VELVET ANTLER : THE PRODUCT AND PHARMACOLOGY

P F. Fennessy

ABSTRACT

Velvet antler has a long history in traditional Chinese medicine. The velvet antler, when harvested at the appropriate stage, is an actively growing cartilage-type tissue and is not of uniform composition The different parts, in fact, have different traditional uses in oriental medicine. There is a developing literature relating to investigations of the pharmacological activity or bioactivity of velvet antler preparations The evidence for such activity is now very strong with convincing evidence for tonic or stimulating (performance improving) activity in both animals and humans and for androgenic/gonadotrophic effects and haematopoietic effects in laboratory animals In some cases, these effects have parallels among the medicinal plants, such as *Eleutherococcus* and ginseng. The possible mechanisms of some of the effects are discussed and directions for the future indicated

INTRODUCTION

The basis of Chinese traditional medicine is found in the ancient manuscript of Huang Ti Nei Ching Su Wen, which was probably written around 1000 BC (Veith 1966) Although deer products are not specifically mentioned in this text, the earliest record of their use is over 2000 years ago, in a silk scroll recovered from a Han tomb (Ma Wang Dui) in Hunan province (Kong and But 1985, Li Chunyi pers comm) The emphasis in traditional Chinese medicine on the promotion of health/prevention of illness is in marked contrast to that largely practised in Western medicine, which is more concerned with the treatment of ill-health (Fulder 1980a). In fact the whole tradition of traditional Eastern medicine is one of the pursuit of health rather than the treatment of ill-health (Brekhman 1980) Kaptchuk and Croucher (1987) contrast western and traditional approaches. "the medicine of the scientific tradition is a powerful one, but it reflects our limitation to an analytical view of the world that ignores many other facets of life " Brekhman (1980) uses the term pharmacosanation, meaning the pharmacology of health, in his book which is concerned with the effect of drugs, diet and pollution on health, and the possibilities for the use of prophylactics, mainly of plant origin, in the promotion of health, including the alleviation of these adverse environmental effects Brekhman's approach is summed up by his statement that "nature not only heals but, in providing man with an enormous complex of biologically active substances, gives constant prophylaxis " Partly as a result of Brekhman's and other similar work, there is an increasing interest in medicinal products which have tonic effects or effects on well-being This is one area where velvet antler has traditionally found a niche, but it has also been used in the treatment of a number of conditions including anaemia, arthritis and impotence (Kong and But 1985; Yoon 1989). The use of velvet antler as a tonic and the importance of sexual wellbeing in Chinese tradition, have resulted in velvet being regarded by Western commentators as an aphrodisiac The song from the classical Chinese Materia Medica of the 16th century (Li Shih Chen cited by Brekhman 1971) makes the case for the use of spotted deer velvet antler·

"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 "

However this reputation is unfortunate since in the western countries, it has generally resulted in velvet antler being disregarded as a serious candidate for pharmacological activity or application In this respect, it is somewhat ironic that Yoon (1989) notes that about 70% of velvet antler users through his Korean clinic are children

The different terms used to describe the various types of antler and antler products are important Velvet (*lu rong* in China or *nog yong* in Korea) refers to velvet antler, antler refers to hard antler (*lu jiao* or *nog gag* or *nag gag*, the latter being cast antler), antler glue (*lu jiao jiao*) refers to the extract of hard antler while the residual powder remaining after extraction of the glue is known as *lu jiao shuang* There are also some cases in the literature where *Cervi cornu* is used to describe all categories of antler but more specifically the term refers to hard antler. Velvet antler is also known as *rokujo* in Japan or *pantui* in Russia Pantocrin, originally a Russian product, is an alcoholic extract of the velvet antler of spotted (sika) deer, Maral deer or Asiatic wapiti while Rantarin is an equivalent product from reindeer antler

This review provides general information on the composition of velvet antler and its medicinal uses The pharmacological data are reviewed in more detail and possible research directions highlighted The deer antler, with its very rapid growth, is a fascinating tissue, and studies of both growth itself (see Suttie *et al.* 1991) and the pharmacological investigations with the accompanying search for bioactive substances will likely prove a very rewarding area There is always the possibility that the study of such a unique tissue will provide new insights into the control of differentiation, growth and metabolism in different animal systems.

COMPOSITION OF ANTLER

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 bony antler (Fennessy and Suttie 1985). 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 degree of mineralisation or calcification of the velvet antler is generally regarded as an indicator of the likely pharmacological quality, with heavily calcified velvet antler being downgraded However this is mainly dependent on the stage of growth as is indicated by the relative ash (or mineral) content in the lower portion of velvet antlers cut at different stags of growth after casting (Figure 1) The effect of stage of growth on lipid content (by ether extraction) is also shown in Figure 1 The inverse relationship between ash and lipid is clearly apparent There are also strong opinions that there is considerable variation in mineralisation between strains and species of deer at the same stage of growth but this has not been quantified The compositional changes from the tip to the base are reflected in the Chinese (Pinney 1981, Fan and Hu 1991) and Korean (Yoon 1989) systems of broadly classifying the parts of the velvet antler (Figure 2). The tip is known as *la pian* or wax piece (with the colour and texture of honey), the next section *xie pian* or blood piece, the next *feng pian* (*feng*, literally bee referring to the honeycomb appearance) and the base *gu pian* or bone piece (Li Chunyi 1991, pers comm.). There is some confusion in the recent literature (eg, Fennessy 1989, Fan and Hu 1991) as to the nomenclature of the upper two sections Once the velvet antler is harvested blood drains from the tip region very quickly, although inverting the antler will affect this; however depending on the drying methods, the dried product can have considerable blood in this section However the traditional Chinese drying methods result in the tip remaining virtually devoid of blood, hence its description as the wax piece The changes in composition down the antler, particularly the degree of calcification are apparent in Figure 3 showing the approximate composition of the four sections of a typical New Zealand red velvet antler cut at the A grade stage

