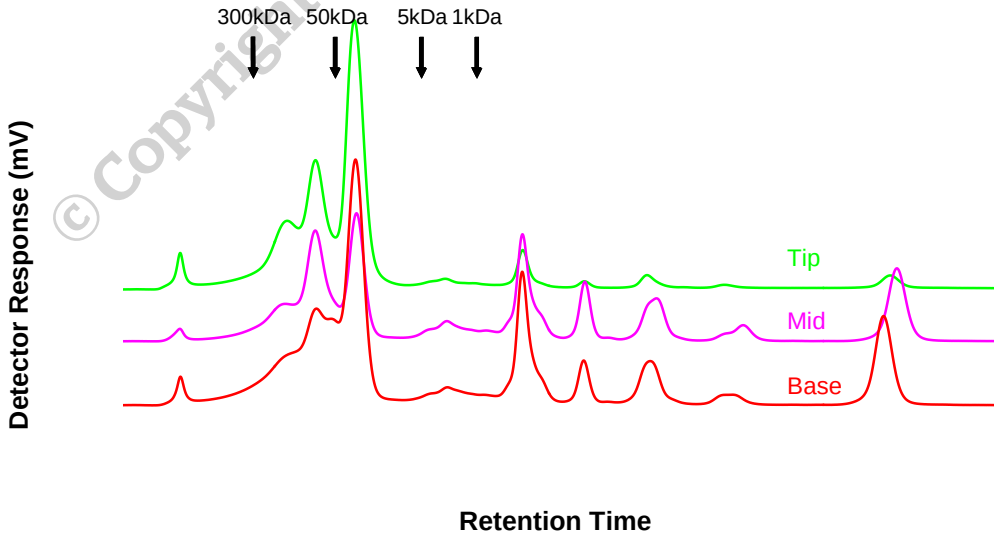


Figure 4. Protein profiles of different sections of a freeze dried velvet antler

The protein profiles of different sections of freeze dried velvet were determined by GFC on a Superose 12 column (Pharmacia), and have been overlaid on the same vertical scale. The approximate molecular weight scale depicted by the labelled arrows was based on calibration of the column using a mixture of proteins of known molecular weights.



Individual proteins/polypeptides

Deer velvet has been shown to contain a wide variety of growth factors and signalling molecules, as well as their receptors, as might be expected in such a rapidly growing and developing organ. These include insulin-like growth factor I (IGF-I) and IGF-II, transforming growth factor α (TGFα) and TGFβ, members of the fibroblast growth factor (FGF) family, bone morphogenic proteins (BMP-2, BMP-4 and BMP-14), parathyroid hormone-related peptide (PTHrP), vascular endothelial growth factor (VEGF), pleiotrophin, dermatopontin, pigment epithelium-derived factor (PEDF), cyclin-dependent kinase inhibitor 1C (CDKN1C), c-myc and c-fos, Indian hedgehog, nerve growth factor (NGF), and neurotrophin 3 (NT3) (Ko *et al.* 1986; Kong *et al.* 1987; Elliott *et al.* 1992; Elliott *et al.* 1993; Feng *et al.* 1995; Mundy *et al.* 1995; Elliott *et al.* 1996; De Alwis 1997; Feng *et al.* 1997; Garcia *et al.* 1997; Huo *et al.* 1997; Francis *et al.* 1998; El-Ashrey 1999; Faucheux *et al.* 2000; Lord *et al.* 2001; Mundy *et al.* 2001; Faucheux *et al.* 2002; Allen *et al.* 2004b; Barling *et al.* 2004a; Barling *et al.* 2004b; Barling *et al.* 2004c; Faucheux *et al.* 2004; Barling *et al.* 2005; Clark *et al.* 2006; Gu *et al.* 2007; Hao *et al.* 2007; Lai *et al.* 2007; Li *et al.* 2007a; Lord *et al.* 2007; Yan *et al.* 2007; Haines 2009). Most studies have focussed on the antler tip (*i.e.* the antler growth centre), but it was demonstrated by Gu *et al.* (2008b) that IGF-I is produced in all parts of the antler, with expression being highest at the tip and in the upper portion, and much reduced in the mid and base portions.

Mundy *et al.* (1995; 2001) purified and sequenced several novel bone growth factors isolated from deer velvet and from conditioned media of antler cells in culture. These polypeptides showed homology with other known growth factors (IGF-I, IGF-II and bFGF), as is discussed in the section on *Strong Bones* (page 51).

A number of biologically active polypeptides have been purified from velvet by Wang Ben Xiang's group in China, as is discussed in the sections on *Healthy Joint Function*, *Strong Bones*, and *Aiding Recovery After Tissue Injury* (pages 47, 51 and 57, respectively). However, published amino acid sequences could only be found for two of the polypeptides, so only those molecules are considered here. Both were 32-amino acid polypeptides, the first purified from red deer velvet (Weng *et al.* 2001a; Weng *et al.* 2002), while the other was isolated following the same procedure from sika deer velvet (Guan *et al.* 2006). Both polypeptides promoted the growth of multiple types of cells *in vitro*, and the *in vivo* skin wound healing activity of the total polypeptide fraction from red deer velvet was attributed mainly to the 32-amino acid polypeptide due to its strong stimulating effect on epidermal and fibroblast cells (Weng *et al.* 2001b). The two polypeptides were structurally very similar, with amino acid sequences that differed in only four positions, and both appear to be fragments of a serum protein, haemoglobin α-chain. This deduction is based on their almost complete homology with amino acids 2-33 of haemoglobin α-chain from Canadian wapiti[1], and with amino acids 1-32 of the homologous protein in reindeer[2]. Thus the sequence differences between the two isolated peptides probably reflect differences in the sequences of haemoglobin α-chain in the two deer species.

[1] *UniProtKB/TrEMBL Q4TU70 (Q4TU70_CEREL)*

[2] *UniProtKB/Swiss-Prot P21379 (HBA_RANTA)*

Global studies using proteomics or microarray analysis of gene expression

Recently proteomics (Park *et al.* 2004) and gene expression analysis techniques (Lord *et al.* 2004; Molnar *et al.* 2007; Gu *et al.* 2008b) have been employed to investigate the proteins in velvet on a global scale. These studies have revealed the identities of a large range of proteins present in velvet, many of which play important roles in the growth and development of the unique organ. Whether the identified proteins also have useful biological activities of interest to consumers of velvet remains to be established.

6.4 Collagen

Collagen is a major constituent of deer velvet, consistent with its nature as a cartilaginous tissue that rapidly develops into bone. Of the family of over 20 proteins that are related by the presence of repeating (Gly-X-Y)n sequences, four types of collagen (I, II, III and X) have been identified in velvet (Price *et al.* 1996; Rucklidge *et al.* 1997; Sunwoo *et al.* 2001). It is thought that consumption of the collagen in velvet provides tolerance to cartilage-derived antigens and relief of arthritis symptoms (refer to the *Healthy Joint Function* section on page 47).

Sunwoo *et al.* (1995) have shown that collagen concentrations are lowest in the antler tip and highest at the base in Canadian wapiti velvet (Table 2). Similar results were obtained for velvet from sika deer (Jeon *et al.* 2005).

Table 2. Collagen and glycosaminoglycans concentrations in Canadian wapiti velvet antler

All values are percentages on a dry matter basis (Sunwoo *et al.* 1995). Means in rows with different superscripts are significantly different (P<0.05). GAG = glycosaminoglycan.

Component	Antler Section			
	Tip	Upper	Middle	Base
Collagen	10.01±0.52[a]	14.35±1.38[b]	25.83±0.84[c]	31.99±1.26[d]
Uronic acid	1.24±0.17[a]	1.36±0.11[a]	0.16±0.02[b]	0.11±0.01[b]
Sulphated GAG	3.73±0.47[a]	4.67±0.27[b]	0.34±0.03[c]	0.26±0.03[c]
Sialic acid	0.61±0.01[a]	0.30±0.06[b]	0.25±0.03[b]	0.09±0.02[c]

6.5 Amino Acids

Amino acids are the building blocks of all proteins, and are important nutritive components of the diet. Owing to its very high protein content (~60%) deer velvet is rich in amino acids, including those that cannot be synthesised by humans and other mammals (*i.e.* 'essential' amino acids).

The contents of protein hydrolysate amino acids[3] in velvet from different deer species and/or different portions of the antler have been reported by multiple authors (Jung *et al.* 1992; Ahn 1994; Sunwoo *et al.* 1995; Chen *et al.* 1998a; Chen *et al.* 1998b; Shin *et al.* 1999; Sunwoo *et al.* 2001; Wang *et al.* 2003b; Lunitsin *et al.* 2004; Wang *et al.* 2004; Jeon *et al.* 2005). Glycine and proline are major amino acids found in velvet, reflecting its high collagen content. Velvet is also rich in glutamic acid, aspartic acid, alanine, arginine and leucine.

Free amino acid (FAA) concentrations were measured the portions of New Zealand red deer velvet that are shown in Figure 1 (Suttie *et al.* 1993b; Suttie *et al.* 1994). The FAA data are presented in Table 3. There were significant differences in concentrations between the sections for most of the FAA measured. Typically, concentrations were higher in the tip and upper sections (1-3) compared with lower sections. The tip itself had the highest concentrations, and this is consistent with its greater value in traditional medicine. A similar result was demonstrated in Siberian sika deer velvet by Jung *et al.* (1992), who also found differences in FAA levels between velvet of different countries.

[3] *Amino acids released from proteins by hydrolysis with strong acid.*

Table 3. Free amino acid (FAA) concentrations in sections of New Zealand red deer antlers

Values given are the means (n=4) in µmol/g (Suttie *et al.* 1993b). SED is the standard error of the difference between any two means in the same row. Statistical differences are shown as ns = not significant, * = P<0.05 and *** = P<0.001; ND = not detected. (Note: sections 1, 2, 4 and 8 are main beam sections; 3 and 7 are tines – see Figure 1).

Amino Acid	Antler Section							
	1	2	3	4	7	8	SED	Sig
α-Amino-n-butyric acid	0.08	0.11	0.06	0.03	0.02	0.02	0.03	*
α -Aminoadipic acid	0.33	0.27	0.29	0.12	0.07	0.03	0.03	***
Alanine/Histidine	22.45	13.65	16.37	6.89	5.34	2.34	0.79	***
Arginine	1.92	1.47	2.04	0.95	1.05	0.37	0.12	***
Asparagine	2.01	1.34	1.25	0.41	0.33	0.07	0.14	***
B-Aminoisobutyric acid	0.37	0.54	0.70	0.41	0.25	0.05	0.06	***
Carnosine	0.15	0.25	0.12	0.19	0.03	0.02	0.07	*
Citrulline	1.02	0.65	1.16	0.62	0.34	0.13	0.05	***
Cysteine	0.32	0.17	0.23	0.09	0.06	0.03	0.05	***
γ-Amino-n-butyric acid	0.15	0.09	0.12	0.06	0.11	0.07	0.01	***
Glutamic acid	25.52	12.68	10.73	3.46	2.13	1.14	1.16	***
Glycine	10.00	7.73	8.77	5.13	4.03	1.85	0.57	***
Hydroxylysine	0.25	0.25	0.26	0.16	0.16	0.04	0.07	ns
Hydroxyproline	0.98	1.54	1.10	0.51	0.39	0.46	0.19	***
Isoleucine	2.07	1.54	1.92	1.09	0.74	0.26	0.08	***
Leucine	4.62	8.12	7.95	5.99	3.98	1.06	0.78	***
Lysine	4.22	3.56	4.67	3.89	2.22	0.65	0.20	***
Methionine	1.03	1.53	1.26	1.13	0.76	0.19	0.19	***
1- Methylhistidine	0.29	0.23	0.17	0.13	0.03	ND	0.19	ns
3-Methylhistidine	1.45	0.92	1.11	0.56	0.27	0.21	0.11	***
Ornithine/Trptophan	1.60	1.00	1.15	1.05	0.32	0.18	0.12	***
Phosphoethanolamine	ND	0.03	0.05	0.02	ND	0.01	0.03	ns
Phenylalanine	1.42	2.68	2.79	1.95	1.27	0.37	0.25	***
Proline	3.56	3.27	4.39	2.59	1.90	0.85	0.18	***
Phosphoserine	0.11	0.66	0.70	0.35	0.23	0.09	0.13	***
Serine	4.96	2.89	3.35	1.70	1.46	0.51	0.21	***
Taurine	7.53	5.37	7.41	4.61	4.38	2.07	0.47	***
Threonine	4.37	3.02	3.21	1.76	1.29	0.55	0.18	***
Tyrosine	1.66	1.24	1.63	0.90	0.63	0.23	0.07	***
Valine	5.65	4.63	5.19	3.46	2.26	0.87	0.26	***
Essential	25.29	26.56	29.02	20.22	13.57	4.33	1.68	***
Total	111.4	83.42	92.10	51.34	37.32	15.32	4.32	***

6.6 Lipids

The lipid fraction of velvet antler is highly complex. Russian studies reviewed by Archer and Palfreyman (1983) indicate that free fatty acids, mono-, di- and triglycerides, neutral lipids, gangliosides, lecithin, cephalin, phospholipids, cholesterol, steroids and prostaglandins have been detected. These lipids have also been extracted and identified in velvet in multiple studies in other countries (Kim *et al.* 1977; Hattori *et al.* 1989; Ivankina *et al.* 1993; Yamasaki *et al.* 1994b; Chen *et al.* 1998b; Shin *et al.* 1999; Sunwoo *et al.* 2001; Wang *et al.* 2004; Xu *et al.* 2007; Zhou *et al.* 2008; Zhou *et al.* 2009a; Zhou *et al.* 2009b; Zhou *et al.* 2009c).

The fatty acid profile of velvet antler has been reported by a number of authors (Kim *et al.* 1976a; Ivankina *et al.* 1993; Sunwoo *et al.* 1995; Lee *et al.* 2007a) and is broadly similar to that found in a range of animal tissues.

Sphinomyelin is a sphingophospholipid found in animal cell membranes, especially in the membranous myelin sheath which surrounds some nerve cell axons, which is thought to have anti-cancer properties. Invermay studies have shown that concentrations of sphingomyelin are highest in the antler tip and upper sections compared with elsewhere in the antler (Table 4), and that the ratio of the two bands detected by thin layer chromatography differs between antler sections (Suttie *et al.* 1993b; Suttie *et al.* 1994). This is of interest because it means that sphingomyelin varies both qualitatively and quantitatively in velvet antler sections.

Table 4. Sphingomyelin (SM) concentrations in New Zealand red deer velvet

Values given are means (n=4) in mg/g. Antler sections as shown in Figure 1. SED is the standard error of the difference between any two means in the same row. *** = P<0.001. (Note: sections 1, 2, 4 and 8 are main beam sections; 3 and 7 are tines – see Figure 1).

	Antler Sections							
SM	**1**	**2**	**3**	**4**	**7**	**8**	**SED**	**Sig**
Band 1	1.57	1.05	0.92	0.87	0.32	0.15	0.082	***
Band 2	1.36	0.73	0.78	0.48	0.25	0.21	0.077	***
Total	2.92	1.78	1.70	1.35	0.57	0.36	0.150	***

Tsujibo *et al.* (1987) isolated lysophosphatidyl choline from velvet and suggested that it may be involved in causing any hypotensive activity of velvet antler. Min *et al.* (2001) have shown that at least four different lysophosphatidyl cholines, varying in fatty acid moiety, suppressed the morphogenic transition from yeast to hyphae in *Candida albicans* without affecting growth of the yeast, suggesting that this active ingredient has potential as a mycostat.

