

## Research Articles - A Literature Review

### Velvet Antler: A Literature Review

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### Introduction

In the United States, the North American elk and red deer, members of the *Cervus* species, are farmed to produce velvet antler teas, extracts, capsules and tablets for health related products. In 1999, velvet antler was scientifically substantiated by research and clinical studies, in compliance with FDA regulations, "to support healthy joint structure and function". But its clinical applications do not stop there: due to its bioactivity and chemical components, velvet antler is likely to have much broader, and as significant, uses in the near future.

Velvet antler obtained from either the North American elk or red deer is chemically synonymous, and is utilized commercially for identical purposes. Many other countries have produced velvet antler for preparation as a traditional oriental medicine: New Zealand, Asian and European velvet antler farming produces a flourishing crop which is economically valuable, and which has been perpetuated for at least 2000 years. Currently, New Zealand produces about 450 tons of velvet antler yearly; China, about 400 tons; Russia, 80 tons, and the United States and Canada, about 20 tons each. Korea is currently the largest exporter of velvet antler, grossing up to 1.6 billion dollars (U.S.) in sales (Burgio).

Currently the use of reportedly tonic and rejuvenative medicines are enjoying increasing demand in international markets. The many conditions for which velvet antler has been used include anemia, arthritis, insomnia, amnesia, topical wounds, and pain.

In traditional medicine of the orient, red deer antler has been used to treat male impotence and female infertility. Emphasis on sexual and reproductive function has placed velvet antler in the category of aphrodisiacs. However, in traditional herbalists' terms, an aphrodisiac is not necessarily an agent that promotes libido. It is instead an agent that aids the ability of men and women to reproduce. Velvet antler has also been used as an immune modulator, erythropoietic agent, particularly in cases of anemia, and to improve blood circulation, muscle strength, and mental alertness. (Fisher et al., 1998). Velvet antler is not used solely by adults: it is estimated that about 10% of Korea's velvet antler is used for preventive and restorative purposes in children (Church, 1999).

Traditionally, different regions of the antler are used for different conditions due to a nutrient profile specifically concentrated in different parts of the antler. The tip and the middle regions are used as pediatric tonics, the upper and middle section is applied to degenerative inflammatory conditions, such as arthritis and osteo-myelitis, and the base is prepared for the elderly to increase calcium intake and reduce the likelihood that they will suffer from conditions exacerbated by calcium loss.

Empirical evidence and some clinical research suggests that velvet antler may have therapeutically valuable hypotensive, erythropoietic, immune stimulant, antiinflammatory, antiaging, metabolic, protective, and rejuvenative effects (Church, 1999). Today, velvet antler is regarded as a treatment for osteoarthritis, a possible tumor preventive, and for physical and athletic strength and endurance, in both the Orient and in western medicine.

Since the earliest velvet antler research in Russia in the 1930s, scientists and pharmacists have attempted to provide sound scientific reasoning for these reported therapeutic effects. As a result, over 250 articles have been published on the manufacture, composition, and biochemical effects of velvet antler. The information available has been recorded by Chinese, Japanese, Korean, and Russian researchers, whose information often overlaps. This review of the literature should serve to close the language barriers and fragmentation that multicultural investigation sometimes incurs. (top)

## Multicultural Use

### China

Velvet antler is regarded in China as preventive medicine. It is yang in property, and an androgenic agent. In order to understand the Chinese concept of yang and how it relates to health, it is important to note that so far Chinese medicine has differed from western medicine in that its emphasis is in prevention or restoration as opposed to the western emphasis on eliminating the offending agent. Because the Russian literature on velvet antler, as well as Japan's and Korea's, is based on Chinese concepts of health and medicine, a brief review is necessary.

Chinese medicine restores harmony between conflicting forces, in order to secure health. The practice is that of an intricate system based on complex philosophies that are thousands of years old. It utilizes herbs, physical therapies and exercises to promote health. Its primary focus is on the concept of qi, the life force, and the continual balance of the opposing natures of yin and yang within the unified system of nature.

In order to determine what is causing illness, a traditional Chinese practitioner looks for imbalances in heat/cold, moisture/dryness, and excess/deficiency of these three life forces. The causes of these imbalances are determined by five organ networks: the liver, heart, spleen, lungs, and kidneys. In TCM, when the organ networks are out of balance or are functioning in the absence of sufficient qi, illness ensues. Treatment aims to correct imbalance by providing complimentary balance in an approach similar to that of Hippocrates's, who taught that balancing the classical humors brought health. For example, if the disease is a cold condition, then the treatment uses substances such as herbs or physical therapies, to create warmth.