MEDICINAL USES

In traditional Oriental medicine, the different parts of the antler have different uses The upper two sections are used as preventative medicines (tonics) in children and young people while the middle portion (honeycomb) is used in the treatment of arthritis and osteomyelitis (being particularly indicated in bone- and joint-related ailments) while the lower part is regarded as being of particular benefit to older people subject to calcium deficiency (Yoon 1989; Young 1990) Velvet antler is also indicated for use in childbirth (to aid delivery), anaemia (particularly postnatal), menopausal disorders, impotence and spermatorrhea (Pinney 1981, Ng 1982a, b, Kong and But 1985, Yoon 1989, Young 1990)

As a medicinal product, velvet antler is dried and processed and used in a variety of preparations. There has been considerable development in drying methods in New Zealand over the last 10 years with virtually all velvet antler now being subject to slow oven drying The actual methods are commercially sensitive

Traditional methods were generally designed to avoid spoilage during the slow drying process In some cases they included procedures for skinning the antler or removing the blood Other methods involved frequent immersions in boiling water followed by drying (using heat or in the open air), steaming of velvet antler over boiling water, steaming and scalding in hot salted water followed by drying (Brekhman 1971) Although no details were given, studies cited by Yudin and Dobryakov (1974) indicate that boiling of the antlers, one of the traditional steps sometimes used, is contraindicated in terms of its effects on pharmacological activity

There are several methods of preparing the dried antler for use, including slices, powders or extracts. Very often it is included as a minor component (by weight) of prescription medicines while over-the-counter preparations also often include velvet antler in mixtures with other traditional medicines, particularly herbs (Kong and But 1985; Yoon 1989).

PHARMACOLOGY

While the use of velvet antler in Oriental medicine has a long tradition, scientific evaluation of its purported pharmacological and bioactive effects is more recent. However the reported effects, mainly in studies with laboratory animals are now numerous, originating mainly from the USSR, but also from Korea, China, Japan and Hong Kong Much of the Russian work is concerned with Pantocrin or Rantarin

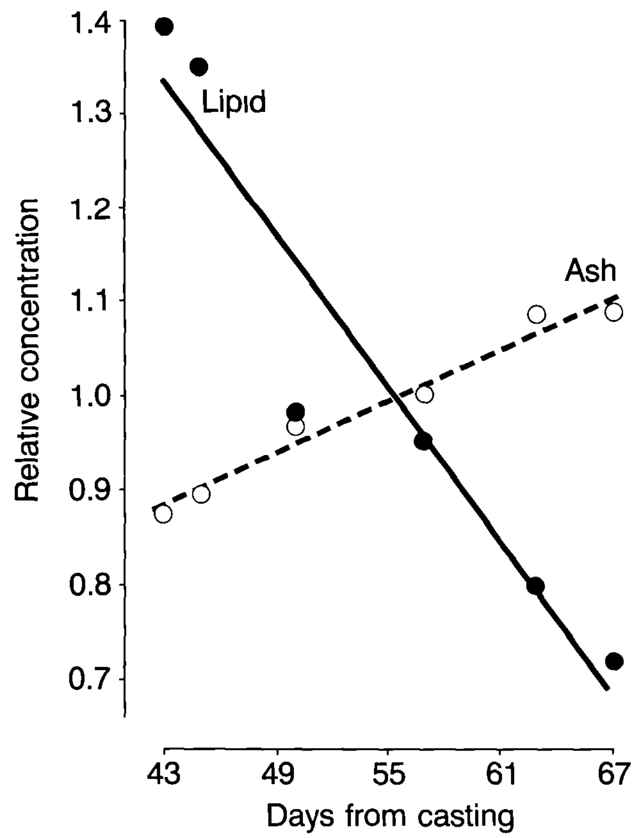

FIGURE 1. Relative concentration of total ash (O) and total lipid (●) in the base portion of velvet antler from 2 year old red deer stags expressed relative to the paired antler cut at 55 days after casting Data are for 6 pairs of antlers with one from each pair cut at 55 days and the other at 43 to 67 days after casting, relative ash = 0.0091 Days + 0.49, $r^2 = 0.96$; relative lipid = -0.0272 Days + 2.51, $r^2 = 0.88$).

Pharmacological and bioactive effects

The reported pharmacological effects and evidence for bioactivity include the following

stimulating and tonic effects
androgenic/gonadotrophic effects
haematopoietic effects
hypotensive/cardiovascular effects
anti-stress effects
growth-stimulation
retardation of aging
accelerated recovery from injury.

Traditionally velvet antler has been regarded as having tonic or general performance-improving effects on the whole body. This now has scientific backing in that a number of studies have revealed such effects in both animals and humans. For example, Brekhman *et al.* (1969) showed that pantocrin increased the working capacity of mice on an "endless rope" system following either a single dose or a 12 day course. Interestingly, the pharmacological effect of rantarin in the stimulating activity assay was only about half of that of pantocrin in studies reported by Yudin and Dobryakov (1974) However, with studies on average healthy sportsmen where static-load bearing (holding a weight at rest) and dynamic activity (on an exercise cycle) were assessed, rantarin was markedly superior to pantocrin In the studies reported by Yudin and Dobryakov (1974), control athletes on the exercise cycle performed 15 kg/m dynamic work whereas those given pantocrin increased this considerably to 74 kg/m and those given rantarin increased to 103 kg/m Similarly, athletic performance in a 3000 m run was improved following pantocrin treatment (Brekhman *et al.* 1969) Taneyeva (1969, cited by Brekhman 1971) has also shown that the mental capacity of young men was improved following pantocrin administration in a test involving a data correction procedure In this respect, the effects are similar to those reported following treatment with an extract of the plant, *Eleutherococcus senticosus*, a member of the Araliaceae, the same family as ginseng (Fulder 1980b). Like velvet antler, Eleutherococcus is not claimed to be curative but restorative Korobkov (1974, cited by Fulder 1980b) states that in respect of their use by athletes, Eleutherococcus and similar substances have "nothing in common with doping, their action is primarily aimed at accelerating the restorative processes after intensive activity and at increasing the body's resistance to unfavourable external influence." For example, a number of Russian studies in large work places have shown that an extract of the root of Eleutherococcus can reduce the incidence of influenza and acute respiratory disease and so reduce work losses due to illness (Brekhman 1980)