Wang (1996) reported that phospholipids of velvet origin could aid memory and learning in mice. He showed that phosphatidyl ethanolamine, sphingophospholipid, phosphatidyl choline, lysophosphatidyl choline and phosphatidyl inositol from velvet antler reduced monoamine

oxidase (MAO) activity in mice. This mechanism may partly explain any anti-ageing health benefit of velvet antler.

Gangliosides are complex carbohydrate-containing lipids found in cell membranes, most concentrated at the surface of brain cells, which are involved in cell signalling processes. In Korea, gangliosides are considered to be important biologically active components, particularly for assisting growth and brain development in children Velvet has been shown to contain gangliosides GD_{1a}, GD_{1b}, GM_1, GM_2, GM_3 and GM_4 (Yoo *et al.* 1993; Han *et al.* 1994; Shin *et al.* 1999), and Jhon *et al.* (1999) fully characterised the molecular structure of three GM_3 and two GD_3 variants isolated from velvet antler.

Suh *et al.* (1999; 2000) have shown that an ethanol fraction of velvet antler containing monoacetyldiglycerides enhanced *in vitro* phagocytosis in peritoneal macrophages. This could help explain at least any effect of velvet antler on immune function.

6.7 Glycosaminoglycans

Glcosylaminoglycans (GAGs) or mucopolysaccharides are polymeric carbohydrates comprised of repeating disaccharide units made up of a hexuronic acid or hexopyranose combined with a hexosamine (which may, or may not, be sulphated). GAGs form an important component of connective tissues, usually covalently linked to a protein in macromolecules called proteoglycans. A major GAG, chondroitin sulphate, has clinically been shown to be a useful treatment for arthritis.

Numerous studies have investigated GAGs in deer velvet (Frasier 1973; Frasier *et al.* 1975; Kim *et al.* 1975; Kim *et al.* 1976b; Zhao *et al.* 1992; Hill 1993; Sunwoo *et al.* 1997b; Sunwoo *et al.* 1998a; Sunwoo *et al.* 1998b; Sunwoo *et al.* 2001; Sunwoo *et al.* 2004; Ha *et al.* 2005; Cao *et al.* 2006; Lee *et al.* 2007a). The results have shown that chondroitin sulphate is the major GAG in velvet, with hyaluronic acid, dermatan sulfate, keratan sulfate, and heparan sulphate being found in lesser amounts. Chondroitin sulphate has even been found in fossilised antlers (Scott *et al.* 1981). Sunwoo *et al.* (1995) demonstrated that sulphated glycosaminoglycans are concentrated in the tip and upper portion of the antler (Table 2), and Lee *et al.* (2007a) reported that levels of GAGs were higher in antlers removed at an early stage of development (after 40 days of growth) than at a more normal removal time (after 60 days of growth).

6.8 Polyamines

Wang *et al.* (1990a; 1990b; 1996) provided evidence that several polyamines (spermine, spermidine and putrescine) are present in deer velvet and that these were RNA-polymerase stimulants.

6.9 Nucleic acid components

Velvet contains a variety of free nucleic acid components, including bases such as guanine, uracil, adenine, cytidine and hypoxanthine amongst others (Wang *et al.* 1988c; Hattori *et al.* 1989;

Yamasaki *et al.* 1994a; Hashimoto *et al.* 1997; Zhou *et al.* 2009b; Zhou *et al.* 2009c). Wang *et al.* (1988c; 1996) showed that hypoxanthine and uridine were the monoamine oxidase B inhibitors in velvet, and as a result partially responsible for the anti-ageing activity ascribed to velvet (see the *Ageing* section on page 83).

6.10 Vitamins

Velvet contains retinoic acid (Allen *et al.* 2002b), the active form of Vitamin A that regulates many cell activities, and antler cells were shown to produce 1,25-dihydroxyvitamin D (Sempere *et al.* 1989). Lee *et al.* (2007a) analysed Vitamin A (retinol) and Vitamin E (tocopherol) in velvet removed 40 and 60 days after casting of the previous antler. Vitamin A levels were the same at both stages of development whereas Vitamin E levels were higher in the 60 day antlers.

7 DOSAGE RATES

7.1 Overview

It is almost impossible to present a definitive comparison of the dose rates used for deer velvet around the world. This is because the use of velvet has evolved over 2,000 years and historical records may not specify doses. Furthermore, there are differences in the way deer velvet is obtained, processed and administered, and it is frequently given in combination with other remedies.

Recently, however, Suttie and Haines (2004) reviewed the available information in which dose of the velvet preparations used were clearly stated by the authors. The dosages were then 'normalised' by converting them to milligrams of deer velvet powder equivalent ('mg VPE'), to enable the doses of the various forms of the velvet products used to be compared. This was done making use of yield information, which was either given in the papers or was inferred for standard preparations such as Pantocrine. The authors recognised the pitfalls of this approach, as extracts may have concentrated particular ingredients (or removed others), leading to efficacies that would not be observed in a subject consuming deer velvet powder. Nevertheless this approach enabled, for the first time, an appraisal of dose that was presented in a form comparable to the typical usage of deer velvet as a Western Dietary Supplement.

7.2 Doses of Deer Velvet Recommended by Medical Practitioners

In Traditional Chinese Medicine (TCM), the recommended dose is 900–1,200 mg/day taken as a powder or 3,000–4,500 mg/day boiled in water, soup or Chinese wine (Bensky *et al.* 1986). In Korea, adults over 16 years are typically prescribed 8,000 mg/day, with other herbal ingredients, for periods of 15 days. Children under 16 receive half that dose. The dose can be increased or decreased to suit individual requirements, or if side effects such as indigestion are experienced (Peter Yoon personal communication).

Using data presented in Brechman (Undated, ~1971), Suttie and Haines (2004) calculated that Pantocrine contains about 111 mg VPE/ml. In Russia, Pantocrine is prescribed either as the liquid, or as tablets which contain either 0.5 or 1.0 ml of the liquid. Skulkova (quoted by Archer and Palfreyman 1983), indicated that the typical Pantocrine dose is 25–40 drops or 1–2 tablets twice daily about 30 minutes prior to a meal. Using the conversion factor given above, these correspond to doses of 250–440 mg VPE/day and 220–440 mg VPE/ day, respectively. Pantocrine can also be injected at a similar dose level. Reshetnikova (1954) reported that the dose was up to 660 mg VPE/day for periods of treatment up to one month.

There are no medical practitioner recommendations for deer velvet powder in Western countries. Most deer velvet capsule manufacturers recommend 1 to 4 capsules of dry powder each day. This is equivalent to 250–1,200 mg/day depending on the size of the capsule and the precise recommendation. The most commonly recommended dose is two capsules or about 500 mg/day, but there is no researched basis for this.

7.3 Research Support

Positive effects of velvet have been reported in animal trials (as is discussed in other sections of this document), but the data presented often does not allow the precise dose of velvet to be calculated. For several in which this was possible, Suttie and Haines (2004) found that very high doses were typically given in order to produce statistically significant results. These tended to be at least 125 mg VPE/kg/day, and ranged as high as 3,300 mg VPE/kg/day. For a human weighing say 75 kg, the equivalent doses would be huge, rendering the comparisons of questionable value.

Only a few reported human efficacy studies have been conducted with velvet. Mostly these have been performed in healthy subjects and have investigated effects on athletic or sexual performance, and cognitive function. The doses of velvet given and outcomes of these trials are presented in Table 5. From this, it is evident that doses of 2,000 mg VPE/day are likely to be required to effectively increase performance.

However, no published studies have examined the effectiveness of smaller doses taken for longer term periods, as typically recommended by dietary supplement manufacturers, so no conclusion can yet be drawn about this usage of velvet. Similarly, insufficient studies have been performed in which patients suffering from medical conditions to indicate whether velvet is an effective treatment in such situations.

Table 5. Summary of human efficacy trials using velvet at various dose levels

Data are from Suttie and Haines (2004), updated to include a study in male and female rowers (Syrotuik *et al.* 2005). The calculation of dose per kg bodyweight is based on a 75 kg person.

Dose		Number of trials	Effectiveness
mg VPE/day	mg VPE/kg/day		
< 1,000	13	3	No effect
1,000 – 1,500	13 – 20	3	Small effect, borderline statistically significant
> 2,000	27	3	Clear effect, statistically significant (where statistics are provided)

8 OVERVIEW OF HEALTH BENEFITS

8.1 Traditional Chinese Medicine

According to the principles of Traditional Chinese Medicine (TCM), velvet antler is an herb which tonifies the Yang. It is used for conditions of deficient Yang, particularly Kidney Yang. These deficiencies manifest themselves as systemic exhaustion, depression, cold, lower back pain and a weak pulse. They may also include impotence, spermatorrhea and low white cell counts in the blood. Chinese medical scholars believe that velvet antler functions to support:

- Regulation of the adrenal cortex and energy metabolism,
- Sexual function,
- Growth and resistance.

Overall, a role in returning abnormal physiological states to normal is emphasised. In other words, as discussed in Section 4 above, velvet is used in TCM for its restorative benefits.

8.2 Russia

Deer velvet supplements have been used in Russia for generations, but scientific studies on velvet's efficacy began in the 1920s and were led by Professor S M Pavlenko (Letchamo *et al.* 2004). Since then, extensive literature has accumulated on velvet antler composition and on its benefits both in small animals and humans. The Russian medical system has made heavy use of velvet products, as have the Russian space research program, the military, and national sports teams. The Russian literature that has been translated into English was written mainly in the 1960s and 1970s. This literature focuses on the health benefits and effectiveness of an alcohol extract of velvet called Pantocrine.

This leads to difficulty of interpretation and comparison of the data on its benefits for humans because of the form of the product. Since velvet antler contains many active substances and these vary in their solubility in water and alcohol, the way in which velvet antler is processed affects its composition and most likely its effectiveness. Effects of an alcohol extract of velvet like Pantocrine may differ from those of an aqueous extract or dried velvet powder.

8.3 Specific Health Benefits Reviewed in this Manual

In Western cultures, interest in velvet antler as a dietary supplement has grown steadily in recent years, and the sections below review the research that has been carried out to investigate its potential for this use. The scientific information has been selected on the basis of completeness of the data, its apparent reliability, and also the ease with which it can be compared to other studies. Whenever possible, reviewed data are from reputable scientific peer-reviewed journals.

The general health benefits that have been identified and are examined in subsequent sections of this manual are:

- Support for growth
- Supporting immune function

- Healthy joint function
- Bone health
- Blood health
- Athletic performance
- Aiding recovery after tissue injury
- Support for memory function
- Support for blood pressure and cardiovascular health
- Anti-ageing effects

9 SUPPORT FOR GROWTH

9.1 Health Benefits

In Asia, velvet antler is taken:

- ❖ to support growth of children, and
- ❖ as a weight-gaining tonic for elderly people, invalids and athletes.

In Korea, a great deal of velvet antler is given to children by Oriental Medical Doctors to support growth and development, as well as to enhance the immune system and support mental ability. Velvet antler has also been used to improve strength of athletes (see the *Athletic Performance* section on page 73). Recent research has confirmed that velvet antler has the potential to enhance the growth of young laboratory animals.

9.2 Suggested Physiological Rationale

Velvet antler, particularly if processed at a low temperature, is likely to contain high levels of mixed growth factors. Although it is currently unclear what happens to these relatively small peptide factors during the digestive process, one could speculate that they may be involved in any growth effect of velvet antler. Additionally, or alternatively, components of velvet antler may alter the expression of growth factors within tissues and exert effects by indirect mechanisms.

9.3 Research Support

Velvet antler powder and velvet antler extract have been shown to aid growth in a dose-dependent manner in growing mice (Mineshita 1938), chickens (Bae 1975; Bae 1976; Yartsev 1989) and rabbits (Gavrin 1976). A patented formulation, which contained velvet extract together with emulsifiers delivered in β-cyclodextrin, enhanced the growth rate of young rats while a 'standard velvet extract' did not show a similar effect (Hsu *et al.* 2003). An ethanol-insoluble fraction of a water extract of velvet prevented a proportion of the weight loss observed in rats with adenine-induced anaemia (Yokozawa *et al.* 1994). Sung *et al.* (2003) demonstrated that powdered velvet antler significantly increased the growth of adult rats (starting weight ~300 g), although it had no significant effect on the growth of young animals (starting weight ~187 g).

Other studies have also shown no effect of velvet supplementation on the growth of young rats (Ahn 1994; Zhang *et al.* 2000), while a study described in more detail below did show a positive effect of velvet extract (Suttie *et al.* 2001). These conflicting results highlight that the dose and nature of the velvet product consumed, along with the physiological status of the recipient, are likely to play a major role in any effects on growth caused by velvet.

In vitro studies have revealed that New Zealand velvet antler extracts enhanced the growth of antler cells in a dose-dependent manner (Suttie *et al.* 2001). Similarly, Sunwoo *et al.* (1997a) demonstrated that an aqueous extract of Canadian wapiti velvet antler promoted the proliferation of bovine fibroblast cells in culture. Randel (2002) reported a stimulating effect of commercially available velvet extract pills on Normal Human Dermal Fibroblasts (NHDF cells), and

he proposed that this bioassay be used as a quantitative measure of velvet antler cell growth-stimulatory potency. Wang Ben Xiang's group in China have shown that polypeptides from velvet antler stimulate proliferation of epidermal cells, fibroblasts and rabbit costal cartilage cells (Guo *et al.* 1998; Zhou *et al.* 1999; Weng *et al.* 2001a; Weng *et al.* 2001b; Zhou *et al.* 2001; Weng *et al.* 2002; Guan *et al.* 2006). Comparable fractions from Chinese sika deer and from red deer velvet antler were equally potent at stimulating the proliferation of rabbit costal cartilage cells, but the red deer preparation provided stronger stimulation of the proliferation of epidermal cell than the sika velvet extract (Zhou *et al.* 2001). This demonstrates that the efficacy of velvet from different species of deer may vary.

Some growth studies in more detail

Growth of chickens

The effects of an extract of velvet antler on the growth of chickens was studied by Bae (1975). Groups of chicks were fed 0 (control), 3.75, 7.5, 18.75 or 75 mg extract daily for 8 weeks.

The results are shown in Table 6. At the close of the 8-week study the chickens weighed 1.7–1.8 kg, so at that time the doses were equivalent to between about 2–40 mg/kg for the velvet-treated groups. All doses were effective, but the 18.75 mg dose (about 11 mg/kg) gave the greatest response and resulted in an increase in weight gain of about 6%.

Table 6. Body weight changes in chickens fed experimental diets containing different concentrations of velvet extract for 8 weeks

Data are from Bae (1975). Means with different superscipts differ significantly.

	Dose of velvet extract (mg)				
Measure (g)	**0 (Control)**	**3.75**	**7.5**	**18.75**	**75**
Initial Body Weight	41	41	41	41	41
Final Body Weight	1,725^{a}	1,768^{ab}	1,779^{bc}	1,821^{c}	1,773^{bc}
Feed Intake	3,968	4,000	4,084	4,162	4,062

Growth of young rats

Suttie and Haines (2001) carried out a study to determine whether or not feeding an aqueous extract of New Zealand velvet antler to young male Wistar rats would stimulate growth. A secondary objective was to investigate if heat inactivation of the extract would influence the extent of any growth stimulation. The rationale for this was that, although the active ingredients for growth were not known, it was speculated they might be heat-labile polypeptide growth factors, for example IGF-I. If heat inactivation blocked activity, then some informed speculation on likely active substances could be made.