Chinese treatments are often used in complex and very specific formulas, taking into account the "flavors" of the ingredients and their corresponding properties and actions. The formulas are derived from plant, mineral, and animal extracts even though they are all called "herbs" and are used to treat every possible kind of ailment. In compounding them, herbal pharmacists take into account not only what disorder the medicines are to alleviate, but also how each ingredient affects others in the formula, and how the addition of certain substances can reduce or cause side effects.

The most respected medical text that contains these principles and philosophies, Pen Ts'ao Kang Mu, was written in the 16th century and discusses the use of elk and moose antler in the form of powders, pills, extracts, tinctures, and ointments. In many instances, the products were mixed with other herbs. Antler was considered a universal tonic, but also held an important place in the list of medicaments meant to produce sexual virility. Li Shih Chen, author of Pen Ts'ao Kang Mu, wrote of a pantui, or velvet antler potion, that:

If you never curbed the passions\*,  
 And squandered the ocean\*\*,  
 The magic potion of nine metamorphoses,  
 By concentrating slowly, will offer you heaven...  
 The spotted dragon\*\*\*,  
 A pearl on his brow,  
 Will restore the lower cave—  
 The portals of the jasper palace  
 \*sexual excess  
 \*\*impotence  
 \*\*\*spotted deer

The Chinese and Korean peoples have for centuries regarded the antlers of both the spotted and maral deer as being one of the most important medicinal substances available. In Korea, it is still considered valuable in the treatment of anemia, to stimulate the immune system, to treat infertility and impotence, to improve circulation in patients with heart disease, to improve muscular tone, glandular function, lung efficiency, and nerve function (Kamen, 1998).

In the early 1980's, an estimated 200,000-300,000 spotted and red deer were farmed to make medicinal products in China, with a yield of approximately 100 tons of dried deer velvet annually. Half of this was exported, and the remainder was prepared at pharmaceutical companies into products that were dispensed throughout rural and urban hospitals. In the 1980s, velvet antler was considered the second most important ingredient in TCM (the first is ginseng).

### Russia

The use of velvet antler in Russian medicine dates back to the late 1400s. There, the antlers were referred to as horns of gold. The reputed use and effect of most animal horns, including velvet antler, as aphrodisiacs goes much farther back in Eastern history, and stimulated a demand for production, which necessitated the advent of deer farming. Deer farming was introduced to Russia in the 1840s, with the Caspian red deer being the favored species for antler production. Generally, the three species used are: spotted deer (*Cervus nippon hortulorum* Swinhoe), maral deer (*Cervus elaphus sibiricus* Sev.) and Canadian deer (*Cervus elaphus xanthopygus* Milne-Eds., or wapiti). Systematic study of antler as a

medicinal raw material began in the Soviet Union in 1931 when pantocrin, an extract prepared from velvet antler, was first discovered.

## Pantocrin

Pantocrin is an alcohol extract that is light yellow, or whitish gray in pill form. It is also available as 1ml or 2ml ampules. Tablets contain 1% of extract; a 0.15g tablet is equal to 20 drops of pantocrin. Pantocrin has been prescribed internally in doses of 25-40 drops, 1-2 tablets twice daily, taken one half hour before eating. A typical course of treatment lasts from 2 to 3 weeks, but usually 3 courses are given, with 7-10 day break periods observed between courses. Dosage recommendations vary according to indication and whether or not the product is being used adjunctively.

## Japan

Lu jung is a Japanese medicine made from velvet antler that is used to rejuvenate the body and provide individuals with added energy. In the late 1960s, rulondin, a Japanese version of the pantocrin extract, was prepared by the Taiho Pharmaceutical Company (TPC) and was used as an injectable treatment for male sexual disorders. Later, the company began to manufacture pantocrin under the trade name Pantocrine, and conclusions from research performed by TPC led to the formulation of three products, pantocrin injection, pantocrin capsule, and pantocrin drink, which are used as cardiovascular agents. (Fisher et al., 1999). (top)

## Velvet Antler Processing and Composition

Velvet antler is soft growing antler tissue which is cast off every year and re-grown by *Cervus* spp (deer). In Latin, the word from which antler is derived, *anteoculae*, means "in front of the eyes," and this is where they grow, from thick, bony cores that rise from skin covered pedicels. Antlers differ from horns in that horns are permanent (Church, 1999).