There is now considerable evidence for the gonadotrophic effects of velvet antler Androgens (testosterone and its metabolites) are known to stimulate the development of the seminal vesicles and prostate of the sexually immature mouse or rat, or retard the degeneration of these organs in the newly castrated animal (Martikainen *et al* 1990, Shima *et al* 1990) Velvet antler preparations (Kong and But 1985, Table 1), pantocrin (Brekhman and Taneyeva 1969) and rantarin (Yudin and Dobryakov 1974) and extracts of ginseng root (*Panax ginseng*) have all been shown to have such androgenic effects (Brekhman 1980).

The haematopoietic effect of velvet antler has been observed in a number of experiments in that preparations of velvet antler have been shown to stimulate red blood cell synthesis and increase erythropoietic activity in cases of drug-induced anaemia in rabbits and rats (and also in untreated animals) (Yong 1964, Song 1970; Kim *et al.* 1979; Shin *et al* 1979) It seems likely that such erythropoietic activity may well be responsible for at least part of the stamina-improving effects of velvet antler preparations discussed earlier. In this sense, the responses are akin to those ascribed to blood-doping where an athlete is re-transfused with his own blood just prior to competition (Burns 1990) The use of erythropoetin itself is a more direct, albeit much more dangerous, approach.

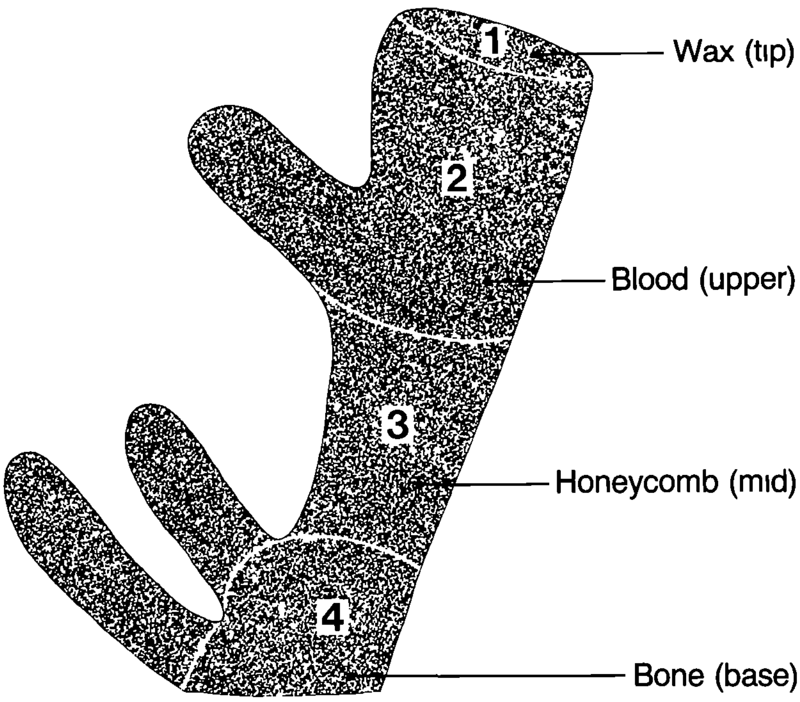

FIGURE 2 Oriental system for classifying the sections of velvet antler

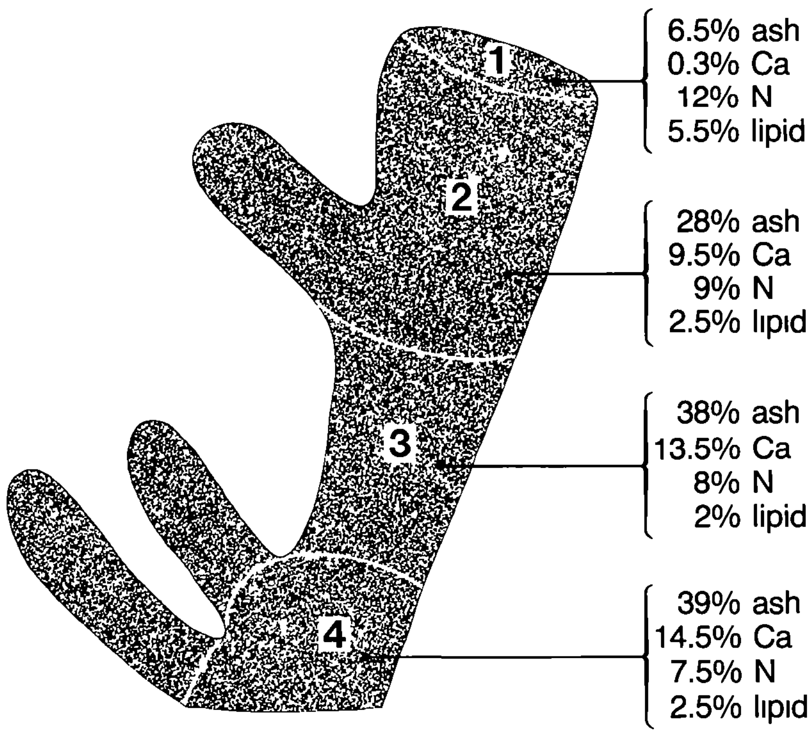

FIGURE 3. Approximate composition (ash, calcium, nitrogen and lipid content) of the four sections of a typical NZ red velvet antler cut at the A grade stage (c 55-70 days after casting) The bez tine is excluded from analysis. The tip constitutes 2 5-3.0% by dry weight, and the other three sections about one-third each.