Seventy male albino Wistar rats about 6 weeks old, each weighing about 105 g, were randomly allocated to one of seven treatment groups (see below). The animals were housed in group cages with four to six rats per cage. The rats were fed *ad lib.* a purified casein-based diet with either no

velvet antler extract or various concentrations of velvet antler extract added (see below). Deionised water was available for drinking at all times.

An aqueous velvet antler extract was prepared, and half of it was inactivated by raising its temperature to 120°C for 2 hours. The active or heat-inactivated velvet antler extracts were added daily for 6 weeks to the purified casein diets at one of three dose rates, *i.e.* 10, 30 or 100 mg/kg bodyweight ('Low', 'Medium' and 'High' dose rates respectively). A control group was fed the casein diet containing no added velvet antler extract.

The treatment groups were as follows:

- Control
- Low Inactive
- Medium Inactive
- High Inactive
- Low Active
- Medium Active
- High Active

The rats were each weighed at the start of the study and weekly thereafter. At the close of the study the rats were killed and body organs were weighed and the femur was dissected for total calcium analysis. During the final week of the study, each rat was individually confined for 24 hours in a metabolism cage for the collection of urine samples. These samples were used to measure calcium and hydroxyproline excretion.

The rats were healthy throughout the trial and no health problems were noted. All 70 rats completed the trial.

The mean body weights of each group of rats, expressed as percentages of the body weight of the control animals, are shown for each week of the study in Figure 5. The group fed the high concentrations of active velvet antler extract grew significantly more throughout the study than the control group or the group fed the heat-inactivated extracts. During the first 3 weeks they rapidly achieved a 12% body weight advantage over the control animals, and then maintained most of this advantage during the rest of the study. The group fed the medium concentration of active velvet extract also grew significantly more during the final 3 weeks of the study compared with the control group or those groups fed the heat-inactivated diets. The overall weight gain also differed significantly (Table 7) among the groups. The groups fed the heat-inactivated extracts did not grow faster than the control and no dose response was observed. In contrast those groups fed the medium and high doses of active velvet antler extract grew significantly more in a dose-dependent manner than the control group.

Liver weight was significantly greater in the groups fed the medium and high doses of active velvet antler extract, but there were no significant differences in testes weights (Table 7). The calcium content of the femur was significantly greater in the group fed the high dose of active extract.

Hydroxyproline concentrations in urine were lower in the groups fed the medium and high doses of active velvet antler extract and also in the group fed the high dose of inactive antler extract. In

contrast urinary calcium was significantly lower only in the group fed the high dose of active extract (Table 7).

Figure 5. Effect of velvet extract supplementation on the growth rate of young male rats

Young rats were fed high, medium or low doses of active or heat-inactivated velvet antler extract or no velvet antler extract (control).

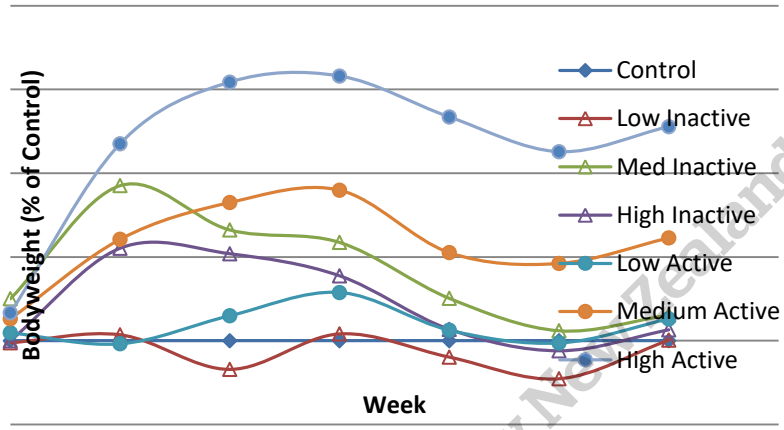


Table 7. Effect of velvet extract supplementation on weight gain, body organs, femur calcium, and urinary excretion of calcium and hydroxyproline of young male rats

	Treatment							
Measure	**Control**	**Inactive Low**	**Inactive Medium**	**Inactive High**	**Low**	**Medium**	**High**	**SED**
Weight gain[1]	221	221	223	223	224	236	253	11
Liver weight[1]	13.7	14.3	13.2	13.9	13.5	15.2	17.1	1.0
Testes weight[1]	3.12	3.21	3.11	3.13	3.07	3.13	3.25	0.13
Femur calcium[2]	129	129	132	132	131	130	144	4
Hydroxyproline[3]	5.1	4.4	5.2	3.4	5.6	3.7	3.9	0.5
Urinary calcium[3]	2.0	2.4	2.8	3.2	2.9	3.0	1.6	0.4

[1] g; [2] mg; [3] µmol/L

Feeding active velvet antler extract to male rats resulted in dose-dependent increases in weight gain. Heat-inactivation abolished the positive effect of the extract on weight gain. It can therefore be concluded that the growth response was due to the presence of heat-labile substances, possibly growth factors, present in the velvet extract.

In Bae's study in chickens (described above), all doses were effective but the 18.75 mg dose (about 11 mg/kg) gave the highest response, and resulted in an increase in weight gain of about 6%. In the present rat study, a dose of 30 mg/kg (medium active treatment) gave a 7% increase in weight gain. Thus, although a comparison between studies is not perfect because of the different species and velvet extracts used, the results of the present study in young rats are in broad agreement with Bae's findings. The results are at odds, however, with those of Sung *et al.* (2003). In their study the growth of young rats was not increased by supplementation with the 'recommended dose' of velvet powder, although that of adult rats was significantly enhanced. This may be due to a difference in dose rates between the two studies or it may be that the growth-enhancing factors were concentrated in the water-based extract used in this study as compared to the velvet powder used by Sung *et al*.

In the present study, liver weight but not testes weight was significantly increased by treatment with active velvet antler extract. In contrast, Bae (1976) found that testes weight of chickens but not liver weight was increased. This may reflect a difference between rats and chickens or a difference between the compositions of the two velvet extracts. In the present study the liver effect is consistent with an overall anabolic effect.

Taken together, the urinary calcium excretion and femur calcium data suggest that the high dose of active velvet antler extract increased calcium deposition and decreased urinary excretion. In data not shown, the mineral density of the bone was not altered by velvet antler extract treatment, so the most likely interpretation of the urinary calcium and femur calcium data is that it reflects an overall anabolic effect rather than a specific effect on bone.

The urinary hydroxyproline data show that the high dose of inactive velvet antler extract as well as the medium and high doses of active extract reduced excretion. A decrease in hydroxyproline excretion can reflect an increase in bone matrix synthesis. This is suggestive of one or more heat-stable factors in velvet antler having some influence on bone metabolism. Potentially these may include small heat-stable peptides or even polar steroids.

In conclusion, an extract of New Zealand velvet antler increased growth when fed to laboratory animals. This supports New Zealand velvet antler having the potential to benefit growth.

Growth of immunised rats

The effect of supplementation with Gycosant™, a patented velvet antler preparation (Sim 2000), was investigated in young rats that underwent an immune challenge (vaccination) (Sunwoo *et al.* 2000; Sim *et al.* 2001; Sim *et al.* 2002). Twenty four weanling Wistar rats were fed *ad lib.* a semi-synthetic diet containing 0% (control), 0.5%, 1% or 3% Glycosant™ powder for 54 days (6 rats per group). Partway through this period, at weeks 5 and 6, each rat was immunised by intra-peritoneal injections of ovalbumin emulsified with an equal volume of Freund's incomplete adjuvant.

Prior to the immunisations, feeding antler powder diets did not significantly affect growth rate (Figure 6) or feed intake. However, final body weights were significantly greater in the groups fed antler powder than the control animals (Table 8), which showed a greatly reduced growth rate following the immunogenic stress (Figure 6).

These data suggested that there are factor(s) in the antler powder that enhance the growth performance of recently immunised rats. Additional effects, on their immune systems, blood, and cholesterol metabolism, are discussed in subsequent sections.

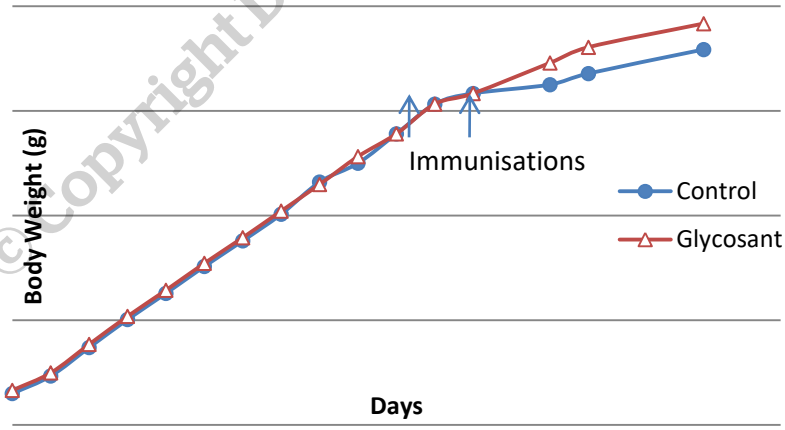
Table 8. Initial and final body weights of immunised rats fed Glycosant™

Initial and final body weights of young rats fed for 8 weeks with Glycosant™ (0.5%, 1% or 3% of diet) or without Glycosant™ (Control), and immunised with ovalbumin on days 35 and 42. Data are means ± SEM (Sim *et al.* 2001).

	Treatment			
Measure	**Control**	**Gycosant™ 0.5%**	**1%**	**3%**
Initial body weight (g)	80.6 ± 3.7	81.2 ± 3.6	81.1 ± 2.7	80.6 ± 2.1
Final body weight (g)	402.9 ± 6.1	433.7 ± 8.3	436.5 ± 6.7	434.1 ± 8.1

Figure 6 Growth rate of immunised rats fed Glycosant™

The growth rates of young rats fed for 8 weeks with Glycosant™ (3% of diet) or without Glycosant™ (Control), and immunised with ovalbumin on days 35 and 42. Groups of rats fed 0.5% or 1% Glycosant™ showed almost identical growth curves as the 3% Glycosant™ group, and are omitted from the graph. Reproduced in part from Sim *et al.* (2001).



10 IMMUNE FUNCTION

10.1 Health Benefits

Velvet antler is often used as a tonic by Koreans at the beginning of and during winter. In Traditional Chinese Medicine (TCM), velvet antler is frequently prescribed as a tonic in situations of stress and fatigue. The TCM Materia Medica indicates that velvet antler administration increases the number of red and white cells. Recent research has some apparently immuno-supportive effects demonstrated in laboratory animals, but the practical implications of these results for humans are not yet known.

10.2 Suggested Immunological Rationale

It may be that velvet antler supports the humoral immune system through its white blood cells and macrophages. A variety of molecules in velvet (lipids, polypeptides, proteoglycans) that span a broad molecular weight range have been identified as having immunomodulatory activity, and it is likely that multiple mechanisms are involved. The precise nature of these, and their interplay, has not been established though.

10.3 Research Support

A study was conducted in Korea by Shin *et al.* (2001), in which the immunostimulating activity of antler extracts were evaluated by the carbon clearance test method established by Wagner *et al.* (1985). ICR mice weighing 25-30 g were dosed orally for 4 consecutive days with velvet antler extracts dissolved in phosphate-buffered saline (PBS) solution. Forty eight hours after the dose, each mouse was intravenously injected with carbon suspension at a dose of 10 µl/g bodyweight. Blood was withdrawn from the orbital vein, and the carbon concentration in the blood was estimated by use of a spectrophotometer. From the optical density at 660 nm, the linear regression coefficient (RC) was calculated by plotting -logE against time. The immunostimulating activity was expressed as the ratio of the regression coefficient of the treated animals (RCtr) to that of the control group (RCc). Zymosan given by intra-peritoneal injection (50 mg/kg of bodyweight) was used as a positive control substance.

As shown in Table 9, the ethanol extracts of antler exhibited a significant enhancement of carbon clearance activity in a dose-responsive manner. The regression coefficient ratio of the group treated with 5 mg/kg/day was 1.18, which represents moderate immunostimulating activity. The regression coefficient ratio of the group treated with 10 mg/kg/day, however, was 1.58, which represents very strong activity. This activity was almost equipotent to Zymosan, a known phagocytosis enhancer. The water extract of antler showed a moderate amount of enhancement of carbon clearance when given as an oral dose of 10 mg/kg each day

The results of the above study backed up those of an earlier experiment by the same group (Shin *et al.* 1989), which showed a weak immunopotentiating effect of velvet powder in the carbon clearance test when orally administered at a dose 500 mg/kg to mice.

Table 9. Effect of ethanol and water extracts of velvet on carbon clearance in mice

Regression coefficients are means ± SEM of five mice (Shin *et al.* 1989). RCtr/RCc (the ratio of RC for treated mice to that of control animals) provides an assessment of immunostimulating potency: values less than 1.0 = not active; 1-1.5 = active; over 1.5 = very active.

Treatment	Dose	Regression Coefficient [a]	RCtr / RCc
Experiment 1 (Ethanol Extract)			
Control		0.0216 ± 0.0017	–
Antler	5 mg/kg/day, p.o.	0.0256 ± 0.0023	1.18
	10 mg/kg/day, p.o.	0.0342 ± 0.0028	1.58
Zymosan	50 mg/kg, i.p.	0.0350 ± 0.030	1.62
Experiment 2 (Water extract)			
Control		0.0208 ± 0.0013	–
Antler	10 mg/kg/day, p.o.	0.0256 ± 0.0010	1.23
Zymosan	50 mg/kg, i.p.	0.0304 ± 0.0016	1.46

Also in Korea, Suh *et al.* (1999; 2000) isolated and characterised monoacetyldigycerides from chloroform fractions of antlers from sika deer. They synthesised one of the monoacetyldiglycerides, *rac*-MADG, and two of its enantiomers (D-MADG and L-MADG), and investigated the effects of these on phagocytosis by mouse peritoneal macrophages. Compared with control macrophages, macrophages treated with *rac*-MADG and in particular with L-MADG showed enhanced phagocytosis. The results suggested that L-MADG enhances the phagocytosis of peritoneal macrophages *via* the secretion of interferon-α.

Japanese scientists reported that a high molecular weight fraction of a hot-water extract of velvet antler had anti-complementary activity (Zhao *et al.* 1992), and thus had effects on the innate immune system. Chondroitin sulphate moieties were shown to be important for the activity of the complement-activating proteoglycans.

In China, Wang (1996) reported that intra-peritoneal injections of Pantocrine (0.5-2 mg/kg) stimulated the phagocytic function of macrophages in both normal and immune-deficient mice. Similarly, Li *et al.* (2004) showed that alcohol velvet extracts of either Chinese wapiti or New Zealand red deer velvet were active stimulators of macrophage phagocytosis, when given to mice by oral administration.

Pan *et al.* (2007) isolated polypeptides from velvet and administered these to mice by daily intra-peritoneal injections (400 mg/kg) for 20 days. The velvet polypeptides promoted the proliferation of T and B lymphocytes, and also enhanced the secretion of IL-12 (a T cell stimulating factor) by activated peritoneal macrophages isolated from the mice. The isolated velvet polypeptides were thus concluded to possess immunopotentiation activity.

