

Deer antlers: traditional Chinese medicine use and recent pharmaceuticals

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Abstract. Deer velvet antlers (VA) have been used as a type of traditional Chinese medicine for over 2000 years, mainly for treating yang-deficiency syndromes. However, VA still largely remain a traditional remedy with scant science, although getting more attention as time goes. In recent years, our group has been trying to develop some efficacious drugs/functional food based on unique biological phenomena of VA, such as, for example, dead tissue (hard antler base) being attached to living tissue (pedicle) for over half a year without causing inflammation, a large-size wound (up to 10 cm in diameter) being left on top of a pedicle stump after previous antler casting healing within a week only with a negligible scar, and severely osteoporotic skeleton caused by intensive antler calcification fully reversing after the completion of antler calcification. Successful translation of these unique phenomena to clinical use would greatly benefit human health.

Additional keywords: animal physiology, animal production.

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Introduction

Deer velvet antlers (VA), known as ‘Lu Rong’ in Chinese, are a common ingredient in traditional Chinese medicine (TCM). According to reports, there are more than 500 TCM prescriptions containing VA, which is considered the number-one animal-derived TCM (Kong and But 1985). Prescriptions containing VA can be traced back to the first Chinese Materia Medica, ‘Shennong Bencao Jing’ (~100 AD; Fig. 1a). However, use of VA appears to have been infrequent until deer were raised on farms, starting in the mid-16th century in China (Ming Dynasty period). In his *Compendium of Materia Medica* (Fig. 1b), Li Shizhen wrote that VA is good at reinforcing the kidneys to strengthen yang, promoting essence production, enriching blood, supplementing the marrow, and invigorating bone health. Within the TCM system, VA is prescribed by a doctor to a patient for treating yang-deficiency syndromes. In Asia, VA is dried and sold as whole sticks (Fig. 1c, d), slices (Fig. 2a) or powder (Fig. 2b). The slices are then either put in water and boiled with other herbs, and consumed as a medicinal soup (Fig. 2c), or in alcohol and used as aqueous alcohol extracts (Fig. 2d). The powder can also be encapsulated (Fig. 2e, f) and consumed as a nutritional dietary supplement.

Although VA remains a traditional remedy with scant science, its health claims are currently under intensive investigation through modern molecular biology, including, for example, transcriptomics, proteomics and metabolomics, and using *in vitro* and *in vivo* models and modern analytical

facilities. Besides the use of VA in TCM, more recently, western-style pharmaceuticals derived from VA have been under development by our group in China, based on the antler's unique biological phenomena. Three types of pharmaceuticals, which our laboratory is developing from VA, are described here.

Hard antler base-derived substances to reduce inflammation of glandular organs

Each year, antlers (or antler buttons if velvet antlers have been removed during their growth phase for TCM use) die due to full calcification in autumn (Goss 1983). Interestingly, the deer's immune system does not sequester these dead tissues, but, rather, allows them to remain firmly attached to the living pedicle tissues until the spring of the following year (Li *et al.* 2004), a period that exceeds half a year (Fig. 3). Macroscopic and microscopic examinations have shown that there are essentially no detectable inflammatory cells accumulated along the line (Fig. 4) between dead tissue (hard antler base/button) and living tissue (pedicle; Li *et al.* 2005). Further research has found that hard antler bases/buttons are very rich in anti-inflammatory factors, such as, for example, IL4, IL10 and IL13, and can effectively inhibit expression of pro-inflammatory factors, such as TNF- α , IL-1 β and IL-6 (Q. Quan, H. Zhao, D. Wang, Z. Wang and C. Li, unpubl. data), which may explain why these dead tissues can be tolerated by the living tissues, without causing inflammation and sequestration. *In vivo* experiments have shown that extracts from antler button-derived powder (ABDP) can effectively



Fig. 1. Chinese Materia Medica, and commercially processed sika deer velvet antlers. (a) Shennong Bencao Jing. (b) Compendium of Materia Medica. (c) Er Gang (two-branch antler). (d) San Cha (three-branch antler).