## Harvest

In the wild, stags grow and cast off a set of antlers every year. Approximately 8 weeks after the antlers begin the growth cycle, they reach the most nutrient abundant growth stage and are ready to be harvested. To do this, the stags are brought into indoor pens. The deer are minimally restrained and the new antler growth is hygienically removed, cooled and frozen. (Suttie et al., 1994). Genetics is the most common cause of variation in these time tables. Velvet yield is subject to a number of intrusions, including parasites, nerve supply injury, and season (Burgio).

## Drying

Velvet antler is dried prior to its manufacture into various medicinal forms. The method of drying used to involve boiling the antlers and then allowing them to dry 60-70°C, and is sometimes referred to as preservation. In 1963, one investigator noted that the drying process increased active substances, and that the active principles in pantocrin are the phosphates, biogenic bases, amino acids and their by-products, produced in the process of preservation (Fisher et al., 1999). Studies reported by Russian chemists in 1974 (Yudin and Dubryakov, 1974) suggest that boiling antler tips destroys bioactive potential, however, and newer methods of extraction used today involve a freeze-drying process that does not include boiling water (Suttie and Haines, 1996). Additionally, a food-grade drying process has been developed by researchers at the University of Alberta (Sim and Sunwoo, 1999). Such a process is currently sought after as a means of preserving the collagen content of velvet antler, which is therapeutically active but destroyed in the heating phase of most drying methods.

## Composition & Quality Assessment

Dried velvet antler is composed of approximately 34% ash, 12% moisture, 54% organic material, of which 10% is nitrogen and 3% fat. Composition varies from species to species and with antler maturity and region of antler studies (tip, upper, middle, base) (Church, 1999).

The growing antler contains a number of necessary cells, including fibroblasts, chondroblasts, chondrocytes and osteocytes. The tips of the antlers begin as undifferentiated mesenchymal cells which are transformed into cartilage. Later, the cartilage is turned to bone, due to the effects of testosterone. Velvet antler is antler that is still in its cartilaginous stage. So far, it has been rather difficult to ensure the cartilage-versus-bone content of harvested antlers. Food, climate, time of year, age of stag and the various concentrations of substances in different regions of the antler itself, are factors that have yet to be harnessed with assurance.

## Calcification and Lipid Levels

Researchers are currently formulating specific chemical markers for the quality control of cartilaginous velvet antler products. Heavy calcification means that the antlers had begun maturing into bone, and products made from these are

downgraded pharmaceutically. Lipid levels in the velvet antler are also an important consideration in velvet antler quality, and change as the antlers mature and on the region of the antler that is under evaluation. The tip section, or wax piece, contains higher lipid, uronic acid, sulfated glycosaminoglycan, and sialic acid levels than other regions of the antler. These levels decrease moving down the antler to the middle region, which is also called the blood piece, to the bottom (bone or base) region. (Church, 1999.)

Of the bioactive substances contained in velvet antler, collagen, glycosaminoglycans, lipids (specifically polysaccharides), growth hormone and prostaglandins are of increasing interest to pharmacists and physicians.

## Collagen

The level of collagen present in harvested velvet antler is a determining factor in the age and therapeutic value of the antler. As stated earlier, lesser amounts of cartilage indicate that the antler has advanced from its pliant, growing stage into its hard, bony, mature phase. Cartilage is a visco-elastic material that has an extracellular matrix of collagen fibers, which are contained in proteoglycan aggregates. Collagen, therefore, is a primary component of cartilage, responsible for about half of the dry weight of cartilage. (Yasui and Nimni, 1988.)

The cells that make up cartilage, the chondrocytes, are fed by the distribution of nutrients through the collagenous network. Chondrocytes are highly differentiated cells that are used to synthesize a specific mix of collagen and proteoglycans to make cartilage. The material that they help to produce includes chondroitin sulfates and other glycosaminoglycans, as well as type II collagen. (Yasui and Nimni, 1988.)

Type II collagen is identified as a cartilage-specific molecule and is associated with hyaline cartilage, the most common type of cartilage. It is also necessary to the formation of elastic cartilage, the type of cartilage around the ear. In humans, hyaline cartilage comprises the transitional skeleton of embryos, which is later replaced with bone. It also covers the articular surface of the trachea, larynx, and the sides of ribs (Yasui and Nimni, 1988).

Particular chronic degenerative conditions are attributed to alterations in collagen synthesis and to changes in cellular metabolism that could precipitate such alterations. These conditions include both osteoarthritis (OA) and rheumatoid arthritis (RA). The degeneration in either case has been postulated to be caused by changes in endogenous cellular environments which inhibit human production of type II collagen, or in which the collagen itself contributes to the degeneration.