Kim *et al.* (1995) conducted a number of experiments to investigate the effects of velvet extract on the following indices of immune function: lymphocyte production and maturation (blastogenesis) in spleen, thymus, lymph node, and bone marrow cells of Balb/C mice, the haemagglutination reaction against sheep red blood cell (SRBC), the plaque forming cell (PFC) assay against SRBC, and on IL-2 production. Velvet extract demonstrated a potent mitogenic activity on spleen and lymph node cells, but had only mild activity on the thymus and born marrow cells. The active mitogenic component of the velvet extract was shown by use of ultrafiltration to consist of materials with molecular weights over 5,000 Dalton. Velvet extract was shown to significantly increase the mitogenic effect on the lipopolysaccharide (LPS)-stimulated spleen cells, but decrease the mitogenic effect on the concanavalin A (Con A) stimulated spleen cells at concentration of 0.3%, 1% and 3%. Velvet extract did not show a positive haemagglutination reaction and was found to inhibit the Con A-induced haemagglutination reaction against SRBC. It significantly increased the number of PFC at concentrations of 0.1% and 1%. When IL-2 or IL-4 production was determined after the proliferation of CTLL-2 cells, velvet extract was not shown to stimulate the production of IL-2. From these results, it was concluded that velvet was capable of increasing antibody production by B cells, but not IL-2 production by helper T cells.

This conclusion is not supported, however, by the results of Sim and Sunwoo (2001) in an experiment in which rats were immunised against ovalbumin (see page 41 for details of the protocol). Titres of specific anti-ovalbumin antibodies were lower in velvet-treated animals, as were total levels of immunoglobulins at the highest dose of velvet. More research is thus required on the effect of velvet on the humoral immune system.

Other Korean researchers (Kim *et al.* 2004c) used bioassay-guided fractionation after silica gel column chromatography to identify an immunomodulator in velvet. Structural analysis was performed with one- and two-dimensional nuclear magnetic resonance techniques and tandem mass spectrometry coupled with fast atom bombardment. The phosphatidylcholines sub-fraction, isolated from a 70% ethanol extract of velvet, induced the proliferation of spleen cells in synergy with Con A. According to the structural analysis, the phosphatidylcholines were classified as a family (1,2-alkyl-sn-glycerol-3-phosphocholines) containing arachidonyl (C20:4), stearoyl (C18:0), oleoyl (C18:1), linoleoyl (C18:2), palmitoyl (C16:0), and myristoyl (C14:0) chains in their fatty acyl chains. Because the unsaturated fatty acids showed an inhibitory effect on the immune system, dialkyl phosphatidylcholines with different chain lengths from C10:0 to C20:0 that stimulate the proliferation of spleen cells were examined extensively. Among other saturated phosphatidylcholines used, dimyristoyl phosphatidylcholine (C14:0) induced the proliferation of spleen cells more efficiently, whereas dimyristoleoyl phosphatidylcholine (C14:1) effected little change in the proliferation of spleen cells. Collectively the results suggested that phosphatidylcholines with saturated fatty acyl chains are immunostimulating factors and that they may modify the proliferation activity of known mitogens. Further, the chain length and saturation of the fatty acids may play important roles in the proliferation of spleen cells.

11 HEALTHY JOINT FUNCTION

11.1 Health Benefits

Velvet antler has been and still is widely used to assist healthy joint function in China. Lately, arthritis sufferers in Western countries have also begun to take velvet to alleviate their symptoms. Recent *in vitro* and *in vivo* studies support this use, and have suggested that velvet antler may indeed be beneficial to joint function.

11.2 Suggested Physiological Rationale

The precise mechanism of any effect of velvet antler on joint function is not known, although immunoregulatory and anti-inflammatory activities and an apparent ability to inhibit connective tissue degradation may play important roles. Deer velvet contains chondroitin sulphate, which has been shown to be clinically effective for treatment of arthritis. However, the effective doses of velvet administered in studies described below did not deliver enough chondroitin for it to solely, or even primarily, be responsible for the observed responses.

11.3 Research Support

Yudin and Dobryakov (1974) concluded that Pantocrine showed marked anti-inflammatory activity.

Wang (1996) reported that intra-peritoneal injection of velvet antler polysaccharides (100 mg/kg) inhibited the swelling induced in the forepaws of mice by dextran and egg white injection. In contrast, oral administration had no effect, which suggests the active polysaccharides did not survive the digestion process.

Intravenous administration of 10–50 mg/kg of a heat stable 68-amino acid polypeptide purified from velvet antler also showed a pronounced anti-inflammatory effect in rats (Zhang *et al.* 1992; Zhang *et al.* 1994). This occurred in adrenalectomised rats as well as in normal rats, although the reduction in swelling caused by dextran and cotton pellet granulomas was not as marked in the adrenalectomised animals (Table 10). In these rats, though, the effect of the antler polypeptide was similar to that of the steroid positive control, dexamethazone. The authors inferred from these results that the anti-inflammatory effects of the polypeptide are not completely dependent upon the pituitary-adrenal system.

There is a report that velvet powder had a pronounced analgesic effect when given orally to rats (Shin *et al.* 1989). A contribution to pain relief by velvet would obviously be of benefit to arthritis sufferers. However the doses administered to the rats were very high (500 mg/kg or more), so the relevance of the observation to standard use in humans is impossible to judge.

Table 10. Effect of a polypeptide (PAP) isolated from velvet antler on hind paw swelling of normal and adrenalectomised rats

Treatments were administered by intravenous injection. Data presented are the means of groups of six animals ± standard deviation (Zhang *et al.* 1994). *P<0.05, **P<0.01, ***P<0.001 *vs* control.

Group	Dose (mg/kg)	Swelling of hind paw	
Normal rats			
Control	0	22.5 ± 2.1	
PAP	5	18.4 ± 3.3	***
	10	12.3 ± 4.1	***
	20	8.2 ± 3.2	***
Adrenalectomised rats			
Control	0	20.7 ± 2.4	
Dexamethazone	1	16.0 ± 3.1	**
PAP	10	17.2 ± 3.6	*
	20	14.5 ± 4.1	**

Rheumatoid arthritis

In Korea, hot water extract of deer velvet is a widely used treatment for some immune-related diseases such as rheumatoid arthritis. Studies in immunisation-induced animal models of rheumatoid arthritis have shown that velvet extract was able to inhibit the development of the disease, when given by intra-peritoneal injection (Kim *et al.* 2003; Kang *et al.* 2006; Suh *et al.* 2007; Kim *et al.* 2008a; Kim *et al.* 2008b) or bilateral Shinsu (B23) acupuncture (Kim *et al.* 2004d; Kim *et al.* 2005). Velvet treatment had significant effects on a range of factors associated with the onset of arthritis in the animals, including suppression of the excessive rises in inflammatory mediators (Kim *et al.* 2003; Kang *et al.* 2006; Suh *et al.* 2007), inhibition of abnormally high activities of synovial fluid proteases (Suh *et al.* 2007; Kim *et al.* 2008a), prevention of oxidative damage to synovial fluid proteins by reactive oxygen free radical species (ROS) (Kim *et al.* 2008a), and inhibition of leukocytosis (Kim *et al.* 2008b). In rodents with collagen-induced arthritis it inhibited the formation of anti-collagen antibodies (Kim *et al.* 2003; Kang *et al.* 2006; Suh *et al.* 2007), and in adjuvant-induced arthritic rats velvet extract alleviated reductions in bone minerals, strength and trabecular bone formation and the increase in osteoclast number (Kim *et al.* 2005).

A registered medicine (Cervusen®) containing deer velvet (70% by weight) in combination with deer sinews (10%) and Korean ginseng (20%) also provided protection against arthritis when administered orally to rats in a modified adjuvant-induced arthritis model (Ghosh *et al.* 2001). Measures of acute inflammatory activity were decreased in rats treated with 2 or 5 mg/kg Cervusen®, and the destruction of cartilage and bone in knee joints of these animals was also substantially reduced.

The use of deer velvet powder to alleviate symptoms of rheumatoid arthritis has also been investigated in two human clinical studies. The first was an initial phase II trial (Allen *et al.* 2002a;

Allen *et al.* 2004a) that was intended to assess the safety of velvet taken together with standard rheumatoid arthritis medications, and to provide data that could be used to estimate required sample size for a subsequent larger trial. Forty patients with stage II rheumatoid arthritis were randomly assigned to groups of 10 patients each. One group received placebo and the other three groups received 2, 4, or 6 capsules (each containing 215 mg) of velvet powder daily for one month. In addition, all subjects continued to take their conventional arthritis medications (*e.g.* non-steroidal anti-inflammatory drugs, disease-modulating arthritis drugs, and analgesics). At the end of the study, there were no significant differences between groups in number of adverse events or health status. However, the greatest improvement was in the group receiving 6 capsules of velvet, and the least was in the placebo group. It was concluded that elk velvet antler could be taken safely in conjunction with a number of rheumatoid arthritis medications and warranted further study to assess efficacy.

In a follow-up triple-blind placebo-controlled study (Allen *et al.* 2008), 168 patients with stage 2 to 3 rheumatoid arthritis and suffering residual symptoms after standard treatment were randomly assigned to receive either velvet (1000 mg) or a placebo, daily for 6 months. Measures included patient assessment of pain, tender and swollen joint counts, patient and physician assessments of disease activity, patient questionnaires of functional ability and quality of life, and blood tests for C-reactive protein (a marker of acute inflammation). No significant differences between groups were found for any of these parameters in the study, and the pattern of change of the measures across time points was essentially the same for both groups. This resulted in the overall conclusion that velvet antler does not effectively manage residual symptoms in patients with rheumatoid arthritis. However, the authors did note that, because of ethical considerations arising from the severity of the disease in the patients, they were unable to compare velvet to standard medications; all patients needed to continue receiving standard treatments in addition to the experimental treatment. This meant that only small changes due to velvet treatment might be expected. Furthermore, the study was somewhat underpowered to demonstrate statistically significant results, as the investigators only managed to recruit 168 patients instead of the target 220 that were estimated to be needed from the analysis of the results of their initial trial. Of interest, some individuals in the velvet group reported that they felt markedly better following treatment, whereas none in the placebo group described a similar improvement. These factors led the study authors to suggest that deer velvet may have a positive effect in some individuals with rheumatoid arthritis.

Osteoarthritis

A double-blind, placebo-controlled human study was conducted to determine if the velvet containing product Cervusen® was effective in ameliorating clinical symptoms in osteoarthritis (OA) sufferers (Edelman *et al.* 2000; Edelman *et al.* 2002). Following baseline examination, 54 patients were randomly assigned to receive either Cervusen® (2 x 350mg capsules/day) or placebo (2 x 350 lactose capsules/day) for 6 months. Clinical assessments were conducted at 1 and 3 months post-baseline, and at the end of the study. No adverse side-effects were reported for the duration of the study. Cervusen-treated patients showed improvements relative to baseline in self assessments of pain, and in both self and physician assessments of global

improvement, which were all significant at 3 and 6 months No significant improvement from baseline was observed for the placebo-treated group for any of the parameters examined. The authors suggested that the lead time required to reach clinical efficacy, along with their pre-clinical data, were suggestive that Cervusen® provided symptomatic relief in osteoarthritis by disease modification achieved through oral tolerisation to cartilage derived antigens.

Moreau *et al.* (2004) have provided evidence that velvet may also be effective for treatment of OA in dogs. Canadian elk velvet antler powder was evaluated on client-owned dogs with OA in a double-blind, and placebo-controlled study. Thirteen dogs received a placebo for 30 days and then velvet for 60 days. Twenty-five other dogs received velvet for 60 days. Gait analysis measured with a force plate, clinical signs assessed by an orthopaedic surgeon, performances in daily life activities and vitality assessed by the owners, and complete blood analyses were obtained at days 0, after 30 days of placebo and/or 60 days of velvet treatment. On placebo, the 13 dogs did not show significant improvement; however, their gait, their performances in daily life activities, and their vitality were significantly improved on velvet supplementation, based on changes in values exceeding those observed when placebo was administered. The 25 dogs on velvet for 60 days showed similar improvements. No clinical changes were revealed by blood analyses. Administration of velvet powder was considered to be effective in alleviating the condition in arthritic dogs. Based on this study, Sanderson et al. (2009) concluded in a recent review of treatments for the management of canine OA that there is a "moderate level of comfort" for the efficacy of velvet in modifying the structures involved in the disease, but cautioned that further high quality studies need to be conducted.

12 STRONG BONES

12.1 Health Benefits

Osteoporosis is a metabolic disorder characterised by loss of bone density and associated increased risk of fracture. It is a significant public health problem, affecting 10 million women in the US alone with a further 34 million at risk of developing the disease. A range of drugs are available for treatment, but most have quite serious side effects. In China and Korea, deer velvet has long been highly valued for its bone strengthening effect. Given this background, and the low toxicity of the product in its various forms, it is no wonder that Western consumers are also beginning to consider the use of velvet for treatment of osteoporosis and other bone-related problems.

12.2 Suggested Physiological Rationale

Healthy and strong bones require a carefully regulated balance between bone resorption and bone formation. These processes are primarily facilitated by two cell types, osteoclasts and osteoblasts, respectively. Chondrocytes are also important bone-related cells, which produce cartilage. Deer velvet might be expected to have an effect on osteoporosis, and bone in general, by directly or indirectly affecting the proliferation or maturation of any or all of these cell types. Strong evidence is being accumulated that shows deer velvet does indeed exert such influences on all three cell types.

12.3 Research Support

In vitro studies

Multiple studies have demonstrated that deer velvet contains factors that have direct effects on bone-related cells *in vitro*.

Total polypeptides isolated from Chinese sika deer (*Cervus nippon* Temminck) velvet by Wang Ben Xiang and co-workers were found to promote the proliferation of chondrocytes derived from rabbit ribs and embryonic human joints, as well as osteoblast precursor cells of embryonic chick calvaria (Guo *et al.* 1998; Zhou *et al.* 1999). A polypeptide consisting of 59 amino acids and having a molecular weight of 7,262 Dalton was purified from the mixture and was found to strongly stimulate the proliferation of all three cell types. In addition, a smaller polypeptide (molecular weight ~3,600 Dalton, as determined by SDS-polyacrylamide gel electrophoresis) was isolated that had weaker stimulatory activity with the two types of chondrocytes, and which did not affect the proliferation of the osteoblast precursor cells (Zhou *et al.* 1999). Comparable polypeptide fractions isolated from sika deer velvet and from red deer velvet were equally effective at stimulating the proliferation of rabbit costal chondrocytes, although there were differences in their compositions and their activities with epidermal cells (Zhou *et al.* 2001).

Chen *et al.* (2008) demonstrated that addition of velvet polypeptides to cultured rat chondrocytes affected the expression of proteins that control the cell life cycle, and resulted in postponing of senescence of the chondrocytes.

Other Chinese researchers separated a water-based velvet extract into five fractions based on their molecular weights, using gel filtration chromatography (Chen *et al.* 2004). The two fractions that contained the largest proteins were found to promote the proliferation of a rat osteoblast-like cell line (UMR 106), while the other three lower molecular weight fractions were inhibitory. After further purification the most active of the growth promoting fractions was identified as containing deer serum albumin (Lin *et al.* 2005). In addition to stimulating the proliferation of UMR 106 cells, the deer serum albumin isolated from velvet was shown to increase the secretion of IGF-I by the cells by about 50%. These activities were affected by the processing of the deer velvet, with greater activity displayed by extract from freeze-dried velvet than from velvet that was exposed to heat during traditional processing (Ke *et al.* 2008).

