PHARMACOLOGY OF VELVET

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INTRODUCTION

The earliest record (about 2100 years ago) of the use of deer products in human medicine is found on a silk scroll recently recovered from a Han tomb in Hunan province in China. The oldest **pents'ao** (c200 AD) includes references to deer velvet, hard antler and various antler glues (an extract of hard antler) (Kong and But 1985). The historical use of antler products extends through many of the Oriental countries, particularly China, Korea, Tibet and Japan. Recent published research, particularly from South Korea, Japan and the Soviet Union, has provided experimental evidence for some of the effects claimed for velvet antler preparations.

In order to avoid confusion, some common definitions are necessary: velvet refers to velvet antler, antler refers to hard antler and is also known as deer horn or Cervi cornu while antler glue refers to an extract of hard antler. However, in some cases, it appears that the term Cervi cornu may also apply to velvet (antler). The velvet antler is also known as "rokujo" in Japan or "pantui" in Russia.

THE TISSUE

The growing velvet antler is composed of a number of different cell types including fibroblasts, chondroblasts, chondrocytes, osteoblasts and osteocytes (Banks and Newbrey 1982). The growing antler tip under the epidermal/dermal layer is composed of a few millimetres of undifferentiated mesenchymal cells which start to differentiate very quickly into cartilaginous tissue. Subsequently the cartilage is replaced by bone, under the influence of testosterone and its metabolites and the velvet is shed leaving the mature hard boney antler. Consequently when velvet antler is harvested at the appropriate stage for use as a high quality product in traditional Oriental medicines, it is an actively growing cartilage type tissue and is not of uniform composition.

THE PRODUCT

The compositional changes from the tip to the base of the antler are reflected in the Chinese (Pinney 1981) and Korean (Yoon 1989) systems of classifying the parts of velvet (Figure 1). The calcium and phosphorus contents of a typical velvet antler are given in Table 1. The maturation of the antler in terms of calcification is clearly evident. Overall A grade velvet antler has a dry matter (DM) content of about 28 to 33% and calcium and phosphorus contents of 7-9% and 4-5% of the dry weight respectively.

An interesting feature of the mineral analyses is the relatively high concentrations of selenium in the antler tip regions (blood piece) of the main beam and trez tine; in samples analysed at Invermay they range from about 0.3 to 0.6 mg/kg DM compared with an overall concentration of about 0.06 mg/kg DM equivalent to a 5 to 10 fold concentration in the growing tip. On an undried tissue basis, the concentrations in the tip (0.06 to 0.12 mg/kg tissue) are higher than normal (ie, adequate) levels of blood selenium (greater than 0.01 mg/litre of blood).