Fig. 2. Commercially available velvet products in Chinese markets. (a) Slices. (b) Powder. (c) Slices in the soup. (d) Slices in alcohol. (e) Powder in soft capsules. (f) Powder in hard capsules.



Fig. 3. Cycle of production of hard antler buttons in commercial Chinese deer farms. (a) A standard three-branch sika velvet antlers. (b) Velveting by using a saw under local anaesthesia. Note that a 3–4-cm-high base (arrow) of the velvet antler was left on top of the pedicle after velveting. (c) The velvet antler base (arrow) on top of the pedicle in the autumn. Note that the button has become completely hard and dead. (d) Hard button (arrow) on top of the pedicle in the spring of the following year. Note that the button is going to cast from the attached pedicle.

ameliorate or even cure inflammation of some glandular organs, including hyperplasia of mammary glands, mastitis, mumps and prostatitis. Recently, we tested ABDP extracts on hyperplasia or mastitis of mammary glands in laboratory mice and achieved satisfactory results (Q. Quan, H. Zhao, D. Wang, Z. Wang and C. Li, unpubl. data). For example, administration of ABDP extracts significantly reduced hyperplasia of mammary glands, and the effects surpassed those of the currently used Western medicine, tamoxifen, in a clinical setting (Fig. 5). Currently, new drugs have

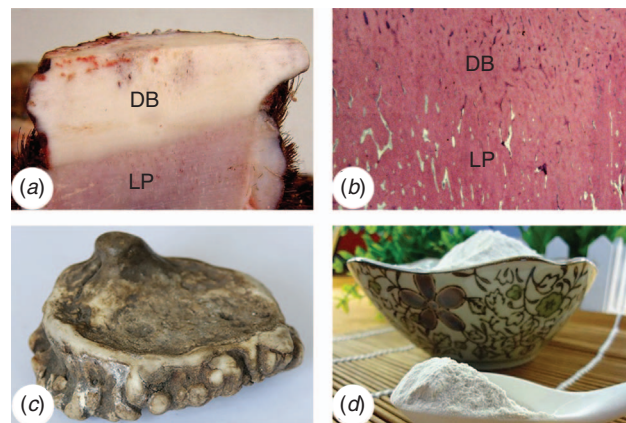


Fig. 4. Histological examination of the junction between the dead button and the living pedicle; cast button and button powder. (a) Macroscopic photo showing the junction between the dead button (DB, white colour) and the living pedicle (LP, pink colour). (b) Microscopic photo showing the junction between the dead button (DB, channels filled with dark red-coloured blood) and the living pedicle (LP, no fillings detected in the channels). (c) Cast button. (d) Ground button powder.

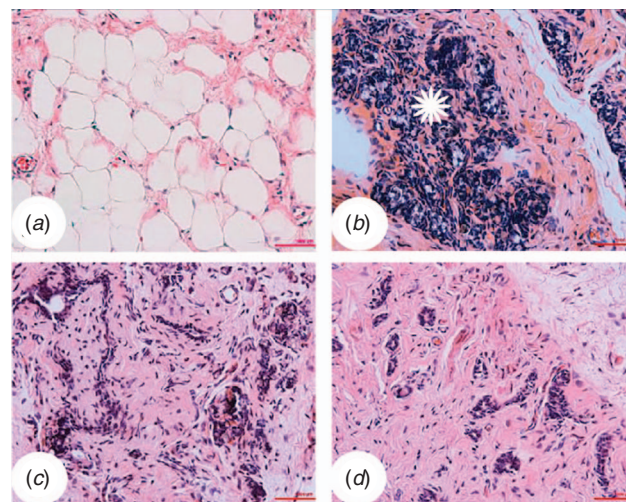


Fig. 5. Effects of hard button extracts on hyperplasia of mammary gland in rats. (a) Healthy mammary-gland tissue. (b) Hyperplastic mammary-gland tissue induced by lipopolysaccharides. Note that hyperplastic acini occupies most of the area of the gland (asterisk). (c) Hyperplastic mammary-gland tissue treated with two phenoxamine. Note that the degree of hyperplasia is significantly reduced. (d) Hyperplastic mammary-gland tissue treated with antler button extracts. Note that the degree of hyperplasia is significantly reduced, and the effect was even greater than in the group treated with normally used western medicine, two phenoxamine, in clinics.