In-vitro and histologic examination of degenerating chondrocytes reveal that they produce type I collagen, a collagen associated with the formation of fibrocartilage, which is a hybrid of hyaline cartilage and connective tissue. Where hyaline cartilage and type II cartilage decrease, fibrocartilage and type I collagen tend to increase (Yasui and Nimni, 1988). As an auto-antigen, type II collagen exerts significant effects when given to RA patients. It assists T-cell production of T-helper cell-inhibiting cytokines to decrease inflammation (Kalden and Sieper, 1998). This is discussed below, in regard to the use of velvet antler in the treatment of RA.

In velvet antler, type II collagen is the primary collagen type involved in the formation of cartilaginous antler. Through a microscope, it looks like a mesh of fine fibrils. It contains high levels of hydroxylysine and also has a high glucosylation rate. (Yasui and Nimni, 1988.) Types I and X collagen also occur in velvet antler, but as with the cartilage of most vertebrates, type II is the major type (Price, et al., 1996). It is important to note that the heat involved with drying the antlers destroys velvet antler cartilage.

## GAGs

Antlers grow by endochondral ossification, the same way that long bones do. A major non-collagenous protein, proteoglycan, a protein substituted with glycosaminoglycan chains, occurs in the cartilaginous tissue of antler. While its use in the antler is not understood, it has been shown that proteoglycan in cartilage, also called aggrecan, regulates differentiation of chondrocytes and may control calcium concentration in the growth plates where endochondral ossification occurs. Immunohistochemical techniques have isolated decorin, a proteoglycan, in wapiti antler, which has a glucuronate-rich glycosaminoglycan chain. (Sunwoo et al., 1998.)

Glycosaminoglycans (GAGs), and specifically, chondroitin sulfate (CS), are of particular interest to physicians and pharmacists. Made from units of amino sugar, including D-glucosamine and D-galactosamine, GAGs bond to core proteins and form proteoglycans. Cartilage proteoglycans regulate water retention and are integral to the differentiation and proliferation of chondrocytes. The most prominent GAG in velvet antler tissue is chondroitin sulfate. As potent anti-inflammatory agents, CS and glucosamine are used today by patients who have arthritis, with excellent results (Sim and Sun-woo, 1999). Other significant types of GAG in velvet antler include keratan sulfate, hyaluronic acid, dermatan sulfate, chondroitin sulfate proteoglycan and decorin (Sunwoo et al., 1997).

Glycosaminoglycans were isolated from the tip, upper, middle and base of growing antlers. Using cellulose acetate electrophoresis, chondroitin sulfate was determined to be the major glycosaminoglycan occurring densely in the

cartilaginous tip and upper sections of the antler, along with small amounts of hyaluronic acid. The bone and bone-marrow containing middle and base antler sections also contain these compounds, and, in addition, chondroitinase-ACI resistant materials. Chondroitin sulfate in the middle and base sections of antler are of larger molecular weight than CS found in the upper section and tip of the antler (Sunwoo et al., 1997.) The average molecular size is greater in 40% ethanol, versus 50% ethanol, fraction. Finally, bone tissue, as opposed to cartilage, contains CS with larger molecular size. (Sunwoo et al., 1998.)

### CS Absorption

In the rat and the dog, plasma levels of CS rapidly increase following oral administration. Peak levels are reached at the 14th hour in the rat, and at the 28th hour in the dog. In tests, atropism of the radioactivity was observed toward glycosaminoglycan-rich tissues, such as joint cartilage. Analysis of molecular weight of radioactive material showed that compounds with a molecular weight corresponding to CS, poly-, oligo- and monosaccharides as well as of tritiated water, were present in the plasma, urine, synovial fluid and cartilage. High molecular weight fraction represented at least 10% of orally administered CS.

Some authors have noted a marked absorption of GAGs following oral administration; others describe the absorption as negligible. Negligible absorption was observed when GAGs with a high degree of sulfation were used. Heparin, the most sulfated GAG, loses its anticoagulant activity when it is administered orally. CS has a lower sulfation degree; its absorption following oral administration is more significant (Palmieri et al., 1990).

### Growth Hormone and Prostaglandins

Elk velvet antler contains significant concentrations of growth hormone precursors and prostaglandins (Fisher et al., 1998).