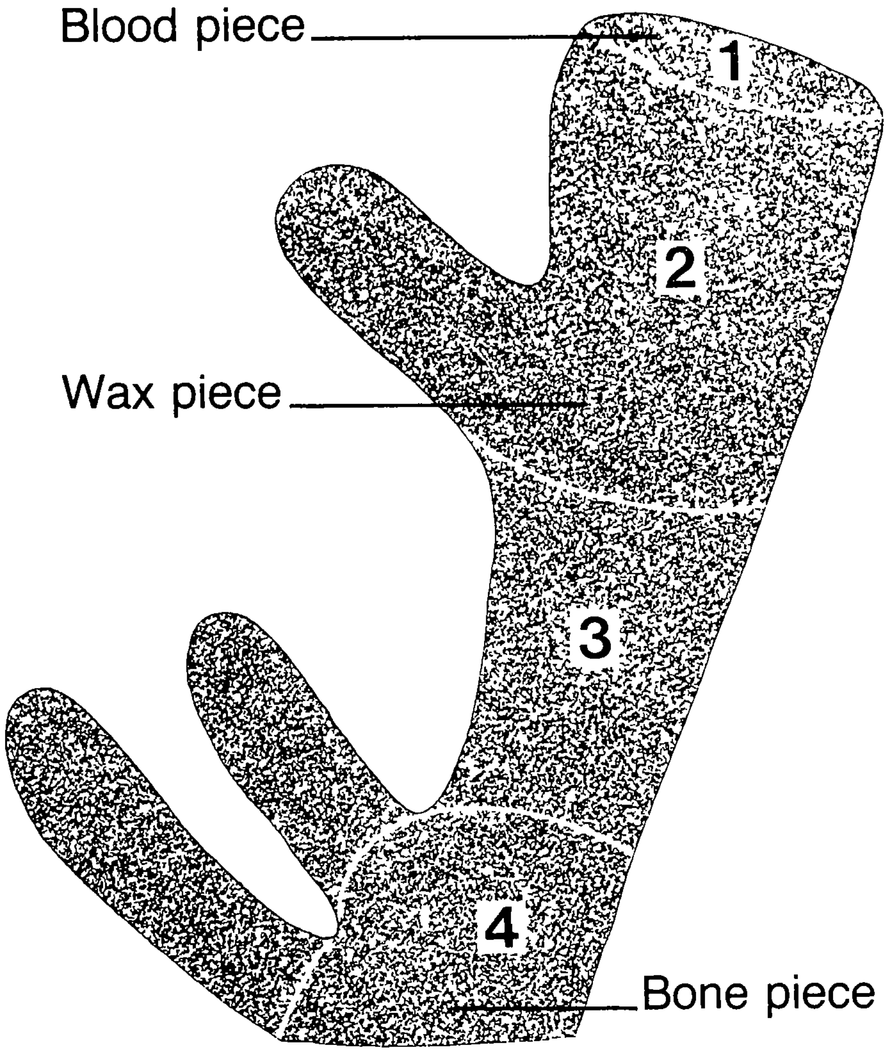

FIG 1. Oriental system for classifying the sections of the velvet antler.

TABLE 1. Calcium, phosphorus and ash contents of a velvet antler cut at the A grade stage classified according to Oriental description of the velvet antler sections.

Velvet antler section	Percentage of dried velvet antler weight	Composition (% of DM) Ca	P	Ash
1	2.2	0.18	0.62	7
2	30	5.2	3.2	27
3 - main beam	24	8.3	4.9	32
3 - brow, bez	26	6.6	3.9	30
4	18	10.3	5.9	37
Total	**100**	**7.1**	**4.2**	**30**

As a medicinal product, velvet antler is dried and prepared in a variety of different ways, much of these being based on tradition. For example, the blood may be extracted or the skin removed prior to drying; this seems to have been one of the traditional methods which protected against spoilage during the slow drying process. Velvet antler may also be immersed in boiling water and then kiln-dried, oven-dried or dried in hot air or under natural conditions.

Velvet antler may be sliced, powdered or prepared as over-the-counter preparations in pill form or as an extract such as the Russian product, Pantocrin (Kong and But 1985; Pavlenko et al. 1969). However, it seems that much of the New Zealand product exported to Korea is purchased by the Oriental medical practitioner as whole dried antler. The different sections of the antler are regarded as having particular features which are helpful for the treatment of specific complaints or in specific situations. Yoon (1989) described his method of preparation of the dried velvet as follows: the hair is first burned off and then the velvet antler is cut into sections for easier slicing and placed in alcohol for about a day; following evaporation, the velvet antler is sliced thinly for use in prescriptions. The Oriental doctor prescribes velvet as part of a mixture along with herbs and other products and it is apparently seldom used on its own.

Pantocrin is a Russian product derived from the velvet antler of spotted (sika) deer, Maral deer and Asiatic wapiti, while Rantarin is an equivalent product from reindeer. Pantocrin is an alcoholic extract consisting mainly of lipid or other fatty substances with the yield of pantocrin from dried antler being about 3%. The comparative composition of velvet antler and Pantocrin are given in Table 2 (Pavlenko et al. 1969). In this respect Sano et al. (1972) reported that Pantocrin liquid (as marketed) contained 1.5% DM plus 0.25% preservative and contained 82% lipids. According to Pavlenko et al. (1969), about one third of the lipid fraction was phospholipids, the most important being choline and ethanolamine.

TABLE 2. Comparative composition of dried velvet antler and Pantocrin (Pavlenko et al. 1969).

