

YUNNAN BAIYAO-WHERE'S THE CLINICAL EVIDENCE? © 2006

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Introducing Yunnan Baiyao or Yunnan Paiyao

Herbology is one branch within the field of integrative, or complementary and alternative, veterinary medicine (CAVM). With the growing interest around integrating these techniques into daily practice, veterinary herbology is gaining attention. One patent Chinese herbal formula, called yunnan baiyao or yunnan paiyao, is commonly utilized to stop bleeding, promote wound healing and relieve pain (18,19,20,27).

Translated as “White Medicine from Yunnan Province” (3,9,12,27), it was developed in the Yunnan Province of China over 80 years ago. A variety of anglicized spellings for this product exist, including:

- yun(n)an baiyao, yun(n)an bai yao, yu(n)nan bai-yao, yun nan bai yao, yun nan bai yao wan
- yun(n)an paiyao, yun(n)an pai yao
- yunnan paiyou, yunnan payao, yunnan piao, yunnan paiao
- hunnan pai yao

The exact herbal formula for yunnan baiyao is not completely clear. The formula is reported to be a ‘highly guarded secret’, but is variably labeled to contain some of the following, suspended in a potato starch base (3,9,15,22,27,29,30):

- pseudoginseng/san qi**/tien chi/tian qi/tian qi ginseng
(*Panax pseudoginseng*, *Panax notoginseng*, *Radix pseudoginseng*, *Radix notoginseng*)
- chinese yam root/Shan Yao (*Dioscorea opposita*)
- wild yam root (rhizome)/Chuan Shan Long (*Dioscorea hypoglauca*, *Dioscorea nipponica*)
- sweet geranium (aerial parts)/Lao Guan Cao (*Erodium stephanianum*, *Geranium thunbergii*)
- galangal (lesser) rhizome/Gao Liang Jiang (*Alpinia officinarum*)
- ox gall bladder/Bai Niu Dan
- borneol/Bing Pian

To the unaided eye, yunnan baiyao appears to be a uniform tan colored powder with a sweetly pungent odor. Microscopic examination reveals a granular nature to the powder, with brown or reddish particulate matter included (15). A 10 mg/ml water-based solution of yunnan baiyao yields a pH of 4.7, and biochemical tests have revealed high concentrations of polysaccharides (starch 97.4%) and elemental calcium (1%) in the yunnan baiyao powder (14,15).

How does Yunnan Baiyao affect hemostasis?

Normal hemostasis requires **platelet function** to form an **initial platelet plug** (primary hemostasis), and functional **coagulation factors** (intrinsic and extrinsic coagulation pathways) forming **fibrin** to stabilize the platelet plug (11). The platelet function, and therefore the ability of the body to perform primary hemostasis, is evaluated clinically by analyzing platelet numbers, platelet aggregation and the buccal mucosal bleeding time (BMBT), also known as template bleeding time (TBT). The efficacy of the coagulation factors, and therefore the intrinsic and extrinsic coagulation pathways, is evaluated by activated coagulation time (ACT), activated partial thromboplastin time (APTT) and prothrombin time (PT). The role of these normal mechanisms is important to prevent excessive blood loss and the subsequent consequences (23,24,26).

Historically, when faced with significant ongoing blood loss, equine practitioners have resorted to intravenous formaldehyde in non-sedated and anesthetized horses (7,16). This technique is not proven to have significant effects on coagulation variables and is associated with dose-dependent side effects in standing, awake horses (21). Regional injection of formalin has been used to stop bleeding and cause sloughing of large, vascular lesions in horses (8). This technique has also been reported to cause

significant side effects (4). Therefore, other clinically simple, inexpensive and effective options to minimize blood loss would be ideal.

Herbal therapies can be used to augment hemostasis when necessary. Yunnan baiyao is one Chinese herbal formula reported to stop bleeding or minimize blood loss in a variety of species (3,6,18,20), including humans. This herbal formula was even carried historically by foreign soldiers as a traumatic hemostatic agent (12,15). In the author's experience, use of yunnan baiyao has allowed patients to return home earlier than without any hemostatic therapies. Preoperative use of yunnan baiyao may decrease the need and the cost for blood products. This would decrease the potential difficulties and side effects of blood replacement and minimize the physiological stresses associated with blood loss (23,24). Many studies have confirmed the positive hemostatic effects of yunnan baiyao. A variety of traditional mechanisms for the positive hemostatic actions of yunnan baiyao have been proposed, including **shortened bleeding times** (5,13,14), an **increased permeability of platelet membranes** resulting in a release of platelet constituents (1,2), and **shortened clotting times** (10,13,14).