### IGF-I

Both insulin-like growth factor-I (IGF-I) and its receptors have been isolated from deer blood during periods of antler growth. In tests, IGF-1 and IGF-2 have been found to assist cell division in undifferentiated cells, and to speed antler growth in fibroblasts and cartilage. IGF-1 increases alkaline phosphatase and cell growth in red deer antler tips. It has been postulated that velvet antler may be a valuable source of unrefined IGF-I, and while the implications of these findings require further elucidation, IGF-I levels decline in humans as we age, with detrimental effects on muscle tissue, thus supplemental IGF-1 may have therapeutically beneficial effects in humans.

### Prostaglandins

Prostaglandins are substances with varying physiologic effects, including vasodepression, smooth muscle contraction or relaxation, inflammation and uterine stimulation. As components of velvet antler, prostaglandins may assist in the capacity of the extract to reduce the swelling associated with arthritis and injury, and with physiological responses in lipid metabolism, as seen in the cholesterol-lowering effects of velvet antler on laboratory animals and in the ability of velvet antler polysaccharides to reduce blood clotting (Church, 1999). (top)

## Indications For Use

### Osteoarthritis (OA)

An estimated 50 million North Americans suffer from osteoarthritis, a progressive disease of cartilaginous tissue. It involves the loss of proteoglycans and deterioration of cartilage. Both the collagenous matrix and bone degrade. Taking oral glycosaminoglycan-peptides (GAG-p), a therapy termed chondroprotection, may help to prevent both cartilage and bone loss by supplementing the body with proteoglycans.

It has been proposed by researchers that therapies for OA, which include anodynes and antiinflammatory agents, should include glucosamine sulfate (GS), or other GAGs &ndash; particularly chondroitin sulfate (CS). In humans, GS is a glucosamine prodrug. Following intravenous, intramuscular and oral administration, GS is distributed into bone and articular cartilage. When ingested orally, up to 90% of GS is absorbed. (Setnikar et al., 1993.)

Chondroitin sulfate has demonstrated slow but gradually increasing reduction in clinical symptoms, lasting up to three months past the end of a controlled study which followed the progress of 146 patients with knee osteoarthritis. Patients were given either diclofenac sodium, an NSAID, or CS. Clinical symptom scores were based on the assessment of the Lesquesne Index, Huskisson visual analog scale of spontaneous pain 4-point ordinal scale for pain on load, and paracetamol consumption. (Morreal et al., 1996.)

The absolute bioavailability of chondroitin sulfate after oral administration is 13.2%. This level of bioavailability in both

man and laboratory animals is consistent with other glycosaminoglycans with low sulfation. After intravenous administration of 0.5g CS to healthy volunteers, plasma level of CS decreased, according to a two-compartmental open model. Studies indicate that the metabolic fate of exogenous CS is the same for humans as is the fate of tritiated CS used in experimental animals. Intestinal absorption of both CS and high and low molecular weight polysaccharides derived from its partial depolymerization and/or desulfation has been confirmed in man. Absorption reaches its peak between the 3rd and 4th hour. (Conte et al., 1991.)

Placebo-controlled, double blind studies that demonstrate GS and CS induced benefits to OA, however, have not determined mechanisms of action. Nevertheless, as a source of chondroitin sulfate and glucosamine sulfate, velvet antler is worthy of consideration in OA therapy (Sim and Sunwoo, 1999). A glycosaminoglycan-rich antler product, GAGRA, is available for commercial use relative to the treatment of OA and arthritis (Sim and Sunwoo, 1999).

### Rheumatoid Arthritis (RA)

In RA, the synovial membrane of multiple joints are inflamed; fibroblasts in the synovium invade and damage both cartilage and bone. In addition to these synovial fibroblasts, T-helper cells may also add to a rheumatoid inflammatory response. T-helper cells are inhibited by interleukin (IL)-4, IL-6, and transforming growth factor beta (TGF-beta), but require the administration of antigens in order to enhance the secretion of these T-helper inhibiting factors while simultaneously causing oral tolerance (Kalden and Sieper, 1998).

As an antigen, collagen type II was used with success in both experimental animal trials and an open study against collagen type II RA (Trentham et al., 1994). Use was based on the fact that orally-administered collagen type II stimulates T-cell production of IL-4, IL-10, and TGF-beta and precipitates oral tolerance (Kalden and Sieper, 1998). One trial involved 60 RA patients in a double-blind setting; those given chicken type II collagen for 3 months enjoyed significant reductions in joint swelling and pain, and 4 patients claimed complete remission. The patients receiving placebo reported neither symptom reductions nor remission (Trentham et al., 1993). Collagen type II was also of significant note in the treatment of juvenile rheumatoid arthritis (JVA): after 3 months of therapy, 8 of 10 patients given oral chicken type II collagen had less pain, swelling and morning stiffness, and increased grip strength and ambulatory endurance (Barnett et al., 1996).