The androgenic and haematopoietic effects of velvet antler preparations may be related. Bardin and Catterall (1981) have reviewed the role of androgens in stimulating haemoglobin synthesis Haemoglobin synthesis in the erythron can be independently controlled by both testosterone and erythropoietin in that the secretion of erythropoietin by the kidney is increased by androgens (probably through the androgen receptor) while the direct steroidal effects on bone marrow are mediated by 5ß-androgen and 5ß-progestin metabolites. Steroids with a 5ß structure are far more potent than their respective 5α epimers in stimulating haemoglobin synthesis (Congate and Solomon 1975, Levere *et al* 1967, Bullock and Besa 1981, all cited by Bardin and Catterall 1981) The potency of the 5ß steroids in stimulating iron incorporation into haemoglobin and the effect of velvet antler preparations in similar systems coupled with the androgenic effects of velvet antler indicate that investigation of the steroid composition and of the steroidogenic effects of velvet antler would be well worthwhile. Interestingly, velvet antler preparations from female reindeer also had gonadotrophic activity in the prostate/seminal vesicle growth assay although the activity was about 30% lower than that for males (Gavrin 1976) Unfortunately no data were reported from castrate reindeer in this work

An intriguing facet of the androgenic effects of velvet antler is that circulating testosterone levels are very low in stags at the time velvet antler is growing (Fennessy and Suttie 1985) The metabolites of testosterone may be important Chinese studies cited by Li and Wang (1990) indicated testosterone and oestradiol concentrations in the blood plasma which were several fold higher and lower respectively than the concentrations of these steroids in the antler tissue, strongly suggesting that the testosterone to oestradiol (aromatase) pathway is operating in the antler itself (see also Fennessy and Suttie 1985) However, overall the steroids likely to be present in the antler will be at low concentrations, and it seems unlikely that they will have direct effects themselves, a possible exception being the 5ß steroids should they be present.

TABLE 1 Effects of an extract[1] from frozen velvet antler of New Zealand red deer (*Cervus elaphus scoticus*) on the weights of the prostrate and seminal vesicles (mg/100 g bodyweight) in the immature rat (T.T Yip, K H Ng and Y C Kong cited by Kong and But, 1985)

		Prostate weight			Seminal vesicles weight		
Expt	Administration	Control	Treated	SED	Control	Treated	SED
2	Subcutaneous	46 2	62 9	4 73**	26 0	25 5	1.82^{NS}
4	Dietary	55 9	65 2	$5\ 01^{(*)}$	27 4	30 9	$4\ 06^{NS}$

[1] Extract was 0 2 ml/day of a 20% lyophilised buffer solution for Expt 2, 0 5 ml/day in Expt. 4 Treatments were for 4 days with autopsy on day 5

Pantocrin has a hypotensive effect in animals under anaesthesia The effect is transient, causing a drop in arterial pressure of up to 50%, it is blocked by prior administration of atropine, an inhibitor of acetylcholine action, and augmented by physostigmine, an inhibitor of the cholinesterases In this respect, recent work by Tsujibo *et al.* (1987) has shown that at least part of the hypotensive activity is due to lysophosphatidyl cholines (LPC), and in particular, the LPC of both the C14 0 and C16 0 fatty acids, both of which had very potent activities in an *in vivo* system using spontaneously hypotensive rats. The velvet antler extracts used in these studies had very high levels of C14 0 LPC It is also likely that in view of the distribution of choline derivatives in animal tissues that extracts of many animal tissues will exhibit hypotensive activity In this respect, Laverty (1982 pers comm) reported that a bovine muscle extract (acidified ethanol) had equivalent effects to a similar extract of velvet antler when administered to anaesthetised rats in an assay for hypotensive activity Consequently the hypotensive effect, although an interesting phenomenon, cannot be regarded as an important effect of velvet antler preparations, and does not take us further in the search for potentially new bioactive substances

The assay for hypotensive activity is the original official method devised by S M Pavlenko in the 1930's for quantifying the biological activity of antler preparations in the USSR (Brekhman *et al* 1969). The hypotensive activity assay involves intravenous administration of a prescribed dose of velvet antler extract (alcohol-free) in anaesthetised rabbits or cats, with recording of the change in arterial pressure There is apparently a very strong relationship between biological activity assessed using this assay and the lipid content of the alcoholic extract manufactured from a range of antlers (Figure 4). The relationship appears to be impressive even considering the fact that the data are mean values However analysis of the other data presented reveals that the biological activity is highly correlated with several of the extract components, including total pentose sugars and free amino acids, and for those extracts for which data were available, total free fatty acids and phospholipids (Table 2). The correlation between bioactivity of the extract and total minerals in the original antler was also strongly negative (r= -0 85; n=19)