Kim *et al.* (2006) conducted an experiment to determine whether traditional Korean velvet water extract may have effects on bone remodelling by inducing the differentiation of resting zone chondrocytes (RC). Confluent chondrocyte cell cultures were pre-treated with velvet extract and then the media were replaced with new media containing 10^{-10}–10^{-8}M 1,25-$(OH)_2D_3$ (a vitamin D3 metabolite) and the cells incubated for an additional 24 hours. This second treatment was chosen because prior studies had shown that only the more mature growth zone chondrocytes (GC) respond to the vitamin D3 metabolite. Following pre-treatment for 120 hours with velvet extract, treatment of RC with 1,25-$(OH)_2D_3$ caused a dose-dependent increase in alkaline phosphatase-specific activity and collagen synthesis, but did not affect proteoglycan production. These increases were not observed in RC that were not pre-treated, or were instead pre-treated with 1,25-$(OH)_2D_3$. The results demonstrated that velvet extract was able to directly regulate the maturation of RC chondrocytes into GC chondrocytes, and may therefore play a role in regulating chondrocyte maturation during bone formation.

In order to investigate the putative anti-bone resorptive activity of deer velvet, Li *et al.* (2007b) investigated the effect of a chloroform (*i.e.* lipid) extract of velvet on osteoclast differentiation in mouse bone marrow cultures. The chloroform extract inhibited osteoclast differentiation in mouse bone marrow cultures stimulated by receptor activator of NF-κB ligand (RANKL) and macrophage-colony stimulating factor (M-CSF). The activation of a number of signalling pathways important in osteoclast differentiation was inhibited by the extract. It also inhibited the bone resorptive activity of differentiated osteoclasts that was accompanied by disruption of actin rings and induction of cell apoptosis. These results support the notion that deer velvet extract may be a useful remedy for the treatment of diseases such as osteoporosis by influencing bone-resorption processes.

Mundy and co-workers (1995; 2001) purified a number of novel bone growth factors from deer velvet and from conditioned media of antler cells in culture, based on their abilities to stimulate the proliferation of either MG-63, MC3T3 and/or C433 cells. MG-63 is a human osteosarcoma cell line, while MC3T3 cells are mouse osteoblasts and C433 is a stromal cell line derived from a human giant cell tumour of bone. One of the isolated peptides ("OT-2") had about 70% homology with IGF-I, while another ("OT-4") was similar to IGF-II. A further peptide ("OT-5") was a novel form of basic fibroblast growth factor (bFGF), which did not bind to antibodies to bFGF on affinity columns and showed some differences to bFGF in cell proliferation assays. The results established

that deer velvet contains a number of novel peptides in addition to known growth factors, which are able to stimulate the proliferation of bone-related cells.

In vivo studies

Wang Ben Xiang's group showed that as well as stimulating the *in vitro* proliferation of chondrocytes and osteoblast precursor cells (see above), the mixture of velvet polypeptides isolated from sika deer velvet hastened the repair of experimental bone fracture repair in rats when injected at the site of injury (Zhou *et al.* 1999). After seven weeks of treatment a significantly higher proportion of fractures had healed in rats injected with 20 mg/kg velvet antler polypeptides as compared to control rats (75% *vs* 25%, respectively). The strengths of the repairs were also enhanced by treatment, as assessed by removing the previously fractured long bones and determining the maximum weights they could support before breaking again. The untreated bones broke again with a loading of 802 g, but the bones of the rats injected with 20 mg/kg velvet antler polypeptides did not break until the load reached 1548 g. The hydroxyproline and calcium contents in the callus were also significantly higher in the velvet treated rats than in control animals, showing that the velvet polypeptides had enhanced collagen accumulation and calcium deposition at the fracture sites.

Mundy *et al.* (1995) injected proteinaceous material extracted from deer velvet above the calvaria of 5 week old mice once a day for 3 days. Four days later a substantial amount of new woven bone was observed on the outer surface of the calvarial bone, and this attained the appearance of lameliar bone over the following 1 to 2 weeks. The velvet extracts so tested were deduced to have therapeutic potential for the enhancement of bone growth and fracture repair in animals and in humans.

In rats with adjuvant-induced arthritis, velvet extract administered by traditional Korean acupuncture alleviated reductions in bone minerals, strength and trabecular bone formation and the increase in osteoclast number associated with the disorder (Kim *et al.* 2005).

Another study by Korean researchers (Lee *et al.* 2005; Jang *et al.* 2006) examined the efficacy of deer antler extract (DA), medicinal herbs extract (MH), and their mixture (DAMH), on bone growth and serum IGF-I *in vivo* in growing rats. Three-week-old female rats (Sprague-Dawley) were divided into four groups and then fed standard (control) diet or experimental diets containing DA, MH, or the DAMH mixture, for 7 weeks. After that time, the wet weights, breaking forces and bone minerals (Ca, Mg and Zn) of the rats' fibia and tibia were found to be significantly higher in the DA-fed group than in the other groups. All three treatments significantly reduced serum ALP and bone-specific alkaline phosphatase (BALP) activities as compared to the control group. Also, serum IGF-I concentrations were significantly higher in DA-fed group compared to the other groups. The deer velvet extract was thus shown to have promoted bone growth, and it was suggested that this might have been as a result of the increase in IGF-I, a major bone growth factor.

A number of studies have examined the effect of deer velvet on bone in a variety of animal models of osteoporosis.

Duan *et al.* (2007) investigated the effect of total velvet antler polypeptides (Zhou *et al.* 1999) on rats with retinoic acid-induced osteoporosis. Male Wistar rats were given retinoic acid (70 mg/kg/day) intragastrically for 14 days before being sacrificed on day 30. Subcutaneous injection of velvet antler polypeptides at doses of 20, 40 or 60 mg/kg/day over the same period as the retinoic acid treatment significantly increased femur bone mineral density in comparison to control osteoporotic rats. At the highest dose of velvet polypeptides, bone calcium content and bone weight coefficient were also significantly elevated back to the levels of non-osteoporotic control animals. In addition, a number of static histomorphometric indices of the trabecular in the tibia of the rats were significantly improved by all doses of the velvet polypeptides, showing that the velvet treatment was able to improve the structure of cancellous bone as well as increase bone mass in the osteoporotic rats.

In a different model of osteoporosis, groups of ovariectomised rats fed a calcium- and phosphorus-deficient diet were treated with hot water velvet extract (625 or 1,250 mg/kg) orally for 5 weeks (Kim *et al.* 2001). Over that time, serum oestradiol levels significantly decreased by 50% in the ovariectomised control group, but were unchanged in the groups given velvet extract as well as in sham-operated and un-manipulated control groups. Serum osteocalcin and calcitonin levels were significantly raised in the velvet treated groups as compared to the ovariectomised control group, and were restored to the levels of the un-manipulated control group. Control ovariectomised rats had significantly raised serum alkaline phosphatase (ALP) activities and calcium levels, and slightly higher serum phosphorus, but velvet treatment normalised these values back to those of the un-manipulated control animals. These findings suggest possible protective and therapeutic effects of velvet extract against bone loss associated with a significant decrease of serum oestradiol level in ovariectomised rats.

Lee *et al.* (2007b) briefly reported on a study in which osteoporosis was similarly induced by feeding a low calcium diet to female rats for 4 weeks after ovariectomisation. Groups of osteoporotic rats were supplemented with velvet extract (2.5% or 5% of diet) for 6 weeks, were treated with 17β-oestradiol (10 µg/kg, positive control) or were untreated (control). Weight gain was not affected by velvet supplementation, but serum oestradiol levels were significantly elevated in velvet extract-fed groups compared to the control group. Femur weight and mineral (calcium, magnesium) contents were significantly increased both by velvet and by oestrogen treatment compared to control, while urinary hydroxyproline and deoxypyridinoline excretions were significantly decreased. Also serum interleukin-6 (IL-6) was decreased both by velvet supplementation and by oestrogen treatment, suggesting that the bone-sparing effect could be partly attributed to the modulation of osteoclastogenesis induced by IL-6. Like the experiment of Kim *et al.* (2001) that is described above, these results support the conclusion that deer velvet has beneficial effects on oestrogen-dependent bone loss and may be useful for treating postmenopausal osteoporosis.

The ovariectomised rat model was also used by Meng *et al.* (2009) investigate the effects of velvet antler powder on osteoporosis. The results were consistent with those already mentioned. After 13 weeks, supplementation with velvet (0.18 or 0.54 g/kg/day) had improved bone mineral density, bone mineral content and serum osteocalcin of the ovariectomised rats, and reduced serum ALP activity. There were significant differences between the high dose velvet group and

the ovariectomised controls for all measures, and for some measures in the case of the low dose velvet treatment. Both doses of velvet significantly increased the width of trabecula bone and bone trabecula area percentage.

13 AIDING RECOVERY AFTER TISSUE INJURY

13.1 Health Benefits

In Traditional Chinese Medicine, velvet antler is used to promote wound healing. Rapid recovery after tissue damage caused by surgery or trauma has obvious benefits for the person involved. It also has considerable social and economic benefits by expediting the return of injured people to a normal lifestyle and to the work force.

13.2 Suggested Physiological Rationale

As with athletic performance, no single effect of velvet antler is likely to explain any benefits it has in aiding wound healing. Any such effects could be mediated by some of the mechanisms discussed in other sections, such as healthy joint functions and blood health.

13.3 Research Support

A rapidly increasing amount of research is being conducted investigating the potential use of velvet for enhancing healing of a variety of types of wounds.

Surgical and internal wounds

In Russia, Arapov (1969) used Pantocrine in surgical practice. Pantocrine was given orally, subcutaneously or it was applied locally in impregnated bandages. Large groups of patients of various ages and both genders were treated. Arapov reported there were a number of positive effects, including a pronounced general tonic effect, and normalisation of both the arterial pressure and the blood picture. Some of the patients were elderly and emaciated by chronic disease such as gastric and duodenal ulcers and malignant tumours of the stomach and rectum. Surgery of such patients is often followed by complications such as distension of the intestine and constipation. During preparation for surgery, they were given Pantocrine (1 ml intramuscularly for 7 to 10 days before surgery). Following surgery the patients remained almost completely free from the usual complications, and became active relatively early. Suppuration of the operation wounds was seldom observed. While the results of this study are interesting they carry little weight as there was no control (untreated) group of patients.

In the laboratory of Wang Ben Xiang in China, polysaccharides isolated from velvet were shown to have anti-ulcer activity in three separate gastric ulcer models in rats (Wang *et al.* 1985; Wang 1996). The effect appeared to involve effects of the polysaccharides on prostaglandin metabolism, as well as a reduction of gastric acid secretion, protecting the mucous membrane from injury.

Bone fractures

Wang's group also showed that velvet from Chinese sika deer (*Cervus nippon* Temminck) contained polypeptides that enhanced the proliferation *in vitro* of rabbit and human chondrocytes and osteoblast precursor cells of embryonic chick calvaria (Guo *et al.* 1998). They further showed that bone fracture repair was accelerated in rats when the polypeptides were injected at the site

of injury (Zhou *et al.* 1999) *(see the Strong Bones section on page 53 for more discussion of these in vivo and in vitro results)*.

Skin wounds

Further work by Wang's group went on to show that the total polypeptides fraction from red deer (*Cervus elaphus* Linnaeus) velvet accelerated healing when topically applied to skin wounds on rats (Weng *et al.* 2001b). It also strongly enhanced the *in vitro* proliferation of epidermal cells and fibroblasts, and a 32-amino acid polypeptide that was considered responsible for this activity was purified from the mixture. After identification of its sequence, the polypeptide was synthesised and its mitogenic effects on epidermal cells and fibroblasts were confirmed (Weng *et al.* 2001b; Weng *et al.* 2002). The pure polypeptide also promoted the growth of chondrocytes (Weng *et al.* 2001a; Weng *et al.* 2001b), supporting the earlier results related to bone fracture repair (Zhou *et al.* 1999).

New Zealand studies have shown that antler extracts have certain angiogenic properties (Clark *et al.* 2004; Suttie *et al.* 2005). This research laid the foundation to explore applications of specific velvet extracts in wound healing, which are produced utilising a novel extraction procedure (Haines 2009). Ongoing work has indicated that velvet is a potential source tissue for the production of extracts with angiogenic activity that have the potential to be used in commercial wound healing treatments, and patent protection has been sought (Coates *et al.* 2004).

In Canada, Mikler *et al.* (2004) investigated the effects of oral and topical elk antler velvet on cutaneous wound healing in an animal model of streptozotocin-induced diabetes mellitus. Wound healing was assessed in the controlled experiment by measuring daily wound contraction and histological and growth factor analysis of wound biopsies. The study found that topical treatment did increase wound contraction speed.

Recently, Gu *et al.* (2008a) investigated the effects of red deer velvet extract on the speed of full-thickness skin wound healing and on the expression of IGF-I, TGFβ , and EGF in the skin wounds during healing. Three groups of rats were topically administered a high concentration of antler ointment, a low concentration of antler ointment, or ointment without velvet. At post-injury days 0, 2, 4, 8, 16, 20, 32, 40 and 60, the skin wound area was measured, the expressions of IGF-I, TGFβ, and EGF mRNA were detected by reverse transcriptase polymerase chain reaction (RT-PCR), and collagen formation by Sirius red dye and the localization of IGF-I, TGFβ, and EGF peptides were inspected by immunohistochemical techniques. Healing of wounds was significantly more rapid in antler treated skin wounds. In addition, the wounds treated with a high concentration antler ointment, low concentration antler ointment or the control ointment closed completely at post-injury day 40, day 44 and day 60, respectively. As shown by RT-PCR, the expressions of IGF-I (days 8 and 16), TGFβ (days 8, 16 and 20) and EGF (days 4, 8, 16 and 32) were obviously up-regulated in high concentration antler-treated wounds compared to control wounds. Similar results could be seen in the histological detection of dye-stained collagen and detection of IGF-I, TGFβ and EGF by immunohistochemistry. These results showed that deer velvet was able to accelerate the repair of cutaneous wounds, and that this may (at least in part) have been due to stimulation of the local expression of growth factors known to be important in the normal healing process.

Nerve regeneration

Early experiments by Takikawa *et al.* (1971; 1972a; 1972b) investigated the effects of the Russian alcohol extract, Pantocrine, on rabbits and rats with experimentally induced whiplash injury. Pantocrine administered as an intra-muscular injection (~1.5 mg/kg/day) from the 3rd to the 21st day after injury significantly improved abnormalities in electronystagmogram (ENG) patterns, and decreases in cerebrospinal glycolysis and enzyme activities of cerebral and spinal tissues, that were caused by the whiplash.

The effect of pre-treatment with velvet extract on regeneration of peripheral nerves was investigated by Chang *et al.* (2002). Groups of rats were orally administered velvet extract or saline (as control) daily for periods of 1, 2, or 3 weeks, after which the sciatic nerve of each leg of the rats was transected. Six hours later, sciatic nerves were taken from the proximal parts of the transected regions for analysis by transmission electron microscopy. A larger proportion of nerve fibres examined showed axonal sprouts at the nodes of Ranvier in rats pre-treated with velvet extract compared to the saline-treated control animals. This was particularly evident in animals given velvet for 2 or 3 weeks and, although most sprouts were short in all groups, some longer sprouts were observed in rats of these two treatment groups. The results indicate that deer antler may be effective for the regeneration of peripheral nerves.