Oral tolerance models have been used as a method of creating antigenspecific tolerance in autoimmune diseases such as multiple sclerosis and uveitis (Trentham et al., 1993). The theory and application of oral tolerance parallels those of allergic desensitization: the allergic patient little by little, through carefully controlled exposure, becomes desensitized to the allergen until the allergy finally abates. As an autoantigen in the etiology of the autoimmune aspect of RA and the primary protein in articular cartilage, type II collagen activates T-cells and also the chronic degeneration of joint cartilage of bones. In reaction to its oral administration, T-cells generated by the immune response contain cytokines that can suppress part of the degenerative response that occurs in RA (Kalden and Sieper, 1998).

Velvet antler is a significant source of type II collagen and worthy of serious consideration in the treatment of RA. Future clinical trials conducted to determine the effects of velvet antler on T-cell production and the autoimmune factors of RA will likely support the use of velvet antler in RA.

### Immune Stimulant and Antitumor Effects

Monocytes in rats given velvet antler extracts reportedly increase (Church, 1999). Monocytes represent 3-7% of leukocytes in blood and are necessary to the immune function of lymph, spleen, bone marrow, and loose connective tissue.

Their increase may serve to enhance immune function. In subsequent studies, immune stimulant activity was ascertained. Intraperitoneal injection of pantocrin (0.5-2 mg/kg) enhanced phagocytosis and immunoglobulin levels in mice (Wang, 1996). After analysis of 8 New Zealand red deer extracts, it was determined that extracts prepared from freeze dried antlers that were harvested from the deer at days 60 or 85 had significant immune stimulant activity (Suttie and Haines, 1996). The studies of the 8 extracts used two dosage ranges, the first entailing extracts that were diluted from 500mg/ml to 62mg/ml; the second, extracts ranging from 62mg/ml to 15mg/ml. The investigators found that all extracts in the first set of dilutions carried some immune stimulant capacity, as did those in the second set, even in dilutions as low as 15mg/ml. The extracts used, however, underwent various types of processing and were obtained from various regions of the antler, so their effects were different. The extract designated as Extract E was freeze-dried and from the antler base, and was both immune stimulant and antiinflammatory, for example. The study had numerous parameters and statistical factors and investigators were unable to say which extract was the most active, nor were they able to conclude the specific mechanism underlying velvet antler's immune effects. However, it is postulated that due to cytokines in the antlers, the response is humoral, involving antibody stimulation, as opposed to being a cell-mediated response. And because of the potential for side effects pursuant to the use of any drug or supplement, it was significant to determine that even at the lowest dilution, immune enhancement was still observed. (Suttie and Haines, 1996).

## Myotropic and Neurotropic Effects

Pantocrin was observed in the late 1960s and early 1970s to have a positive effect on the endurance of laboratory animals. Pantocrin extracts increased the working capacity of mice (Brekhman et al., 1969), and these early findings led to experiments designed to study the effects of pantocrin on athletes.

In Russia, tests included one study in which subjects were given either pantocrin or rantarin (reindeer antler); results were compared to the physical exertions of a control groups of athletes. Athletes given pantocrin exhibited 74kg/m dynamic work potential on an exercise bicycle; those given rantocrine, 103kg/m. The control group performed at 15kg/m. (Yudin and Dubryakov, 1974.)

Spurred on by studies like this, Dr. Arkady Koltun, MD, chair of the Medical Committee for the Russian Bodybuilding Federation, included velvet antler in his studies of anabolic agents and their effects on muscle composition, endurance and strength. Early theorists suggested that the elevated performance levels arose from velvet antler increases in muscle restoration following exertion, and from adaptogenic properties of the velvet antler preparations, which help the body to recoup following physical, external, or biochemical challenge (Fulder, 1980). Dr Arkady's research demonstrated that velvet antler was both myotropic and neurotropic in effect.

Because these effects serve to increase muscle and nerve strength, they do tend to support early theories. Also, pantocrin enables rats and rabbits to recover quickly from whiplash-like injuries. The effect is thought to be due to increases in glycolosis, which is a necessary process in the maintenance of healthy nerve tissue. Humans with cervical injuries reportedly heal faster when administered pantocrin, as well (Church, 1999).

Despite these indications that velvet antler is myotropic and neurotropic, a 1998 study in which the strength training of the Edmonton (Canada) police recruits was supplemented with elk velvet antler (EVA) demonstrated significant increases in neither endurance nor performance. The study did show, however, that the EVA supplement significantly increased testosterone levels in blood plasma.