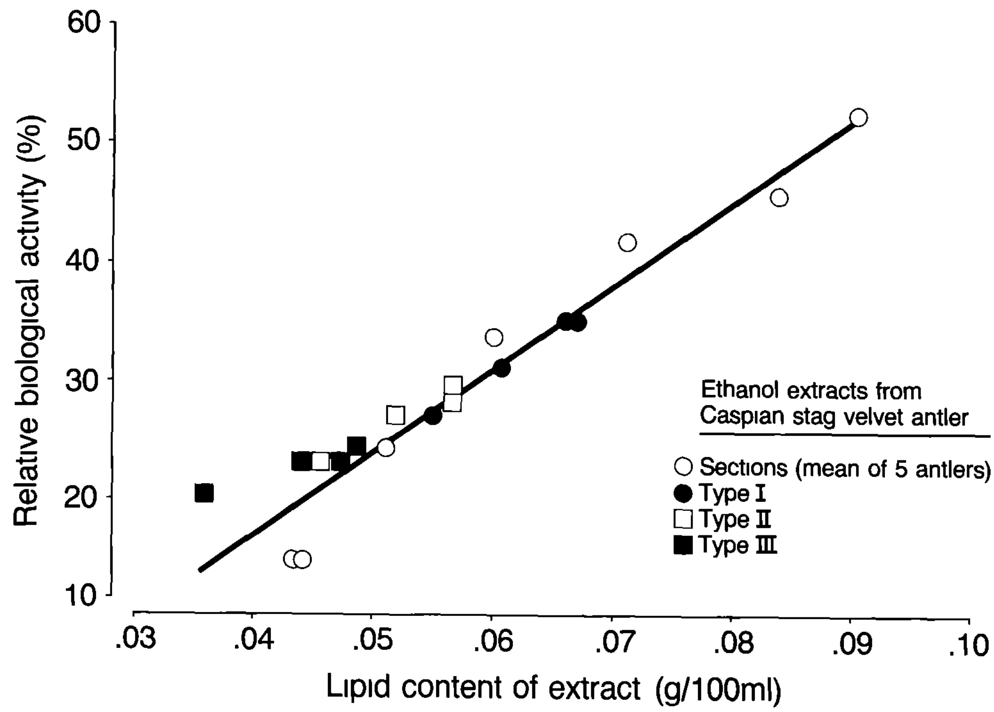

FIGURE 4. Relationship between biological activity in the hypotensive assay (% reduction in blood pressure) and lipid content of the ethanol extract of velvet antler from Caspian stags (sections of antlers refers to the mean analysis of 7 individual sections from 5 antlers, Type I antler has a rounded tip, Type III antler is overgrown with the tip of the main beam being pointed, Type II is intermediate, from Gavrin 1976)

TABLE 2. Correlation coefficients for the linear regression relationships between biological activity in the hypotensive assay and various components of ethanol extracts from the velvet antler of Caspian (*Cervus elaphus maral*) stags; data as for Figure 4

	Correlation coefficients	
	All samples (n=19)	Antler sections (n=7)
Total lipid	0 97	0 98
Phospholipids	-	0 97
Free fatty acids	-	0 97
Triglycerides	-	-0 69
Pentose sugars	0.99	0.99
Free amino acids	0 99	0 99
Organic matter	0 71	0.99

More recently, the gonadotrophic and stimulating effects assays have been used to evaluate the biological activity of velvet antler preparations in the USSR (Brekhman *et al* 1969) For example, studies cited by Gavrin (1976) indicate that velvet antler extracts from moose (*Alces alces*) and Siberian roe deer (*Capreolus c pygargus*) also have potent pharmacological activity recorded in hypotensive, gonadotrophic and stimulating activity assays Brekhman (1971) considers the newer gonadotrophic and stimulating activity assays to be superior to the hypotensive assay for evaluating velvet antler preparations and presents data comparing the three assays for *pantui* from the antlers of spotted deer (*Cervus nippon* ssp) harvested at various stages of growth (Table 3) The comparative assay data reveal a very clear pattern of biological activity which reaches a maximum at the third stage of antler development (described as "depth of flute at the second 3-cm tine" which is interpreted as the early trez tine stage) The gonadotrophic and stimulating activity assays are more discriminating than the hypotensive assay

TABLE 3. Comparative biological activity (units/g *pantui*) of velvet antler from spotted deer according to the stage of growth

Antler development stage (days)[1]		Reduction (%) in arterial pressure[2]	Gonadotrophic activity[3]	Stimulating activity[4]
1	d 20-25	18	376	84
2	d 35-45	49	447	103
3	d 40-50	52	798	126
4	d 55-70	50	556	80
5	d 60-80	50	381	72
6	full velvet	47	312	52
7	hard antler	36	208	25

[1] The stages of antler development are estimated as days from casting according to the description provided. Stage 3 is equivalent to a New Zealand TW stage and Stage 4 to NZ A/B grade

[2] Details of experimental animals not given

[3] The assay systems involve 7 dose levels (logarithmic scale) of ethanol-free pantocrin administered to 6 mice intraperitoneally for 3 days The dose (estimated from the semi-logarithmic plot of percentage change on log dose) which increases the weight of the seminal vesicles plus prostate by 33% is taken as the unit of activity The dose is then calculated as per 1 g of *pantui*.

[4] The assay procedure uses the same approach as for gonadotrophic activity, the unit of activity is that which increases the duration of exercise in the "endless rope" system by 33%.