More recently, two Chinese groups have also reported beneficial effects of Wang's velvet antler polypeptides (see discussion above) on nerve regeneration in rats.

Li *et al.* (2008) evaluated the effects of different doses of velvet polypeptide on motor function, behaviour and pathological changes of spinal cords of rats with spinal cord injury. After seven days significantly more motor activity was recovered in the velvet polypeptide treatment group compared to the control group, and the effect was dose-dependent. Similarly, a dose-dependent reduction of tissue oedema and inflammatory infiltration of the spinal cord was observed, especially at the highest dose (15 mg) of velvet polypeptide.

Lu *et al.* (2008) evaluated the effect of velvet polypeptide in a nerve damage model, in which the sciatic nerve of rats was surgically sectioned and then rejoined. Four groups, each of 18 rats, were either left untreated (control), were injected intramuscularly with 10 µg velvet polypeptide every other day for up to 6 weeks, or were implanted at the surgery site with a PLGA[4] copolymer containing either 3 or 15 mg/g of velvet polypeptide. The recovery rate of the evoked potential of the triceps surae was significantly better for all treatment groups compared to the control group, with the greatest recovery being shown by the 15 mg/g PLGA-velvet polypeptide group. Similarly, all treatment groups showed significantly more nerve regeneration than the control group, as revealed by immunohistochemical analysis of TGFβ1 and IGF expressed in the nerve fibre axons and myelin sheaths of the rats, as well as horseradish peroxidise (HRP) staining of myelinated nerve fibres. Again, the best response was shown by the 15 mg/g PLGA-velvet polypeptide group.

[4] *Poly(lactic-co-glycolic acid), a biodegradable copolymer which is used in a host of Food and Drug Administration (FDA) approved therapeutic devices.*

Sciatic nerve adherence was also reduced by the injection of velvet polypeptide, and eliminated by treatment with either dose of the PLGA-velvet polypeptide compound.

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).

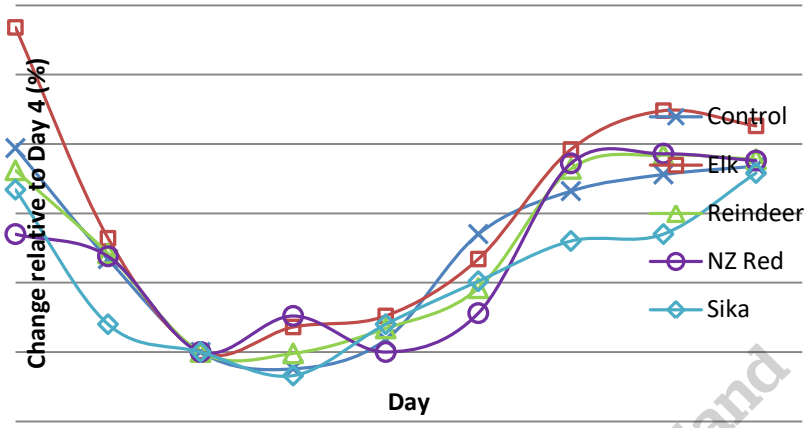


Figure 8. Haemoglobin levels (relative to day 4) in anaemic rabbits given velvet extracts from different species of deer

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

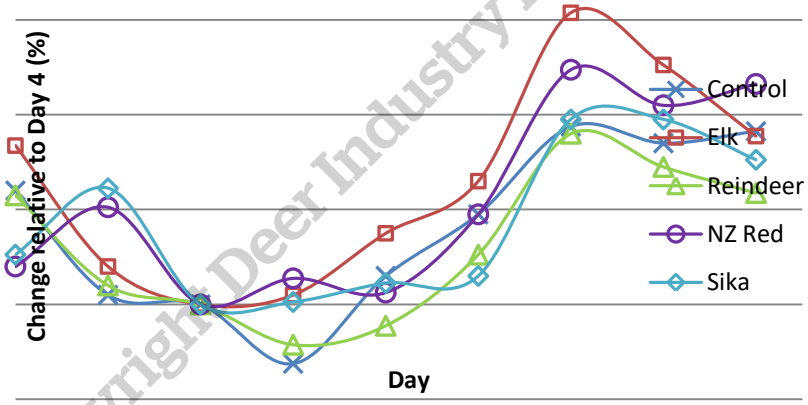


Figure 9. Haematocrit (relative to day 4) in anaemic rabbits given velvet extracts from different species of deer

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

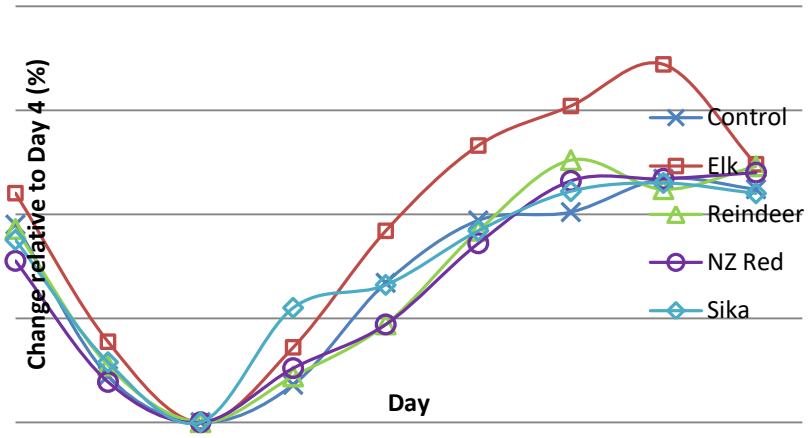


Figure 10. Erythrocyte numbers (relative to day 0) in anaemic rabbits given velvet extracts from different species of deer

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

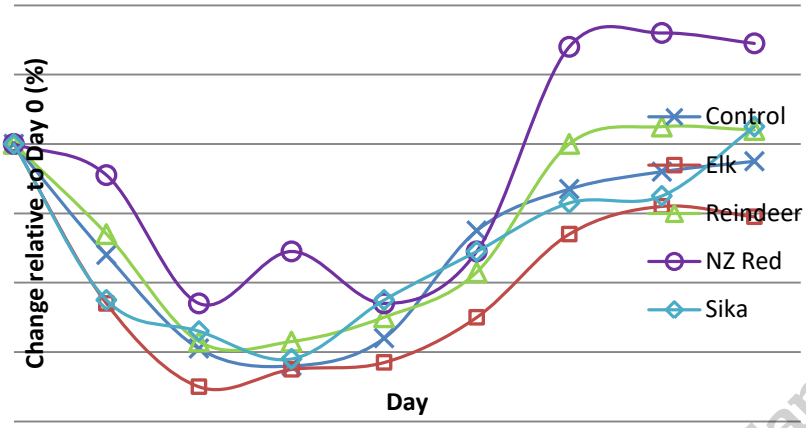


Figure 11. Haemoglobin levels (relative to day 0) in anaemic rabbits given velvet extracts from different species of deer

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

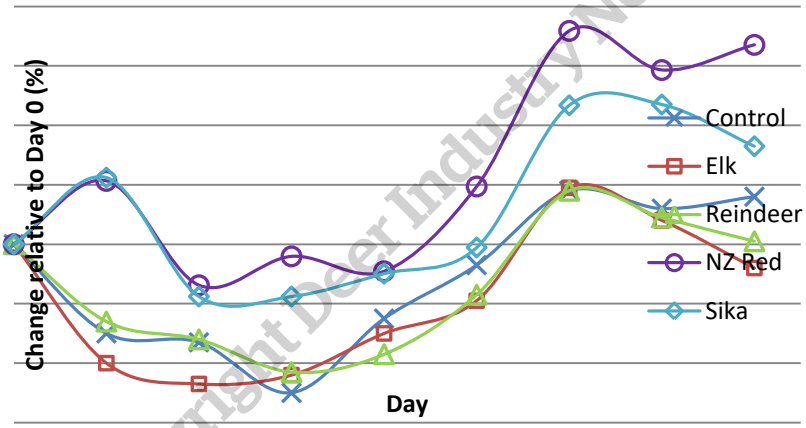
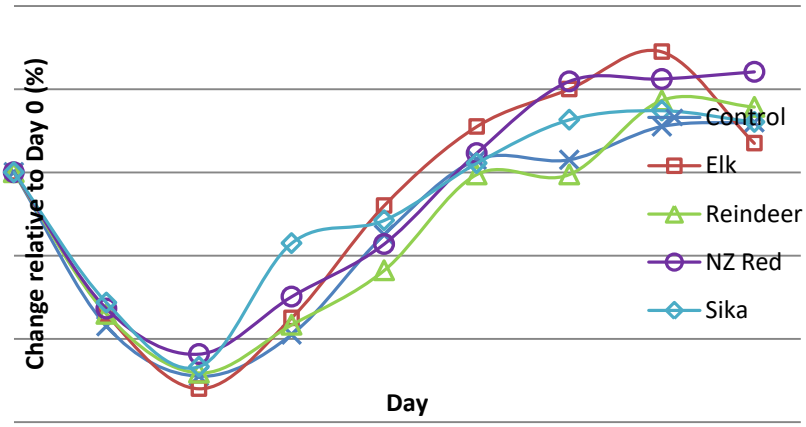


Figure 12. Haematocrit (relative to day 0) in anaemic rabbits given velvet extracts from different species of deer

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

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.

16 NORMAL CHOLESTEROL BALANCE

16.1 Health Benefits

Heart disease is widespread and common in Western countries, because of factors such as a rich diet and a sedentary lifestyle combined with a genetic predisposition in some people. It carries with it a huge social and economic cost. High cholesterol concentrations are known to predispose to heart disease, and diets and dietary supplements that support the maintenance of normal blood cholesterol concentrations may help lower the risk of heart disease. Deer velvet appears to be a product that has some potential in this area.

16.2 Suggested Physiological Rationale

The mechanisms by which velvet antler may help maintain healthy cholesterol concentrations in the body are currently not clear.

16.3 Research Support

Soshnianina (1974) studied the effects of alcohol extracts of velvet antler on cholesterol concentrations in guinea pigs. Treatment with velvet extract lowered liver cholesterol content from 1,610 to 1,311 mg/100g dry tissue. Spleen and brain cholesterol concentrations were also reduced. In contrast, the kidney cholesterol concentrations were increased (from 1,733 to 1,900 and 1,880 to 2,190 mg/100g dry tissue respectively). The author concluded that velvet antler extract was causing cholesterol to be filtered from the blood, thereby increasing kidney levels but lowering levels elsewhere in the body.

Velvet has been shown in a number of experiments to also lower cholesterol levels in rats.

Ahn (1994) fed groups of rats with a diet supplemented with 0.3% of velvet from sika, formosan or red deer to groups of rats. Velvet treatment had no effect on feed intake or growth performance of the rats, but significantly lowered plasma cholesterol levels as compared to control rats given the basal diet. The reductions in cholesterol levels ranged from 20.7% to 32.9% for the three velvet treated groups, but there were no significant differences between the types of velvet.

Sunwoo and Sim (2000; 2001) found that the ratio of high-density lipoprotein cholesterol (HDL-C) to low-density lipoprotein cholesterol (LDL-C) in the plasma of growing rats was significantly higher in a group of rats fed antler powder for 54 days than in a group of control rats, though the plasma total cholesterol concentrations did not differ between groups. They suggested that these findings reflected the involvement of unknown factors derived from the antler powder and that the increased HDL-C to LDL-C ratio might be important for the prevention of coronary heart disease.

Cui (2008) conducted an experiment to investigate the effect of water soluble extracts from different sections of farmed elk (*Cervus elaphus*) antler on lipid metabolism and haematology of 80 rats for 4 weeks. Antlers were divided into four sections (tip, upper, middle and base). Water soluble extract (35 g/60 ml) was prepared from each section of the antler, and was administered

orally to male Sprague-Dawley rats (10 ml/kg body weight) once a day. At the end of the 4 week supplementation period, all groups fed velvet extract had decreased total cholesterol in visceral fat and liver in comparison with the control group. Total cholesterol in serum was also significantly reduced in the groups given extract from upper and base portions of the antler as compared to the control group (54.2 and 53.4 mg/L *vs* 64.8 mg/L, respectively). The composition of visceral fat was also different in the velvet treated groups when compared with the control. These results, albeit obtained with very high doses of extract, provide further evidence that velvet is capable of positively affecting lipid metabolism.

In humans, Broeder *et al.* (2004a; 2004b) reported a significant 12.2% reduction of LDL-C in athletes administered velvet powder which was not observed in control subjects given a placebo (see page 74 for details of the experimental protocol). However, diet was not controlled in that experiment so it is not clear whether the positive effect on cholesterol balance was due to velvet treatment or some dietary factor.

In a non-placebo-controlled trial, Kim *et al.* (2004a; 2004b) treated 10 type 2 diabetic patients with a commercial Korean deer velvet drink daily for 3 weeks. No significant differences were observed in levels of triglycerides, total cholesterol, LDL-C or HDL-C. However, oxidized-LDL, measured as conjugated dienes, decreased in most patients at the end of the trial. (Kim *et al.* 2004b). Similarly, a marked decrease of over 50% in cellular DNA damage was observed following the 3 weeks of treatment (Kim *et al.* 2004a). These results suggest that the velvet drink may have positive effects in reducing oxidative stress in patients with type 2 diabetes.

17 ATHLETIC PERFORMANCE

17.1 Health Benefits

Sports people whether professional or amateur continuously strive to improve physical performance. The discipline of sports nutrition has arisen from the need to combine training, responses to injury and diet to ensure the best possible athletic performance. Velvet antler is well placed to impact on sports nutrition. In Russia, Korea and China, velvet antler is widely used by athletes to enhance performance. In the West, more and more athletes are looking to velvet antler as a training aid, a promoter of recovery after physical activity and injury, and possibly an injury preventive.

17.2 Suggested Physiological Rationale

Athletic performance is a very complex issue. Velvet antler could improve athletic performance in many different ways, for example by assisting strength and endurance (stamina), by enhancing the oxygen-carrying capacity of the blood, by facilitating minor tissue damage occurring either during training or competition, and by boosting the immune system of athletes whose immune system has been compromised as a result of extreme exertion. These broadly reflect the protective and restorative effects of velvet antler.

The effects of velvet antler on athletic performance are likely to be complex and they will be influenced by many factors, such as the type of velvet antler extract and the dose. Not all athletes are likely to benefit from taking velvet, and individual variation in response coupled with the requirements of the athlete will also affect the outcome.

17.3 Research Support

A strong body of evidence supporting the use of deer velvet for enhancement of athletic performance is developing. Importantly, the research includes double-blind studies conducted in humans, as well as animal studies.

Efficacy studies in humans

In Russia, Yudin and Dobyrakov (1974) studied the effect of alcohol velvet antler extracts on the static load-bearing capacity (holding a weight at rest above a gymnasium bench) of healthy sportsmen. The velvet extracts increased the time of work by 2–4 seconds compared with control sportsmen. In tests of dynamic work using a veloergometer, velvet antler alcohol extract (Pantocrine) treatment increased the work output of sportsmen 4- to 5-fold compared with the work output of sportsmen not treated with extract.