The nine week study intended to provide support for the hypothesis that EVA increases muscle mass and strength through anabolic effects. The rigorous training program involved both strength and endurance exercises, and recruits received either placebo or EVA. Venous blood samples were analyzed for cortisol, testosterone, insulin-like growth factor (IGF-I), and various approved physical markers were recorded before and after the 9 week period.

EVA was chosen as a trial substance in strength and endurance training because of its protein content, as athletes have increased protein needs. The proteins in EVA stay in their original form and are not degraded by heat and acids during processing. It is also a rich source of undenatured, intact branched chain amino acids, which may stimulate the increased testosterone levels noted in the results of this study. It is postulated that these amino acids, some of which are branched chain amino acids, stimulate testosterone release from Leydig cells in the testes, due to EVA-prodded signals from luteinizing hormone. Other theories suggest that EVA may block the release of testosterone from the kidneys while raising testosterone half-life, or it may bind with sex hormone binding globulin (SHBG). (Fisher, et al. 1998.)

Antler extract preparations rantarin and pantocrin both exert androgenic effects, which means that they increase the production of testosterone and its metabolites. In this capacity, velvet antler may function in a way that is similar to the supplement androstenedione, which was made famous at the end of the 1998 baseball season by record-holding batter Mark McGwire. Androstenedione is a steroid precursor produced normally by the adrenal glands and gonads, and is converted to testosterone in the liver. While no long term studies on the performance-enhancement use of androstenedione exist, manufacturers and users say that the steroid precursor helps to build muscle mass and reduce recovery time following injury (Josephson, 1998).

Furthermore, a discussion included in a report of similar study, in which velvet antler was given to male university athletes, postulates that the dosages used in tests so far may be too low (Gerrard et al.). The male university athletes received 70mg daily for 10 weeks; the dose of the EVA supplements given to the Edmonton police recruits were not included in the report of the study.

In the university athlete trial, researchers report that while results were not statistically significant in this study, there was a positive trend toward increasing athletic strength. While the study did not firmly demonstrate strength and endurance enhancement, the investigators involved note that velvet antler-induced erythropoiesis should stimulate increases in muscle mass. Further, they suggested that this effect, combined with antunflammatory effects of velvet antler and reported lactic acid removal efficiency, should enhance muscle composition, and exertional stamina and recovery time. (Gerrard et al.)

## Hypotensive

A Japanese study in which 8 out of 10 patients received pantocrin resulted in significant and transient reductions in arterial blood pressure. The systolic reading was lowered by 20 to 70 points, and the diastolic by as much as 10 to

20mmHg. Taking into account all the objective and subjective indices, pantocrin was 80% effective. Another study showed that intravenous administration of alcohol extract from Siberian deer antler at 0.85m1/kg lowers arterial blood pressure by an average of 20-23mmHg, for 126 seconds in cats and 123 seconds in rabbits. (Fisher et al., 1998).

Used intravenously at doses of 0.5-5mg/kg in cats anesthetized with 25mg Na-pentobarbital/kg, pantocrin caused an immediate drop in blood pressure, which returned to normal after two minutes. Given intravenously to rabbits that had been previously treated with atropine and physostigmine, pantocrin's effects were found to be blocked by atropine and enhanced by physostigmine. Further, cervical vagus nerve amputation did not change the effects of pantocrin on blood pressure, neither did electrical stimulation of the right peripheral vagus nerve. (Fisher et al., 1998).

In anaesthetized dogs, 1mg/kg pantocrin injection to the left femoral artery lowered blood pressure comparably to that caused by 0.2mg/kg acetylcholine. Effects were only in the left femoral artery; at 3mg/kg blood pressure lowering effects extended to the right femoral artery. Pantocrin also stimulated an increase in blood flow. Intravenous administration lowered blood pressure in both arteries, and was somewhat blocked by atropine, but did not stimulate an increase in blood flow. The researchers concluded that pantocrin acted directly on blood vessels and on the parasympathetic nervous system due to cholinergic effects. (Fisher et al., 1998.)

The extent of hypotensive effects exerted by pantocrin on humans has been reported by some investigators to be negligible if pantocrin is given in doses prescribed in Chinese medicine (0.5-1mg/kg body weight), and that at high doses (0.15g/kg) precipitate only a mild reduction in blood pressure. Discrepancies in the hypotensive response in humans to pantocrin led to an analysis of the influence of temperature in the production of the velvet antler extract. The product that had the most influential effect on blood pressure was reported to have undergone a 50% ethanol extraction at 121C for 16 hours, and the entire process included centrifuging and vacuum drying the extract. The residue was then dissolved in an NaCl solution .85m1/kg caused a 20mgHg fall in blood pressure in anaesthetized rats. (Church, 1999.)