Other pharmacological data on velvet antler have been reviewed previously (Kong and But 1985; Fennessy 1989) but some aspects are highlighted here There is 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. Yudin and Dobryakov (1974) reported that rantarin alleviated the adverse effects of an undefined stress, in that normal stress-related responses such as hypertrophy of the adrenals, involution of the thymus gland and reductions in the weight of the liver and kidneys were reduced in laboratory animals pretreated with rantarin Also relevant is the report of Wang *et al* (1985, cited by Wang *et al* 1988a) who claimed that the polysaccharide content was responsible for the anti-ulcer effect of a velvet antler preparation In this respect, Frasier *et al.* (1975) showed the developing antler cartilage matrix (of mule deer) contained strongly anionic mucopolysaccharides (possibly heparin, keratin or dermatan sulphates) which were present in the general matrix but especially prominent along the capsular margins Kong and But (1975) cited Russian studies showing that treatment of patients with rantarin prior to surgery for gastrointestinal tumours resulted in significantly lower plasma 17-oxysteroids, indicating a reduced stress response in rantarin-treated patients 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 preparations being from velvet harvested at different stages of growth (Choi *et al* 1979). Thus from a variety of sources, there would appear to be good evidence for the efficacy of velvet antler preparations in the treatment/alleviation of stress-related conditions However the development of suitable animal or *in vitro* models would be a vitally important issue in any detailed investigation of such "anti-stress" effects.

Bae (1975) found that the feeding of velvet antler (equivalent to the mid or base portions based on chemical composition, Fig. 2) 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 Recent studies from Japan (Wang *et al.* 1988a) 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. In this respect, Wang *et al* (1988c) note that the peroxidation of lipids by free oxygen radicals, the formation of malondialdehyde (MDA) and the accumulation of lipofuscin are related and may be associated with aging in animals, treatment with an ethanol extract of velvet antler (rokujo) suppressed MDA synthesis in the liver of chloroform-treated rats, suggesting that the hepatic damage caused by the increase in free radicals could be alleviated by rokujo treatment Further studies (Wang *et al* 1988b) revealed a direct effect on the rate of protein synthesis in the liver and kidney apparently mediated by an increase in RNA polymerase activity (RNA polymerase regulates RNA transcription from nuclear DNA) The studies carried out by Wang and his associates (Wang *et al* 1988a,b,c) appear to be careful and well thought out, and provide a good starting point for further work in this area Effects such as those reported by Wang *et al.* (1988b) in the kidney (and in the liver) are also produced by androgens (Bardin and Catterall 1981), again suggesting that some more intensive research directed towards the steroid-like activities of velvet antler preparations would be worthwhile

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 Kokubu 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) Li and Wang (1990) cited Chinese studies showing that treatment of rats with a velvet antler extract resulted in marked increases in the numbers of monocytes suggesting the presence of components which might affect the immune system

Drying and processing

Unfortunately there are very few published data on the effects of drying or processing methods on the bioactivity of velvet antler preparations The importance of quality control and the likely long-term importance of newer methods of quality assessment with increasing sophistication in the market place, means that the evaluation of the effects of drying and processing methods is now a priority. However the first step is to develop appropriate assay systems suitable for large scale application Gavrin (1976) cites Russian research indicating that the traditional methods of antler preparation involving dipping in boiling water followed by air or heat drying (depending on the climatic conditions) not only preserve the antlers but are also increase the content of biologically active substances During this traditional process, the temperature inside the antlers does not rise above 47-52°C and under such conditions, proteins are not fully denatured, but breakdown into small peptides and free amino acids does occur However Gavrin (1976) also cites work by Dobryakov (1968) which indicated that the biological activity of extracts from dried antlers was reduced compared with extracts from frozen antlers The comparative data presented indicate that the lipid, phospholipids, pentose and free amino acid contents of the extracts were increased by 5 to 14% while the biological activity (hypotensive assay) was increased by 10% in extracts from frozen, compared with preserved dried Type I velvet antler from Caspian stags Tevi (1969) compared a number of extraction methods on dried antlers in terms of the hypotensive effect of the pantocrin extract In this assay system, high temperature extractions (112-120°C) yielded the extracts of highest potency However, the relevance of the hypotensive activity to the overall pharmacological value of velvet antler is questionable

Unfortunately there are no available published data comparing either other assay systems or other methods of processing, particularly drying methods such as freeze-drying

MECHANISMS

Clearly the case for the pharmacological or bioactivity activity of velvet antler preparations is very strong However the critical question confronts us Is there a unifying hypothesis to explain the many and varied effects of velvet antler in animal systems? The hypotensive effect has been explained as at least partly due to the actions of choline compounds It is not unique to velvet antler Other facets of biological activity ascribed to velvet antler are not so easy to explain although Wang *et al.* (1985 cited by Wang *et al* 1988) state that the anti-ulcer effect of velvet antler preparations (rokujo) is due to the presence of certain polysaccharides. Velvet antler likely contains peptide growth factors (eg, epidermal growth factor, EGF, Ko *et al.* 1986), but the concentrations are probably very low and there must be questions about the retention of their biological activity through processing However, there is evidence that the insulin-like growth factors would survive such processing (A Skottner, pers comm to J.M Suttie) In respect of growth factors, however, EGF can replace oestrogen in the stimulation of female genital tract growth and differentiation (Nelson *et al* 1991), a phenomenon which raises some fascinating questions about the interrelationships between steroids and the peptide growth factors Steroids would survive the processing but there are apparently no systematic evaluations of the steroid composition of velvet antler published However it seems most unlikely that steroids present in velvet antler are responsible for the observed androgenic effects but rather that compounds present in the antler are inducing steroid synthesis in the treated animal presumably via effects on the hypothalamus or pituitary and then the adrenal or testis Fulder (1980b) proposed a general theory to explain the effects of these "antifatigue substances" which includes pantocrin, Eleutherococcus, ginseng and other plants such as *Acanthopanax sessiliflorum* and *Schizandra*, in that the biologically active components are generally glycosides, where the active chemical groups are linked to sugar molecules In the case of ginseng the major active compounds are triterpenoid (ie, steroid analogues) - containing glycosides whereas in the case of Eleutherococcus, the glycosides are phenolic or coumarinic Fulder proposes that the primary site of action of the glycosides is the hypothalamus and the pituitary. The most commonly used glycoside in Western medicine is digitoxin, originally isolated from the plant *Digitalis lanata* (foxglove), which has potent effects on the cardiac system The reported effects of the cardiac glycosides on the pituitary are few (Joubert 1981) although some recent work has isolated a hypothalamic digitalis-type substance with inhibitory effects on the Na^+, K^+ -ATPase system (Takahashi *et al.* 1988) This area of the glucoside/glycoside link is potentially important and one where future studies might provide strong clues as to the nature and efficacy of some of the compounds present in some of the traditional medicines of the East