Taneyeva (quoted by Brechman, undated) tested the effect of Pantocrine in athletes running 3,000 metres. The time for 50 men aged between 18 and 23 years old to each complete the run was recorded. A single administration of 20 ml velvet antler extract 30 minutes before a repeat of the run lowered the average time to complete the event from 14 minutes 48 second to 14 minutes 4 seconds. In a second experiment the alcohol velvet antler extract was administered for 12 days and the race was re-run 24 hours after the last treatment. The time taken to complete

the event was reduced in the majority of subjects. Interestingly, improvement was noted in above-average as well as below-average athletes.

Strength training study 1

More recently, a collaborative trial was carried out in New Zealand by AgResearch Invermay and the School of Physical Education at the University of Otago in Dunedin (Sleivert *et al.* 2003). The aim was to determine whether velvet antler could improve gains made during strength training in male athletes. Thirty eight active males were randomly assigned in a double-blind fashion to either velvet extract (n=12), velvet powder (n=13) or placebo control groups (n=13). The velvet was given at a rate of 300 mg extract or 1,500 mg powder daily, which were approximately equivalent doses based on yield of extract. Subjects were tested prior to beginning supplementation and a 10-week strength programme and again immediately post-training. All subjects were measured for circulating levels of testosterone, IGF-I, erythropoietin, red cell mass, plasma volume and total blood volume. Additionally muscular strength and endurance, and oxygen-carrying capacity (VO_{2max}) were determined.

All groups improved equivalently (by 41 ± 26%) in the six-repetition maximum (6 RM) strength test, which determines the maximum weight the subject can lift six, but not seven, times in a row. However, there were significant differences between improvements in isokinetic knee extensor strength (30 ± 21% *vs* 13 ±15%) and muscle endurance (21 ± 19% *vs* 7 ± 12%) in the velvet powder group compared to the control group, respectively. There were no endocrine, red cell mass or VO_{2max} changes in any group. Thus the findings did not support an erythropoietic or aerobic ergogenic effect of deer velvet in these athletes. Given that the subjects were all healthy and did not undergo any aerobic training, these results were not surprising. The effects of deer antler velvet powder supplementation on muscle strength and endurance, though, were supportive of the earlier Russian results.

Strength training study 2

The results of the above study of Sleivert *et al.* also backed up those of an earlier double-blind pilot trial, conducted in 24 healthy male university students by the University of Otago (Gerrard *et al.* 1998). The design of the two studies was similar, except that in the pilot study only velvet extract was compared to placebo control (*i.e.* no third group was given velvet powder), and the dose administered was lower (70 mg extract/day as opposed to 300 mg/day). The pilot study also focussed on the measures of muscle strength and endurance, without the endocrine and aerobic endurance testing. Most of the strength measures improved with training but no significant differences due to the velvet extract were detected. There were some strong trends however. The increase in the total work done by extensor muscles of the extract-treated group was about twice that of the placebo group. There was some evidence that endurance of the extension muscles was also improved. The lack of a statistical significant result may have been related to the relatively low dose of velvet given, as evidenced by significant results subsequently being obtained using similar-sized groups of subjects supplemented with higher doses.

Strength training study 3

In a double-blind study carried out in the United States, Broeder *et al.* (2004a; 2004b) investigated the physiological and potential performance enhancing effects of New Zealand deer velvet supplementation in men. Thirty-two males between the ages of 18 and 35 with at least 4 years of

weight lifting experience were randomly assigned into either a placebo (control) or velvet treatment group.

Control group members received placebo capsules, while the velvet group received 1,350 mg velvet powder once in the morning and again immediately prior to bed-time (*i.e.* 2,700 mg/day). Random assignment was done in matched pairs (1 placebo; 1 velvet). Prior to and immediately following a 10-week period of supplementation, each subject participated in a series of measurements. These procedures included the measurement of maximal aerobic capacity (VO_{2max}), maximal power output on a cycle ergometer, a determination of maximal strength (1-RM) for the bench press and squat, a comprehensive blood chemistry profile, body composition analyses (DEXA), and a 3-day dietary recall. Of the original 32 subjects recruited for this study, 56% of the subjects properly completed all aspects of the study. Dropouts were evenly divided between the two treatment groups, leaving the placebo and the velvet groups each with 9 subjects. At the start of the study, there were no significant differences between the groups in their respective body composition profile variables.

For the placebo group, only the absolute 1-RM values for the bench press and the squat improved after the intervention period. When normalized for kilograms of total body weight, the placebo group did not show any significant differences for the 1-RM measurements in either the bench press or the squat exercises. In contrast, the velvet group showed significant improvements in the 1-RM values, both in absolute terms and relative to total body weight. In absolute terms, the 1-RM for the bench press of this group increased 4.2% while the squat 1-RM improved 9.9%. When expressed relative to total body weight, 1-RM values for the bench press and squat also significantly improved by 4.0% and 10.1%, respectively, in the velvet group.

One of the most interesting findings of this study was the fact that there was also a significant improvement in aerobic capacity in the velvet treatment group. In litres, VO_{2max} increased significantly by 9.8% from the pre- to post-treatment period. When expressed relative to total body weight in kilograms, VO_{2max} was also significantly elevated by 9.4% in the velvet group following the training-supplement intervention. These results differ from those of Sleivert *et al.* (2003), who found no effect of velvet on VO_{2max} in their experiment. The reason for the difference is unclear. Possibly, though, this could be related to the use of a supervised training programme in the study of Sleivert *et al.*, as compared to the self-determined training programme of the present experiment. Further research, including specific aerobic training, is warranted to clarify the potential effect of velvet on aerobic capacity during exercise.

In the velvet group, reductions in percentage body fat, fat weight, and trunk-to-limb fat weight ratio were either significant or neared significance. Also observed was a significant reduction in LDL cholesterol (12.2%), which improved the LDL/HDL ratio by 8.4%. These findings need to be treated with some caution, as diet was not controlled in the study, but the effect on cholesterol balance coincides with results of some animal studies (see Section 16 above). They are certainly worthy of closer examination in studies designed for the purpose.

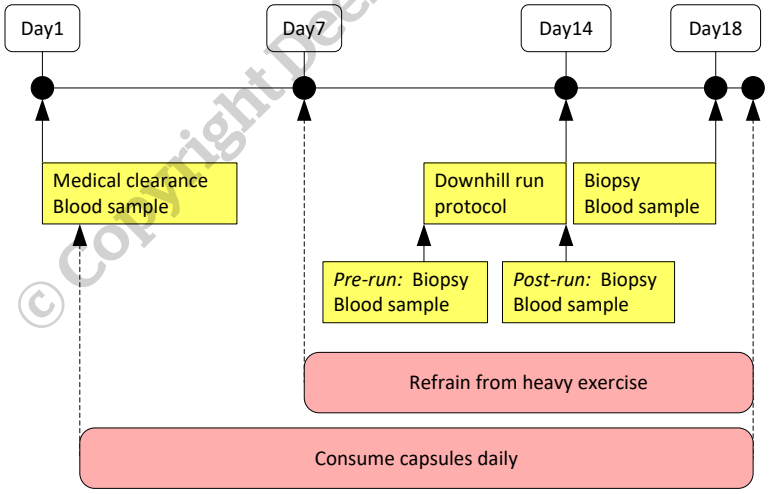
Overall, the results of this study suggested that New Zealand deer velvet may have positive effects on body composition and strength/power in men undergoing resistance training.

Recovery from muscle damage study

An experiment was performed by the University of Otago to determine if velvet products have an enhancing role in athletic performance by affecting repair of exercise induced muscle damage (Gerrard *et al.* 2000). Thirty students were allocated at random into three groups of 10 for the double-blind study (Figure 13). One group ('Powder') was given 1.5 g/day velvet antler powder for 2 weeks, and one group ('Extract') was given 300 mg/day velvet antler extract for 2 weeks. The third group ('Placebo') was included as a control, and took a placebo for 2 weeks. Damage to the quadriceps muscle group was then induced in all subjects by having them run for 35 min discontinuously on a motorised treadmill on a 12% downhill grade. A pre-run muscle biopsy and blood samples were taken before velvet supplementation, immediately after this exercise and again 4 days later. Immediately following completion of the 35 minute downhill run, and on each of the four subsequent days, participants performed five slow, controlled, non-supported squats and gave ratings of muscle soreness (MSR). For this, a scale of 1–10 was employed, where 1=normal, 5=moderately sore, and 10=very sore. Consumption of velvet or placebo continued throughout the 4 day post exercise period. Blood samples were tested for the serological markers of muscle damage, creatine kinase (CK), lactate dehydrogenase (LDH) and aspartate amino transferase (AST). The downhill treadmill run produced ultra structural muscle damage that was ranked in accordance with a scale of 1 (representing normal muscle) to 5 (indicating widespread muscle damage).

Figure 13. Muscle damage study design

The protocol of an experiment conducted by the University of Otago (Gerrard *et al.* 2000) to determine the effect of velvet on recovery from exercise induced muscle damage.



Participants were excluded from the analyses if their initial level of serum CK was greater than 2 standard deviations above the mean reference range for blood CK (140 ± 95 U/L); *i.e.* CK values of 330 U/L or above. This was done because elevated CK values generally indicate that an individual may have experienced strenuous exercise in the recent past or may have some undetermined myopathy. Because previous eccentric exercise may also provide protection against subsequent

damage from eccentric exercise it was necessary to exclude subjects who may have had a recent eccentric exercise experience. Twenty participants completed the study (6 each in the Placebo and Extracts groups, and 8 in the Powder group).

Significant minor to moderate ultra structural damage was reported for the post-exercise muscle biopsy sample. However, there were no significant differences between groups and the treated groups appeared to receive no significant benefit from powdered or extract forms of deer velvet.

In the subjects in all three groups, there was a demonstrable and significant rise in serum CK concentrations 4 days after exercise (Figure 14). However, the CK increase was significantly less 4 days after exercise in the group supplemented with velvet powder than the concentrations in the Extract and Placebo groups, suggestive of a lower degree of muscle damage in the Powder group. No significant differences in the activities of the other enzymes measured (LDH and AST) were evident between groups.

Qualitative measures of perceived muscular discomfort were reported by using a specific muscle soreness rating (MSR) scale. There was a clear pattern of increased MSR at 24 hour post-exercise (Figure 15). While the overall pattern of change in MSR was similar for all groups, the return to a normal level seemed to occur 24 hours earlier in the Powder group.

A regression analysis between MSR and muscle damage rating revealed significant positive slopes for the Placebo and Extract groups (Figure 16). This was to be expected because soreness would be expected to increase with increasing level of damage. However, the analysis produced a non-significant slope for the Powder group. There is no immediately obvious explanation for this although it may be indicative of some kind of analgesic effect specific to powdered velvet, as previously reported by Shin *et al.* (1989).

Thus, the study did not provide unequivocal evidence of protective or restorative effects of velvet products on post-exercise muscle stiffness after acute eccentric loading, but some indications of a beneficial effect of powdered velvet were noted. Relevant to this was the low number of participants that completed the study, which reduced its statistical power. Further research would be needed to determine if deer velvet can in fact accelerate recovery from exercise induced muscle damage.

Figure 14. Creatine kinase (CK) levels in the muscle damage study

Data are mean CK levels at pre-supplementation, post-supplementation, and 96 hours following the downhill run for the Placebo, Powder, and Extract groups in the study of Gerrard *et al.* (2000). Error bars show SEM. * = Significantly different from post-supplementation scores for the group; † = significantly different from placebo group pre-supplementation; # = significant difference in CK rise *vs* placebo group at 96 hours post-run.

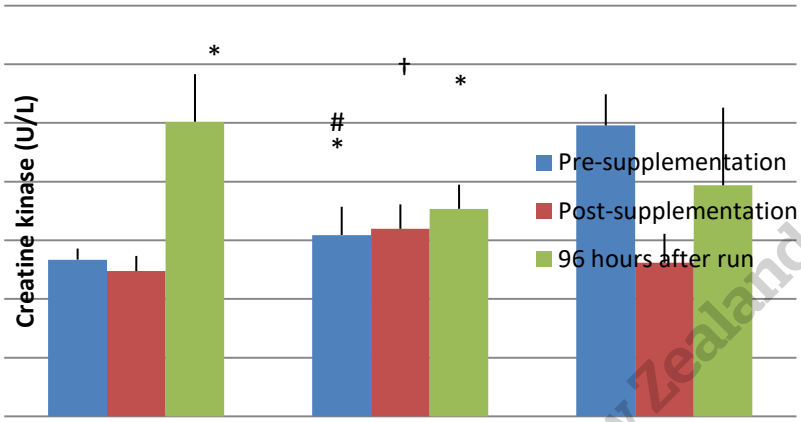


Figure 15. Muscle Soreness Rating (MSR) scores in the muscle damage study

Data are mean MSR scores immediately after, and 24, 48, 72 and 96 hours following the downhill run for the Placebo, Powder, and Extract groups in the study of Gerrard *et al.* (2000). Error bars show SEM. * = Significantly higher than immediately after the run (0 hours) for group; # = significantly lower than immediately after the run (0 hours) for group.

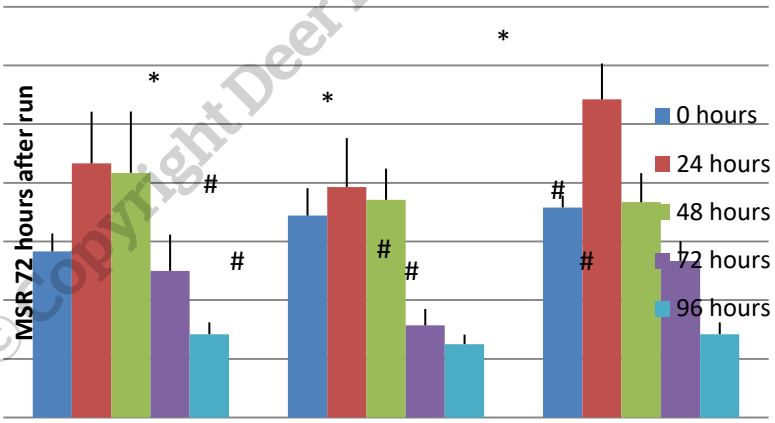
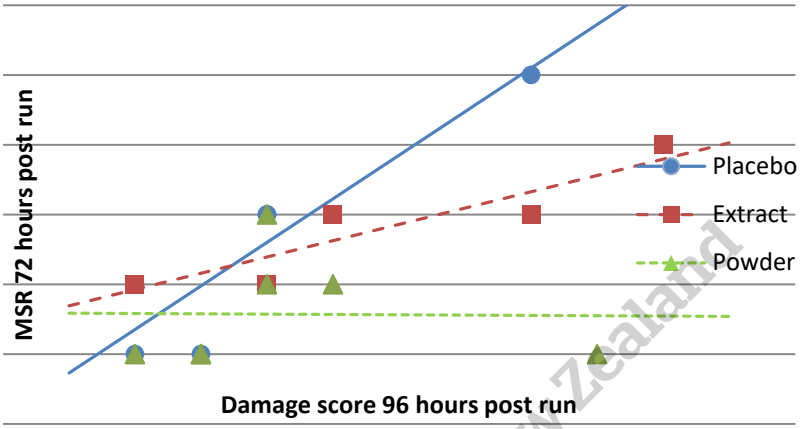


Figure 16. Regression analysis of MSR and ultra structural muscle damage scores in the muscle damage study

Data are individual MSR and ultra structural muscle damage scores, together with fitted linear curves obtained by regression analysis, for the Placebo, Powder, and Extract groups in the study of Gerrard *et al.* (2000). Positive non-zero slopes were fitted to the data for the Placebo and Extract groups, but the slope for the Powder group was not significantly different to zero.