Primary hemostasis of small vessels involves **platelet function**, not the coagulation factor cascade, in the formation of the platelet plug. In vitro rat platelets have been shown to degranulate in a dose-related fashion in the presence of filtered extracts of yunnan baiyao, perhaps by increasing the permeability of the platelet membrane (1,2). This action during platelet release has long been recognized as one of the mechanisms of action of platelet function inducing blood coagulation (11). Clinically, (buccal or template) **bleeding times** are an indicator of platelet function in the role of primary hemostasis. The effect of yunnan baiyao on the platelet function decreased the time needed for primary hemostasis, as indicated by the shortened bleeding times from incised liver lobes after in vivo, **topical** administration of yunnan baiyao in pentobarbitone anesthetized rats (13). Preoperative, **oral** administration of yunnan baiyao to rats also resulted in decreased bleeding times from incised liver lobes within 1 hour of administration and these effects lasted for a minimum of four hours (14). Another study demonstrated that preoperative, **oral** administration of yunnan baiyao caused a significant decrease in the template bleeding time in healthy ponies under halothane anesthesia (5). This confirms that the positive hemostatic action of yunnan baiyao occurs, in part, via an effect on the platelets (primary hemostasis).

The **formation of fibrin** involves **the cascade of coagulation factors** and mediators, allowing the platelet plug (formed during primary hemostasis) to be stabilized. The **clotting time** allows practitioners to easily assess the function of the intrinsic and common pathways of the coagulation cascade. In vitro clotting test using bovine blood demonstrated a reduction in clotting time associated with the use of yunnan baiyao (10). **Topical** administration of yunnan baiyao decreased the in vitro clotting times in blood taken from pentobarbitone anesthetized rabbits and awake humans (13). A dose-related shortening of in vivo clotting time was seen within 30 minutes after preoperative, **oral** administration in pentobarbitone anesthetized rabbits, and these effects lasted for a minimum of four hours (14). In addition to augmenting primary hemostasis, the hemostatic effects of yunnan baiyao may be related to pathways of the coagulation cascade, as indicated by shortened clotting times in these studies.

Other proposed mechanisms for the hemostatic effects of yunnan baiyao include **peripheral vasoconstriction** (13,14), a **particle/precipitant effect** of the polysaccharide base (13,14), or a **calcium mediated effect** (13). The high levels of starch and calcium may partially account for the hemostatic effects of yunnan baiyao, especially when applied topically. To simulate this action of yunnan baiyao, the effect of starch and starch plus calcium solutions were tested on bleeding times and clotting times in two studies. Neither topically administered starch (13), nor orally administered starch (14), at an equivalent dose (by weight), caused a decrease in bleeding times in rats. Topically administered starch plus calcium did shorten the bleeding time in rats (13). In the same study, **topically administered yunnan baiyao** caused a **greater shortening in bleeding time (in vivo) compared to topical** administration of **starch plus calcium** (13). Also, yunnan baiyao **significantly shortened the in vitro clotting time in rabbit blood and human blood when compared to starch or starch plus calcium** (13). Therefore, it is unlikely that the high levels of starch and calcium, contained in commercially available yunnan baiyao, significantly account for the hemostatic actions when administered orally or topically.

Yunnan baiyao is also thought to have **antimicrobial** and **anti-inflammatory** properties (9,20,25,27), although these claims are debated (15). Arasaponin A/B and dencichine, reported to be in the primary components of yunnan baiyao, have anti-inflammatory effects according to one study (28). However, clinical trials evaluating the analgesic effects of this herbal formula have not been published in the Western literature. Another study showed **in vitro cytotoxic effects** of some of the saponin extracts of yunnan baiyao, leading to the possibility of anti-neoplastic effects (16). Anti-neoplastic effects have not been evaluated in vivo, to the author's knowledge.

In terms of Traditional Chinese Medicine (TCM), yunnan baiyao stops bleeding by removing or **dispersing stagnant blood**, which blocks vessels and obstructs the normal path of blood flow. It also tonifies, invigorates and regulates blood via the Liver (9,22,19).

The **positive hemostatic effects** of yunnan baiyao are **well documented**, and although the exact mechanism remains unclear, an **augmented platelet effect** seems to play a role. The oral and/or topical (in vivo) administration of yunnan baiyao to rats, rabbits and horses has not been associated with adverse side effects in studies (5,14). However, **long-term effects of chronic yunnan baiyao use have not been described** in Western medical terms (18,19). Chronic use of yunnan baiyao is not recommended, as it could exhaust the Fire and/or Yin of the individual. The author has used longer term, **pulsed therapy** (ie 1 week on, 1 week off; 4 days on, 3 days off; dosing M-W-F only, etc.) when necessary, especially if no other viable options are feasible. Mild to moderate elevations in liver enzymes (ALP, ALT, AST) have been anecdotally reported with long term use of yunnan baiyao. However, these patients often have received multiple other traditional or non-traditional therapies, or have diagnoses that in and of themselves can be associated with elevations in liver enzymes.

How is Yunnan Baiyao used?

Yunnan baiyao has been used clinically, both **orally and topically**, in everything from birds to elephants. It has been useful for (but not limited to) internal and external bleeding tumors, sheared nails/hooves, surgical bleeds, epistaxis/nasal procedures, gastrointestinal hemorrhage, abdominal trauma, disseminated intravascular coagulation (DIC), avian bumblefoot, VWD and/or thrombocytopenic patients, aural hematomas, oral/dental surgery and spays in estrus.