Component	Composition (g/100 g DM) Velvet antler	Pantocrin
Ash	39	2
Organic matter	61	98
Protein	49	6
Lipid	2.3	65
Amino acids, etc	6	20

MEDICINAL USE

The different sections of the velvet antler are used in different situations largely according to tradition (Yoon 1989). For example, the upper part (1 and 2, Fig. 1) is effective in children and young people being used as a preventative medicine; the middle part is used in the treatment of arthritis and osteomyelitis being particularly indicated in bone diseases, while the lower part is used in old people who are lacking in calcium.

Yoon (1989) notes that about 70% of velvet antler users through his clinic are children but the actual quantity they consume is very small. For example, only about 4-5 g of velvet antler is prescribed per package of medicine which contains about 60-100 g of other medicinal materials, mainly herbs. Medicines containing deer parts are consumed mostly in spring and autumn, with a one year old child taking one package per year while a 4 year old would be prescribed 4 packages per year, and an adult about 20 packages per year. The mixture is usually simmered over a low fire and served as a soup.

In traditional Oriental medicine, velvet antler is indicated for use in childbirth (to aid delivery), anaemia (particularly postnatal), arthritis, impotence and spermatorrhea and other complaints (Yoon 1989; Kong and But 1985; Pinney 1981; Ng 1982a, b).

There are also some interesting new developments, one example being the direct injection of velvet preparations into certain acupuncture points as treatment for specific complaints, a procedure known as "aqua-acupuncture". According to Yoon (1989) this can be a very effective approach requiring much lower amounts of velvet than oral treatment. Pantocin is also used clinically as an injection (Tsujibo et al. 1987).

PHARMACOLOGY

Considerable interest is now developing in the pharmacological activity of velvet antler with the traditional indications for the use of velvet providing a guide for researchers investigating possible activity.

Both the stage of antler growth (and hence the overall composition) and the method of preparation can influence the pharmacological activity of the product. Table 3 shows the biological activity of Pantocrin prepared from antlers at 7 different stages of growth. The **gonadotrophic activity** is based on the capacity of alcohol-free pantocrin to stimulate growth of the seminal vesicles and prostrate of the sexually immature male mouse. The **stimulating activity** is an index of the effect of the same product on the duration of forced exercise by mice using an endless rope system. The data indicate marked changes in both gonadotrophic and stimulating activity with both indices being maximal at about stage 3 (equivalent to early trez tine of NZ red deer or second tine in spotted deer).

Brechman (1971) notes that the evaluation of biological potency using the gonadotrophic and stimulating activity values is superior to that based on the hypotensive effect but he considers that the methods could be further improved. Using the hypotensive effect in cats and rabbits as an index of biological activity of velvet antler preparations, Tevi (1969) has shown that the preparation method can influence bioactivity (Table 4). High temperature extraction was clearly superior in this case, which raises interesting questions about the nature of the factor involved (eg, heat stability). It is possible that the effect is due, at least in part, to the actions of choline/acetylcholine. Tsujibo et al. (1987) showed that at least part of the hypotensive activity is due to lysophosphatidyl cholines (LPC) and in particular the LPC of both C14:0 and C16:0 fatty acids had very potent activities in an in vivo system using spontaneously hypotensive rats; the velvet antler extract contained very high levels of C14:0 LPC. In this respect, acetycholine given intravenously at very low doses (0.01 μg or even less) to cats lowers the blood pressure due to a direct dilatory action on the walls of certain peripheral blood vessels. When larger doses (0.01 - 0.1 mg) are injected, there is a considerable fall in blood pressure which is largely due to a vagus effect on the heart

TABLE 3. Comparative biological activity of spotted deer antlers (pantui) according to the stage of growth (Brechman *et al*. 1969).

Antler development stage[1]		Biological activity (units/g) Gonadotrophic activity	Stimulating activity
1	d 20-25	376	84
2	d 35-45	447	103
3	d 40-50	798	126
4	d 55-70	556	80
5	d 60-80	381	72
6	full velvet	212	52
7	hard antler	208	25

[1] The stages of antler development are estimated as days from casting from the description provided; stage 3 is about equivalent to a NZ red deer T grade and stage 4 to NZ red deer A grade.

TABLE 4. Effect of method of preparation of velvet antler on biological activity assayed by its hypotensive effect in cats and rabbits (Tevi 1969).