Efficacy studies in animals

Scientists in China (Li *et al.* 2004) and Russia (Letchamo *et al.* 2004) have both shown by use of standardised forced swimming tests that velvet enhances the stamina of mice. The Russians classified velvet as an adaptogen that acts for a short term. They further showed that individual mice vary in their ability to respond to adaptogens (including velvet), and classified them as having high, medium or low adaption capacity.

Enhancement of performance in forced swimming tests has also been demonstrated by Korean researchers, as described in the following section.

Weight-loaded forced swimming performance test in mice

Shin *et al.* (2001) tested the effect of 96% ethanol and hot water extracts of velvet on the stamina of mice in forced swimming tests. ICR mice weighing 25-30 g were administered with test samples orally for 5 days consecutively and, 24 hours later, the swimming tests were performed. For each experiment, mice were divided into five groups of 9 animals each. Velvet treated groups were orally administered 50, 100 or 200 mg/kg velvet extract in distilled water daily for 5 days. A further group was similarly given tocopherol suspended in gum Arabic (5 g/L) as a positive control substance, and a control group given just water was also included. On the 6th day the swimming test was carried out with a weight attached to the tail of the animal. A weight [(bodyweight + 3 g) x 0.065] was attached 5 cm from the base of the tail. A stainless water tank was used that was equipped with a circulation pump and a thermostatically controlled heating unit, which maintained the temperature at 33°C. The swimming time was defined as the interval between the onset of swimming and the point at which the animal became fully submerged for 5 seconds.

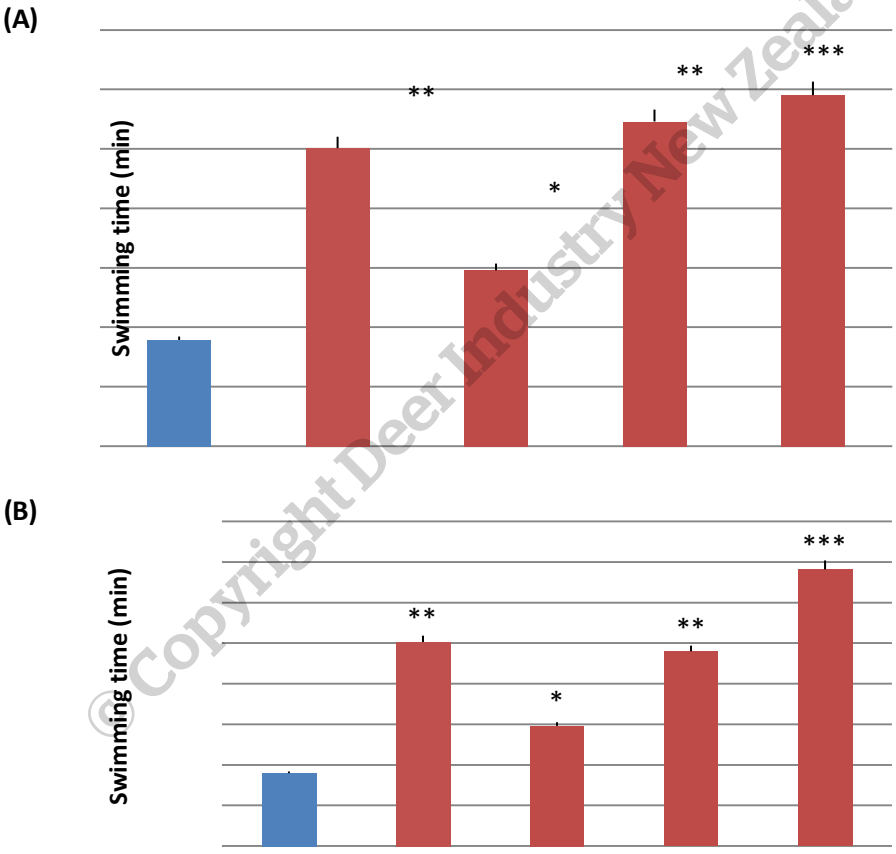
The mean durations of swimming times showed significant dose responsive increases for both the water and the ethanol extract of velvet (Figure 17). For each extract, the swimming performance

of the 100 mg/kg/day dose group was the same as the positive control tocopherol, having mean swimming durations that were over 250% of those of the negative control group.

These results suggest that the heat stable factors in deer velvet that enhance the stamina of animals are either soluble in both water and in ethanol, or else multiple factors are involved. Although evidence is lacking at this time, it is tempting to speculate that these might be small peptides since these are known to be soluble in both solvents.

Figure 17. Effect of velvet extracts on swim duration of mice

Mice were orally administered 50, 100 or 200 mg/kg/day of (A) water or (B) alcohol extract of velvet consecutively for 5 days. Swimming times were estimated 24 h after the last treatment of test samples (Shin *et al.* 2001). Tocopherol (5g/L) in gum Arabic was given to an additional group of mice as a positive control substance. Data are means ± SEM for groups of nine mice each. Significantly different from control group: *P < 0.05, **P < 0.01, *** P < 0.001.



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.

19 AGEING

19.1 Health Benefits

Although the ageing process is inevitable, it is human nature to seek ways of deferring and ameliorating the process. Velvet antler has been used as a tonic for aged people and as an anti-ageing preparation in Traditional Chinese Medicine, and this might well be linked to its supposed support for:

- joint mobility,
- blood,
- brain function,
- and general tonic properties.

As might be expected, some Western consumers who subscribe to complementary medicinal principles are showing a keen interest in using velvet as an anti-ageing dietary supplement.

19.2 Suggested Physiological Rationale

Monoamines are neurotransmitters in the central nervous system and they include serotonin, adrenaline, noradrenaline, dopamine, tyramine and tryptamine. The ageing process is associated with the effect of monoamine oxidase in degrading these neurotransmitters. Monoamine oxidase inhibitors by helping prevent the oxidation of neurotransmitting monoamines and so help prevent age-related degenerative change in the brain. Monoamine oxidase inhibitors are used in Western medicine as antidepressants and antihypertensives. From animal studies, it appears that at least in some circumstances deer velvet may act as a monoamine oxidase inhibitor.

Other oxidations, including those that involve free radicals like lipid peroxidation, are also implicated in the ageing process. Suppression of these oxidation processes provides another potential mechanism for velvet to exhibit an anti-ageing effect.

19.3 Research Support

Wang *et al.* (1988a; 1988b; 1988c; 1988d; 1990a; 1990b; 1996) and also Hattori *et al.* (1989) showed that velvet contains components that inhibit monoamine oxidase B (MAO-B). Specifically, these were hypoxanthine, phosphatidyl ethanolamine, sphingophospholipid, phosphatidyl choline, lysophosphatidyl choline, phosphatidyl inositol and uridine. They used an experimental system in which they made a comparison between the effects of velvet antler extract on a strain of senescence-advanced mice and the effects on a strain of normal mice. The velvet extracts significantly altered the metabolism of the senescence-advanced mice, but not the control (normal) mice. In the senescence-advanced mice, the velvet extract decreased monoamine oxidase activity in liver and brain. It also increased plasma testosterone, decreased the content of malondialdehyde in the liver and brain, increased liver superoxide dismutase activity and increased liver protein content. These changes served to reverse some of the physiological changes associated with senescence in this experimental model. Other research (Chen *et al.* 1992; Wang *et al.* 2003a) has demonstrated inhibition of MAO-B in aged mice, and a patented

velvet formulation in β-cyclodextrin reportedly has greater activity than standard velvet extract (Hsu *et al.* 2003). Recently, supercritical fluid extraction (SFE) has been used to extract MAO-B inhibitors from velvet (Zhou *et al.* 2009c).

A Korean preparation containing dried velvet has been shown *in vitro* to exhibit free radical scavenging activity (Park *et al.* 2005). Similarly, water velvet extract has been shown *in vitro* to reduce lipid peroxidation (malondialdehyde production) and superoxide anion radical production (Chen *et al.* 2003), and to protect myocardial cells against free radical-induced toxicity of doxorubicin (Huang *et al.* 1990).

Kim *et al.* (2004a) conducted an experiment investigating the ability of velvet to reduce the oxidative stress to patients with diabetes. This involved measuring cellular DNA damage, expressed as tail length and tail moment (tail length x percent tail DNA), using single cell gel electrophoresis (COMET assay). Ten patients (4 men, 6 women) participated in the study and consumed two pouches of a commercial deer antler drink every day for 20 days. Blood was collected on the morning before and after the intervention for lymphocyte isolation and blood glucose analysis. Both systolic and diastolic blood pressure showed a tendency to decrease but these changes did not reach statistical significance. Blood glucose level was not affected by the supplementation. After the intervention, the level cellular DNA damage was reduced by over 50%. Although a beneficial effect on lowering blood glucose levels in the patients was not obtained, the results of the short term experiment suggested that deer antler may initially act to reduce endogenous DNA damage. If the same activity is evident in healthy patients, this might provide a mechanism by which velvet is able to exert an anti-ageing effect.

20 TOXICITY AND CONTRAINDICATIONS

20.1 Toxic Effects

In laboratory animals, Yudin and Dobryakov (1974) found that Pantocrine (alcohol velvet antler extract) had a relatively low toxicity, and its LD_{50} was 14.5 ml/kg.

Takikawa and Imai (1977) performed acute toxicity tests using alcohol velvet antler extract on healthy 4-week-old mice and rats. After a 12-hour fast the animals were given alcohol velvet antler extract intravenously or intramuscularly at various doses from 100 to 1,000 mg/kg and 250 to 750 mg/kg respectively. During 3 weeks of observation, no deaths occurred. However, treated mice showed temporary tachypnoea (rapid breathing rate) and 'a resting state' after doses of 100 mg/kg intravenously and 250 mg/kg intramuscularly, and the intensity of these signs increased with the dosage. After being given 1,000 mg/kg intravenously, mice showed exophthalmos (bulging forward of the eyes), epiphora (excessive tear production) and slight tremor. In rats, intravenous administration of 1,000 mg/kg did not induce exophthalmos, epiphora or tremor, but otherwise the same signs as in mice were observed.

Shin *et al.* (1989) reported that, after a single oral dose, velvet powder showed a very weak acute and subacute toxicity in mice (with minimum lethal dose being over 5 g/kg). Furthermore, daily oral administration to rats of velvet powder at doses up to 3 g/kg for 14 days did not cause any significant differences in body weight gain, various organ weights, or serum transaminase activities compared to those of the control rats.

In New Zealand, Zhang *et al.* (2000) demonstrated that, after acute administration of a high dose (2 g/kg) of New Zealand deer velvet as well as after subchronic treatment (90 days) with a moderate dose (1 g/kg), no signs of toxicity and no abnormal changes were observed in male and female Wistar rats either at a gross or histopathological level.

In another New Zealand study (Zhang 2000), deer velvet powder was tested for any toxic effects on the reproductive systems of adult male and female Wistar rats and on the development of foetal rats, using an OECD guideline, *i.e.* 421: Reproductive/Developmental Toxicity Screening Protocol. New Zealand deer velvet was administered in 1 g/kg daily doses by stomach tube. The control group rats received water only. Females and their litters were sacrificed on postpartum day 4, and adult males were sacrificed within the following week. There was no apparent maternal, reproductive, or developmental toxicity in any rat. No clinical signs of toxicity and no effects on body weight, food consumption, or absolute organ weights were observed. No microscopic changes were observed in reproductive organs. There were no differences in mean number of corpora lutea, implantation sites, or live pups per litter, and no gross abnormalities were detected in the pups. The dose of New Zealand deer velvet used here was relatively large and this suggests that it has very low toxicity. The doses were far in excess of any doses anticipated for human consumption.

The toxicity of New Zealand red deer velvet and Chinese wapiti velvet were compared by Li *et al.* (2004). Alcohol extracts were prepared from each type of velvet and, after concentration, were administered to female and male mice (10 each per extract group). Each mouse was given a

single administration of either New Zealand red deer or Chinese wapiti velvet extract at a dose equivalent to 300 g velvet/kg bodyweight. All animals were observed and their behaviour and weight recorded for 7 days. Soft faeces were observed in 70% of males and 40% of female mice from both treatment groups 2-3 hours after administration of velvet. Faecal consistency returned to normal the following day in both groups. No deaths or behaviour abnormalities (including eating and drinking) were observed during the period of investigation. There were also no significant differences in bodyweight between the two groups 7 days after velvet extract administration.

Hemmings and Song (2004) examined the effect of exposure to, followed by consumption of, a diet containing 10% powdered Canadian elk velvet antler (EVA) from the 18th day of gestation to the 88th day after birth in male and female Fischer 344 rats. There were no teratogenic effects of EVA exposure *in utero* or differences in birth outcomes between pups born to regular chow fed and EVA chow fed dams. Growth curves of the EVA fed rats were identical to those of regular chow fed rats, as were developmental milestones of pinna development and eye-opening. Acoustical startle and righting reflexes, developmental and behavioural indices, were identical. Blood glucose levels were comparable in EVA chow fed and regular chow fed rats, indicating that EVA did not affect glucose balance. There were no signs of toxicity in the EVA chow fed compared to regular chow fed rats, as judged from plasma enzyme markers of liver damage: plasma levels of alanine aminotransferase were 50% lower in EVA chow fed rats compared to regular chow fed rats; and plasma levels of γ-glutamyltranspeptidase (γ-GT) were the same. The activity of γ-GT displayed a decrease in the livers of EVA chow fed rats, more so in the male (22%) than in the female (14%), suggestive of an androgenic effect. It was concluded that dietary 10% EVA chow is without long term effect on growth, development and behaviour, is non-toxic and may be hepatobeneficial.

20.2 Precautions

Remarkably few data on contraindications for velvet antler are available. The Chinese Materia Medica indicates that velvet antler should not be taken in 'deficient Yin patterns with heat signs'. From a biomedical perspective these symptoms include rapid but weak pulse, vertigo, tinnitus and dry mucous membranes. However the fact that velvet has been used by young and old male and female alike for 2,000 years with few reports of adverse effects is evidence that velvet is a relatively safe preparation.

The Russian literature as reviewed by Archer and Palfreyman (1983) listed the following contra-indications: serious atherosclerosis, serious heart disease, high blood coagulability (stroke risk), serious kidney disease and diarrhoea. Ryashchenko (1976) stated that excessive alcohol consumption and smoking were contraindicated for those taking velvet antler.

There are anecdotal reports of very occasional anaphylactic responses to velvet antler in some people. This might be expected with any ingested dietary item. These individuals should certainly avoid taking velvet antler in future.

Velvet antler can have a hypotensive (lowering of blood pressure) effect. Therefore anyone with a cardiac abnormality or abnormal blood pressure should consult a doctor before taking velvet antler in case the use of velvet exacerbates their problem.

Some consumers have reported nose bleeds after taking velvet. After visiting China several times to pursue his studies of deer velvet, Dr Jimmy Suttie (personal communication) reported that it is in fact common practice for Chinese people taking deer velvet to gradually increase the daily dose until nose-bleeds occur then reduce the daily dose to that of the day before.

An experiment with rats in New Zealand raised the possibility that deer velvet may increase the size of, but not the number, of pre-existing tumours in the large intestines of rats. However, there is no other research material available about the effects of deer velvet on other types of cancer. Nor is there any published scientific literature that indicates deer velvet causes cancer. The significance of the results of the experiment for human health is not known. However, people who have cancer or are at an increased risk of developing cancer compared to the general population should exercise caution in their use of deer velvet, and consult their health practitioner.

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