As with many herbal therapies, **dose ranges** of yunnan baiyao are poorly defined and widely variable. Dosing is often 'to effect' and may vary depending on the cause of the bleeding. The following dose recommendations have been gathered from a variety of sources, including VIN postings, the CAVM list discussions, textbooks and continuing education talks:

- Dog:** open capsule and sprinkle on superficial wounds, bleeding tumors, etc.
 - one (250 mg) capsule per 10 kg, once to twice a day
 - one capsule per 5 kg daily, given as divided doses, if possible
 - ¼ tsp per 5-7 kg, OR 60-75 mg/kg, at least once a day
 - 75-100 mg/kg daily, given as divided doses
 - <15 kg = 1 capsule P.O. twice a day
 - 15-30 kg = 2 capsules P.O. twice a day
 - >30 = 2 capsules P.O. three times a day
- Cat:** open capsule and sprinkle on superficial wounds, bleeding tumors, etc.
 - ½ -1 capsule P.O. twice a day, adjusting appropriately
- Horse** (500kg): open capsule and sprinkle on superficial wounds, bleeding tumors, etc.
 - 1 bottle (4 gm), or 16 capsules, P.O. three times a day as an oral slurry in water
 - 2 bottles P.O. twice a day for six days, then 1 bottle twice a day for six days
- Birds** (400-1000gm): open capsule and sprinkle on superficial wounds, bleeding tumors, etc.
 - one (250 mg) capsule dissolved in water, given by oral gavage, once a day

How do I get Yunnan Baiyao?

Yunnan baiyao is a **widely available** herb, via mail order or in local Asian markets and health food/co-op stores. When purchasing Chinese herbal formulas, it is important to buy from reputable

retailers; the quality and contents of herbal formulas can vary greatly and heavy metal contamination is a very real possibility.

Yunnan baiyao is an **inexpensive** herb. It is available in foil sheets of 16 gelatin capsules (250mg each), with 5 sheets in a box. This box costs less than US\$10 from most retailers. It is also available in 4 gm bottles of loose powder, which are equivalent to one foil sheet of 16 capsules (9,12,22). Each 4 gm bottle or each foil sheet of 16 capsules comes with one small, red 'safety pill' which is about the size of a peppercorn. This very potent form of yunnan baiyao, called Bao Xian Zi [or "insurance pill for a serious or emergency case" (12)] is equivalent to one 4 gm bottle or 16 capsules of yunnan baiyao. It is unclear as to whether the ingredients of this 'safety pill' are exactly the same as the yunnan baiyao capsules. One reference notes that the components are different, but does not state what those components are (12). Research on the Bao Xian Zi is not documented in the Western literature (searches via PubMed, Medline, etc).

Summary

Yunnan baiyao is an inexpensive, patent Chinese herb known for its positive hemostatic effects in the face of active hemorrhage. A variety of traditional mechanisms for the action of yunnan baiyao have been proposed, including shortened bleeding time, shortened clotting times, reduced capillary permeability, peripheral vasoconstriction, an increased permeability of platelet membranes resulting in a release of platelet constituents, a calcium mediated effect, or a particle/precipitant effect. Most studies seem to indicate an enhanced platelet (primary hemostasis) or coagulation factor effect. Some of these mechanisms and the contents of yunnan baiyao are defined by research, but many open questions remain regarding its use in companion animals. Preoperative use of yunnan baiyao may decrease the need and the cost for blood products. This could decrease the potential difficulties and side effects of blood replacement and minimize the physiological stresses to the patient and the veterinary staff associated with blood loss.

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What is the dose of Yunnan Baiyao?

(Compiled from "Yunnan baiyao-where's the clinical evidence?" © 2006 presented at the 2006 SAVMA Symposium; Lynelle Graham, DVM, MS, Diplomate ACVA; University of Minnesota College of Veterinary Medicine, Department of Veterinary Clinical Sciences)

A variety of traditional mechanisms for the action of yunnan baiyao have been proposed, including shortened bleeding time, shortened clotting time, reduced capillary permeability, peripheral vasoconstriction, an increased permeability of platelet membranes resulting in a release of platelet constituents, a calcium mediated effect, or a particle/precipitant effect. Most studies seem to indicate an enhanced platelet (primary hemostasis) or coagulation factor effect.

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15-30 kg = 2 capsules P.O. twice a day
>30 = 2 capsules P.O. three times a day
- Cat:** open capsule and sprinkle on superficial wounds, bleeding tumors, etc.
½ -1 capsule P.O. twice a day, adjusting appropriately
- Horse:** open capsule and sprinkle on superficial wounds, bleeding tumors, etc.
1 bottle (4 gm) P.O. three times a day with water
2 bottles P.O. twice a day for six days, then 1 bottle twice a day for six days
- Birds** (400-1000gm) open capsule and sprinkle on superficial wounds, bleeding tumors, etc.
one (250 mg) capsule dissolved in water, given by oral gavage, once a day