DIRECTIONS

A more scientific understanding of the bioactive components of velvet antler is necessary to define the nature of the compounds and their effects in animal systems This is necessary both to define the effects of drying and processing methods on bioactivity and so maintain and improve product quality It is also necessary in the search for new bioactive compounds which may be unique to velvet antler and which could provide new insights into the control of differentiation, growth and metabolism One of the prime objectives must be to develop appropriate *in vitro* systems to assay bioactivity of velvet antler preparations This may be difficult in the sense that some of the reported effects of velvet antler would appear to be dependent on an integrated whole animal system There is also the possibility that some of the effects are due to the synergistic effects of two or more components present in the velvet antler The whole area, though clearly one of considerable complexity, is likely to be very rewarding

REFERENCES

Bae, D.S 1975. Studies on the effects of velvet on growth of animals I Effects of velvet of different levels on weight gain, feed efficiency and development of organs of chicken *Korean Journal of Animal Science 17* 571-576.

Bae, D.S 1976 Studies on the effects of velvet on growth of animals II Effects of velvet on the growth of internal organs and blood picture of chicken. *Korean Journal of Animal Science 17* 342-348

Bae, D S. 1977. Studies on the effects of velvet on growth of animals III. Effect of antler on the ability of spermatogenesis of cocks Reprinted paper source? *15*.103-109

Banks, W J. and J.W Newbrey 1982 Light microscopic studies of the ossification process in developing antlers. In *Antler Development in Cervidae*, ed R D Brown Caesar Kleberg Wildlife Research Inst., Kingsville, Texas, pp 231-260

Bardin, C W and J.F Catterall 1981 Testosterone a major determinant of extragenital sexual dimorphism *Science 211* 1285-1294.

Brekhman, I.I. 1971. Pantocrine Medexport, Moscow, 38 pages.

Brekhman, I I , Y I Dobryakov and A I Taneyeva 1969. The biological activity of the antlers of the spotted deer and other deer species. *Izvestia Sibirskogo Otdelenia Akademii Nauk SSSR, Biological Series* No. 10 (2) 112-115

Brekhman, I I. 1980. *Man and biologically active substances The effect of drugs, diet and pollution on health.* Translated by J H Appleby, Pergamon Press, Oxford

Brekhman, I.I. and A.I. Taneyeva 1969 The biological activity of the antlers of spotted deer and other species 1. Some new data on the pharmacological effect of preparations from the antlers of spotted deer. *Izvestia Sibirskogo Otdelenia Akademii Nauk SSSR, Biological Series* No. 5(1) 38-45.

Burns, H J.G 1990 Growth promoters in humans. *Proc of Nutrition Society 49*.467-472

Choi, D Y.; M.K Shin, S.I Lee, H I Lee and W H Kim 1979 A study on the effect of *Cervi Cornu* against CCl_4-induced liver damage in rats *Kyung Hee University Oriental Medical Journal 2* 43-51

Fan and Hu 1991. Assessment of velvet antler quality *Proc. Second International Wildlife Ranching Symposium,* Edmonton, Canada in press.

Fennessy, P.F 1989 Pharmacology of velvet. *Proc of a Deer Course for Veterinarians 6* 96-103.

Frasier, M B., W J Banks and J.W. Newbrey 1975 Characterization of developing antler cartilage matrix 1. Selected histochemical and enzymatic assessment *Calcified Tissue Research 17* 273-288

Fulder, S. 1980a The hammer and the pestle *New Scientist 87 (1209)* 120-123

Fulder, S. 1980b The drug that builds Russians *New Scientist 87 (1215)* 576-579.

Gavrin, V.F 1976. *The utilisation and protection of forest ungulate animals* Forest Trade, Moscow.

Joubert, P H 1981 Effects of cardiac glycosides on autonomic nervous system and endocrine glands In *Cardiac glycosides Part I, Experimental pharmacology, Handbook of experimental pharmacology* ed. K Greef, Volume 56, pp 533-550

Kajihara, M and N Kokubu 1971 Effect of *Pantui* extract (Pantocrin) on several enzyme activities of spinal nerves of rats. *Pharmacometrics 5*·741-745

Kang, W S 1970. Influence of antler (deer horn) on the mesenteric mast cells of rats exposed to heat, cold or electric shock *The Journal of Catholic Medical College 19*.1-11

Kaptchuk, T and M Croucher 1987 *The Healing arts Exploring the medical ways of the world,* Summit Books, New York, 176 pages.

Ko, K M , T T. Yip, S W Tsao, Y C Kong, P F Fennessy, M C Belew and J Porath 1986 Epidermal growth factor from deer (*Cervus elaphus*) submaxillary gland and velvet antler *General and comparative endocrinology 63* 431-440

Kong, Y C and P.P H. But 1985 Deer - the ultimate medicinal animal (Antler and deer parts in medicine) In *Biology of Deer Production*, ed P F Fennessy and K R Drew Royal Society of NZ Bulletin 22, pp 311-324

Li, C. and W Y. Wang 1990 Review of studies on the effective compounds of velvet antler *Chinese special wild economic animal and plant research 4*.19-22

Martikainen, P., N Kyprianou and J.T. Isaacs 1990 Effect of transforming growth factor-ß, on proliferation and death of rat prostatic cells *Endocrinology 127* 2963-2968.