Because freeze dried rump steak had similar effects on blood pressure, it was theorized that hypotensive effects of protein extracts are not caused by cholinergic receptor activity. Instead, it was theorized that hypotensive results obtained from intravenous administration stems from an pantocrin-induced weakening of the cells in vascular walls, due to hyperpolarization. Most researchers agree that hypotensive effects are due to choline compounds (Church, 1999).

#### Antishock

Velvet antler also demonstrates an ability to prevent or reduce both shock and stress responses. Rats given velvet antler prior to exposure to extreme temperatures and to electric shock demonstrated quicker recovery times than those that did not receive antler treatment (Kang, 1970). Tests also show that in laboratory animals, velvet antler may prevent stress-stimulated hypertrophy of the adrenal glands and involution of the thymus (Yudin and Dubryakov, 1974).

#### Miscellaneous Effects

Many other effects exerted by velvet antler on physiological processes have been described and require further, follow-up research. The polysaccharides in velvet antler may play a role in observed antiulcer effects (Wang et al., 1985). Rantarin administered before gastrointestinal surgery aided recovery (Kim and Lim, 1977). Velvet antler extracts protected the liver from carbon tetrachloride toxicity in rats (Church, 1999). Cholesterol levels were reduced in rats given velvet antler in their diets (Church, 1999).

Velvet antler may also help to treat inflammatory liver and kidney diseases in a manner similar to steroid-based pharmaceuticals. Due to its androgenic activity, velvet antler was used to determine its effects on the liver and kidney. Liver tissue already damaged with chloroform was able to recover following velvet antler treatment. It was observed in follow-up studies that protein formation in both the liver and kidney was enhanced, due to effects of velvet antler on RNS polymerase activity. (Wang et al., 1990.)

In chickens, velvet antler increased growth rate slightly, enhanced food conversion, increased weight of testes and reduced the weight of the thyroid (Church, 1999). Tip section preparations have also been observed to stimulate wound healing (Church, 1999). Erythropoiesis, increased red blood cell production, has been observed in anemic rats and rabbits given velvet antler products (Church, 1999); this finding supports the empirical use of velvet antler for anemia in humans.

Velvet extracts also slow tumor growth and demonstrate antitumor activity against Bacillus P-92, a tumor cell line, in mice (Suttie et al., 1994). Fermented velvet antler increases the survival rate of mice that have tumors, from 25-40% (Church, 1999). Polysaccharides in velvet antler may be responsible for the antiinflammatory actions of a fraction isolated from antler in the treatment of mammary hyperplasia (Suttie and Haines, 1996).

Velvet antler may also benefit the elderly through protective effects against senility. In mice, senescence-accelerated mice (SAM) given a hot water extract of velvet antler for 8 days demonstrated improvements in parameters that convey the progression of senility, compared to control mice in whom parameters remained unchanged (Wang et al., 1988). (top)

## Summary Of Biochemical Effects & Implications For Research

Research so far supports a therapeutic role for velvet antler in a number of conditions. Biological effects have been reproduced in some clinical experiments, but further research is necessary in order to determine modes of action, adverse effects, drug interactions and contraindications.

Velvet antler polysaccharides have been associated with antiulcer effects, the choline compounds to hypotensive actions. Glucosaminoglycans, glucosamine sulfate and chondroitin sulfate, have potent antiinflammatory effects and significant clinical implications in the treatment of osteoarthritis and other degenerative muscle, bone and joint conditions.

In addition, studies suggest that pep-tide growth factors, such as epidermal growth factor (EGF), may have a role in wound healing, and may be useful in the estrogen replacement therapies, since EGF supplants estrogen in genital tract development. IGF- I, luteinizing hormones and prostaglandins alter inflammatory events, muscular atrophy and androgen formation. Oxygen metabolism, blood cell formation and muscle tissue enhancement may stimulate rejuvenative and tonic actions that benefit athletes, the elderly and cardiovascular disease patients alike.

Velvet antler awaits scientific determination of its clinical efficacy in the treatment of RA. However, its collagen content indicates that its effects would be beneficial. In light of the collagen and GAG research that has been performed in clinical settings, and due to their concentrations in quality velvet antler products, velvet antler has received scientific substantiation to be marketed as dietary supplement for the support of healthy joint function. (top)

Velvet Antler Is Reputed To Be Extremely Safe.

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