been under development on the basis of the discovery of this unique phenomenon (firm attachment of dead tissue on living tissue) and laboratory findings for treating inflammation of glandular organs in clinics, particularly chronic inflammation.

Antler stem cell-derived substances to induce regenerative wound healing

Casting of a hard antler/antler button leaves a huge wound (which can be up to 10 cm in diameter in northern American wapiti) on the top of a pedicle, in each spring (Fig. 6a).

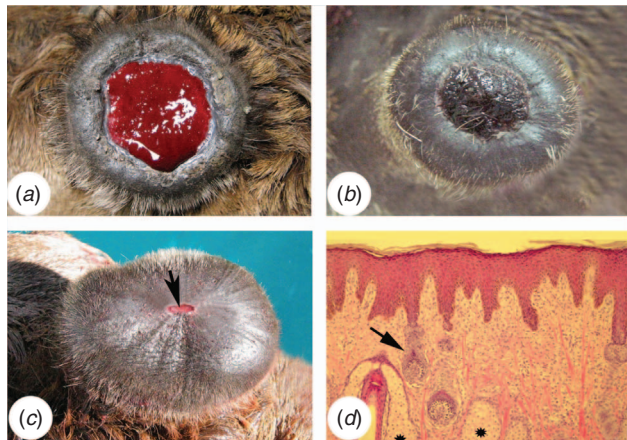


Fig. 6. Wound healing over the top of a pedicle stump. (a) A pedicle stump immediately after the hard button has been lost. Note that fresh blood covers the casting surface. (b) Casting surface on top of a pedicle stump a couple of days after hard antler/button dropping off. Note that distal pedicle skin has migrated centripetally and almost covers half of the entire wound. (c) Casting surface on top of a pedicle stump 6–7 days after hard antler dropping off. Note that wound healing, at this stage, is nearly complete (arrow). (d) Histological section of a sagittally cut healing skin. Note that the skin contains hair follicles (arrow) at different developmental stages.

Astonishingly, this large mammalian wound not only heals within a week, but also leaves behind only a negligible scar (Fig. 6b, c; Li *et al.* 2004). Histological examination has shown that this healing is a regenerative process (Fig. 6d; Li *et al.* 2014). A combination of tissue deletion and transplantation experiments demonstrated that this regenerative wound-healing property relies solely on the existence of the closely wrapped pedicle periosteum (Li 2012), and that the cells from the pedicle periosteum have stem-cell attributes (Li *et al.* 2009). Therefore, these cells have been termed antler stem cells (ASCs; Li *et al.* 2009). Injection of ASCs into rats can help punch-biopsy wounds achieve regenerative healing (Fig. 7). Furthermore, topical application of the conditioned medium from ASCs on wounds can give healing results (Fig. 8) similar to those obtained from ASC injections (Rong *et al.* 2019). New drugs are currently under