Method of preparation	Decline in blood pressure (mm Hg) Cats	Rabbits	Time (secs) for blood pressure to return to normal Cats	Rabbits
Hot alcohol (112-120°C) plus boiling water evaporation	20	23	126	123
Alcohol (38-40°C) plus vacuum evaporation (38°C)	18	6	17	15

(i.e. slowing and decreased contraction). Both effects are abolished by atropine, an inhibitor of acetylcholine action (Keele and Neil 1965). However, the LPC doses used by Tsujibo *et al* (1987) are much higher than the doses of acetycholine given above.

In animal studies, velvet antler or antler preparations have been shown to have a number of effects including the following:

gonadotrophic effects
haematopoietic effects
protection against shock/stress
recovery from liver damage
stimulation of growth
retardation of ageing
recovery from injury

The effect of velvet or antler preparations on the growth of the prostate and seminal vesicles in the immature rat or mouse is an example of the gonadotrophic effect (Brechman et al. 1969; Kong and But 1985). There is also evidence of a stimulation of spermatogenesis in chickens (Bae 1976, 1977). The haematopoietic effect is well-known with velvet preparations stimulating red blood cell synthesis and increasing erythropoietic activity in both intact and anaemic rabbits and rats (Song 1970; Yong 1964; Kim et al. 1979; Shin et al. 1979).

There is some evidence that treatment with velvet or antler preparations can protect against later shock or stress. For example, Kang (1970) reported that antler pre-treatment reduced mast cell degranulation in rats subject to heat stress, cold stress or electric shock. Also relevant is the report of Wang et al. (1985) who claimed the polysaccharide content was responsible for the anti-ulcer effect of a velvet antler preparation. Kong and But (1975) cited Russian studies showing that pre-treatment of patients awaiting surgery for gastrointestinal tumours with Rantarin resulted in a significant reduction in plasma 17-oxysteroids, an indication of a reduced stress response. Velvet antler treatment of rats has also been shown to protect against carbon tetrachloride-induced liver damage with some evidence of different responses with velvet of different sources, presumably due to the velvet being at different stages of growth (Choi et al. 1979).

Bae (1975) found that the feeding of velvet antler (equivalent to part 3 or 4 based on chemical composition; Fig. 1) to broiler chickens resulted in a small but significant increase in growth rate and food conversion efficiency over an 8 week period. Interestingly the weight of the testes was significantly increased while thyroid weight was decreased. Being an extremely fast growing tissue, it could be expected that velvet antler would be a rich source of growth factor activities, and in this respect epidermal growth factor(EGF)-like activity has been isolated from the velvet (epidermal-dermal) layer of growing antler (Ko et al. 1986).

Recent studies from Japan (Wang et al. 1988) have shown marked effects of velvet antler preparations on biochemical parameters related to ageing in senescence-accelerated mice (SAM), a murine model for senility. The hot water extract of velvet antler was administered for 8 days; treated mice showed significant improvements in parameters normally associated with senility, including an increase in plasma testosterone. The effects were generally observed only in the SAM strain and not in the control strain of mice, suggesting that velvet preparations may exert an anti-ageing effect in male senile animals. Further studies (Wang et al. 1986) revealed a direct effect on the rate of protein synthesis apparently mediated by an increase in RNA polymerase activity (RNA polymerase regulates RNA transcription from nuclear DNA).

Japanese workers have also investigated the effects of Pantocrin treatment on the recovery of rats and rabbits from an induced whiplash-type injury. Pantocrin treatment enhanced glycolysis in nervous tissue, an effect actually specific to neural tissue (Takikawa et al. 1972a, b; Kajihara and Kobuku 1971). There is also support for such effects from a double-blind study in humans suffering from cervical injuries, where Pantocrin treatment aided recovery (Ueki et al. 1973).

CONCLUSIONS

There is good evidence that velvet and velvet antler do have potent pharmacological effects. This is not surprising considering the extraordinarily rapid growth rate and differentiation of the tissue during antlerogenesis. Consequently there is considerable scope for investigations into aspects of the growth and differentiation phenomena leading to an understanding of the pharmacology and vice versa. With the increased interest from the general public and within the medical profession in traditional Oriental medicine, there is also some pressure for investigations of the claims made for traditional medicines such as velvet.

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