Ng, C.K 1982a An introduction to anti-cancer medicines and prescriptions In *Tak Tai Ginseng Firm Limited, Health Manual* Tak Tai Ginseng Firm Ltd, Hong Kong, pp. 61-73

Ng, C K 1982b. Common diseases among all ages In *Tak Tai Ginseng Firm Limited, Health Manual* Tak Tai Ginseng Firm Ltd, Hong Kong, pp 84-92.

Nelson, K G ; T Takahashi, N L Bossert, D K Walmer and J A McLachlan 1991 *Proc National Academy of Sciences, USA 88* 21-25.

Pavlenko, S.M ; A B Silayev, L A Filippova and V S Kiselyov 1969 Some data on the chemical properties of Pantui and Pantocrin In *Pantocrin*, Second publication, part II, ed S.M Pavlenko, p 18-22.

Pinney, B 1981 Delegation to China *The Deer Farmer* (Spring) p 22-35

Shima, H , M Tsuji, P Young and G R Cunha 1990 Postnatal growth of mouse seminal vesicle is dependent on 5α-dihydrotestosterone *Endocrinology 127*·3222-3233.

Shin, M K , S.I Lee, W H. Kim and H.I. Lee 1979 Effect of deer horn on the iron bone marrow in experimentally induced anaemic rat *Kyung Hee University Oriental Medical Journal* 2·69-72

Song, S K 1970 Influence of deer horn on erythropoietin activity and radioactive iron uptake in rabbits *The Journal of Catholic Medical College 18* 51-63.

Suttie, J M , P.F. Fennessy, M Sadighi, J L Elliot; I D. Corson and K R Lapwood 1991 Antler growth in deer. *Proc. of a Deer Course for Veterinarians 8*

Takahashi, H ; M. Matsusawa, K Suga, I Ikegaki, M Nishimura, M Yoshimura, N Ihara, H Yamada and Y. Sano 1988 Hypothalamic digitalis-like substance is released with sodium-loading in rats *American Journal of Hypertension 1* 146-151

Takikawa, K ; N. Kokubu, N Tahara and M Dohi 1972a Studies of experimental whiplash injury. II Evaluation of Pantui extracts, Pantocrin as a remedy *Folia Pharmacol Japon. 68* 473-488

Takikawa, K , N Kokubu, M. Kajihara, M Dohi and N Tahara 1972b Studies of experimental whiplash injury. III. Changes in enzyme activities of cervical cords and effect of Pantui extracts, Pantocrin as a remedy *Folia Pharmacol Japon 68*:489-493

Tevi, A S 1969. The influence of temperature factors on the pharmacological activity of extracts from antlers In *Pantocrin*, Second Publication, Part II, ed S M Pavlenko

Tsujibo, H , Y Miyake; K Maruyama and Y Inamori 1987. Hypotensive compounds isolated from alcohol extract of the unossified horn of *Cervus elaphus* L var *xanthopygus* (Rokujo)1. Isolation of lysophosphatidyl choline as a hypotensive principle and structure-activity study of related compounds *Chem Pharm Bull* 35·654-659

Ueki K, S Sato, T. Tsuchida, Y. Sugiyama, A Otsuka, H. Nemoto, S Sano, K Tazawa, N Okada, T Shinohara; K Yamada, K Tomita, K. Suzuki; M Yabuki, T. Kurosaka; M Sato and K Kono 1973. The evaluation of the pantocrin injection to the so-called *hitting wounds* by the matched pair multiclinical trial methods *Journal of the Advances of Medicine (Igaku no ayumi) 86*·230-237

Veith, I 1966 Translation of *Huang Te Nei Ching Su Wen· The Yellow Emperor's Classic of Internal Medicine,* Univ of California Press, Berkeley and Los Angeles

Wang, B X., X.H Zhao, S.B Qi, S Kaneko, M Hattori, T Namba and Y Nomura 1988a Effects of repeated administration of deer antler extract on biochemical changes related to aging in senescence-accelerated mice. *Chem Pharm Bull 36*.2587-2592

Wang, B.X.; X.H. Zhao; S B. Qi, X W. Yang, S.Kaneko, M Hattori, T Namba and Y Nomura 1988b Stimulating effect of deer antler extract on protein synthesis in senescence-accelerated mice *in vivo* *Chem Pharm Bull 36* 2593-2598

Wang, B X., X H Zhao, X W Yang, S Kaneko, M Hatori, T Namba and Y Nomura 1988c Inhibition of lipid peroxidation by deer antler (Rokujo) extract *in vivo* and *in vitro* *Journal of Medical and Pharmaceutical Society for WAKAN-YAKU 5* 123-128

Yong, Y I 1964 The effect of deer horn on the experimental anaemia of rabbits *Journal Pharmaceutical Society Korea 8*.6-11

Yoon, P. 1989 Velvet pharmacology *Proc 14th NZ Deer Farmers Conference*, p 11-13

Young, L M. 1990 Health plan: do you take deer horn with any understanding of it? Translation of article from Korean Airlines Magazine, p 106-107

Yudin, A M and Y I Dobryakov 1974 A guide for the preparation and storage of uncalcified male antlers as a medicinal raw material In *Reindeer antlers*, ed I I Brekhman. Academy of Sciences of the USSR, Far East Science Centre, Vladivostock Translated by M Chapin, Inst of Arctic Biology, University of Alaska, Fairbanks