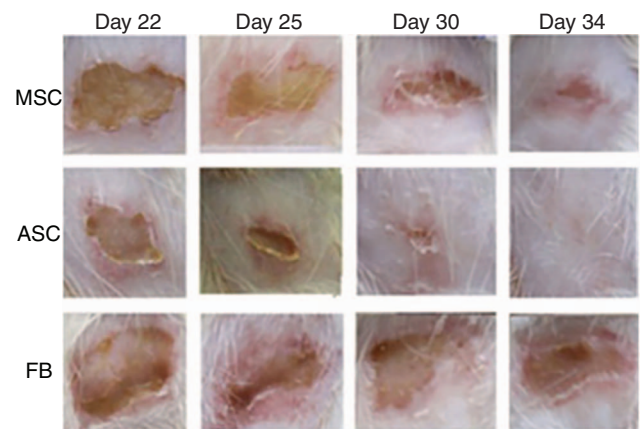


Fig. 7. Effects of antler stem cells on rat wound healing. Note that, on Day 34, wound healing in rats injected with antler stem cells (ASC) is almost complete, whereas in rats with human mesenchymal stem cells (MSC), a quarter of the size of the original wound still remains, and, in rats with fibroblasts (FB), more than half of the size of the original wound remains.

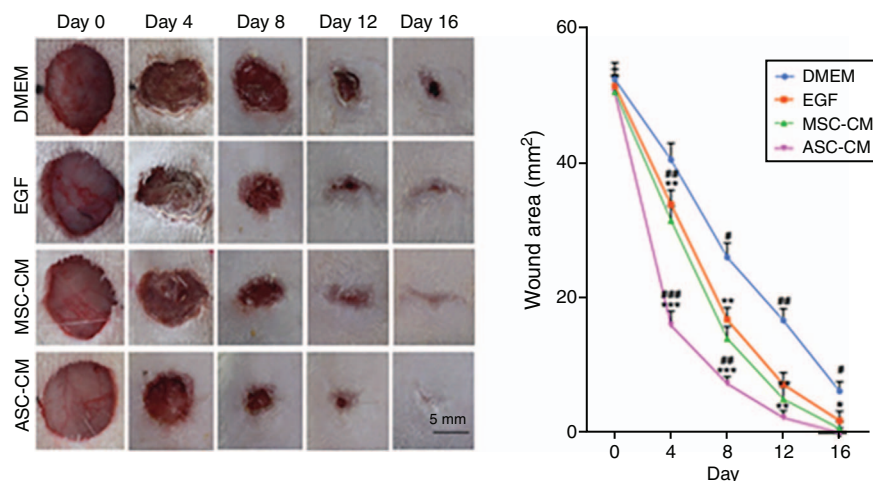


Fig. 8. Effects of antler stem cell-conditioned medium (ASC-CM) on rat wound-healing rate. Overall morphological changes observed during the wound healing are shown, as are changes in wound area during healing. Note that the fastest wound healing rate and the smallest wound area occurred in the ASC-CM group. NC, negative control (DMEM); PC, positive control (EGF); MSC-CM, mesenchymal stem cell-conditioned medium.

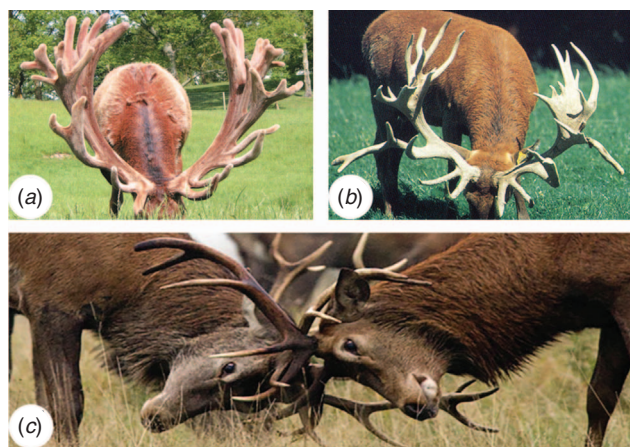


Fig. 9. Red deer antlers and fighting behaviour. (a) Full size of velvet antlers in late summer. (b) Hard antlers in autumn. (c) Deer fighting in the rutting season (autumn).

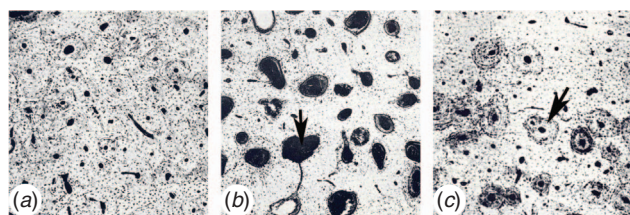


Fig. 10. Histological sections of adult deer sternal bone. (a) Sampled before antler intensive ossification. Note that the well defined osteons are evenly distributed in the bone. (b) Sampled during antler intensive ossification. Note that minerals have been seriously absorbed from the bone around haversian canals and have left many holes (arrow, black colour) with different sizes. (c) Sampled after antler intensive ossification. Note that the holes caused by the loss of a large quantity of minerals due to antler intensive ossification had been essentially refilled (arrow).

development in various clinics, on the basis of this unique phenomenon and the laboratory findings, so as to achieve of scar-less wound healing.

Deer blood-derived substances to reverse osteoporosis

Each year, a mature male deer can grow antlers of up to 30 kg (Fig. 9a), and these antlers must be fully mineralised to become hard in autumn to serve as weapons during the rutting season (Fig. 9b), as males in the rutting season fight fiercely for dominance (Fig. 9c). Research has found that, so as to supply such a huge quantity of calcium in a short period, the entire deer skeleton is subjected to severe osteoporosis. Surprisingly, the severely osteoporotic status of deer skeleton is fully reversed back to normal before the rutting season starts (Fig. 10). The mechanism involved in this reversal of osteoporosis is not fully understood, but irrespective of what the mechanism is, the ability to fully reverse osteoporosis in mammals is unique to deer. This phenomenon is in sharp contrast to the situation in human bones where, once the osteoporotic process starts in aging people, the most effective anti-osteoporotic drugs currently

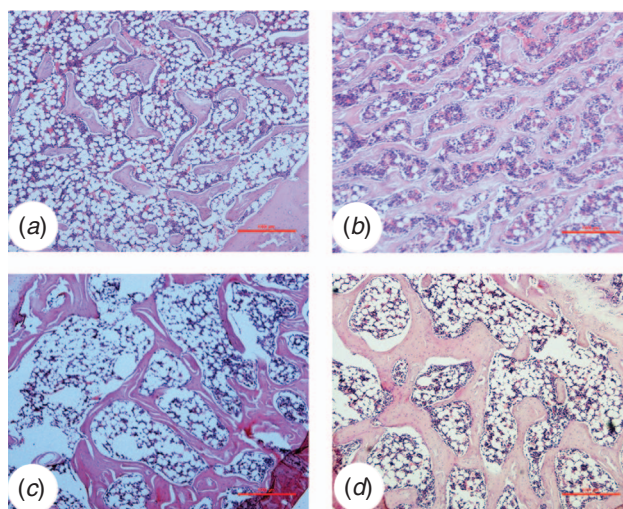


Fig. 11. Histological sections of rat bones, showing effects of the extracts of deer tissue sampled during the reversal period of deer bone osteoporosis from (a) sham-operated rat, (b) ovariectomised rat, (c) ovariectomised rat, but which was subsequently treated with oestrogen; note that oestrogen has significantly restored the collapsed trabeculae; (d) ovariectomised rat, but which was subsequently treated with deer-tissue extracts; note that the extracts have significantly restored the collapsed trabeculae, and the effect is comparable to that of the oestrogen-treated group.

available cannot completely stop it and bring the bone density to normal level (Compston *et al.* 2019). Intragastric administration of the substances derived from deer tissue collected during a special period (commercially sensitive) has been shown to effectively ameliorate the usually inevitable osteoporosis of ovariectomised rats (Fig. 11). On the basis of this unique phenomenon and laboratory findings, new drugs are under development for treating human osteoporosis.

Conflicts of interest

The author declares no conflicts of interest.

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