

Bleeding Risks from Herbs

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Failing to inquire about what herbs an animal has received *before* surgery could lead to bleeding disasters *during* surgery. Specifically, botanicals that interfere with clotting could transform an otherwise routine surgery into a frustrating and lengthy exercise.ⁱ

A false sense of security

While the true clinical impact remains clouded by lack of controlled research in both veterinary and human patients,ⁱⁱ this paucity of safety information may be creating a self-perpetuating cycle of false-negative information.ⁱⁱⁱ The unregulated and untested nature of veterinary plant-based products amplifies uncertainties over product strength, potential misidentification, adulteration, and species-specific or idiosyncratic variations in drug metabolism or effects.^{iv} In particular, products with a multiplicity of ingredients, such as Chinese herbal formulations, especially when administered chronically, exhibit a disproportionately greater percentage and severity of side effects, compared to single herb supplements.^{v vi vii} Harmful drug-herb interactions involving mixtures of herbs heighten the hurdles of identifying the source of the interaction. Mechanisms by which herbs may influence bleeding include direct pharmacologic actions and indirect interactions.^{viii} Indirect (namely, herb-drug) interactions involve either pharmacodynamic or pharmacokinetic influences.

Antiplatelet effects of herbs

Veterinary patients ingesting herbs for longstanding conditions such as arthritis and cancer build higher blood levels. Arthritis remedies typically interfere with arachidonic acid metabolism and therefore may likewise inhibit platelet aggregation, either by inhibiting platelet activating factor (PAF) binding or by limit production of other mediators, such as thromboxanes, adenosine, or prostaglandins.^{ix} Bleeding tendencies increase when taken in conjunction with non-steroidal anti-inflammatory drugs (NSAIDs) or acetaminophen.^x Implicated herbs include ginkgo (*Ginkgo biloba*), garlic (*Allium sativum*), ginger (*Zingiber officinale*)^{xi}, and ginseng (*Panax ginseng*); known as the “4 G’s”. Others include meadowsweet (*Filipendula ulmaria*), willow bark (*Salix alba*), dong guai (*Angelica sinensis*), turmeric (*Curcuma longa*), bilberry (*Vaccinium myrtillus*), and feverfew (*Tanacetum parthenium*).

Warfarin-herb interactions

Concerns multiply when patients receive warfarin. Originally derived from the sweet clover plant, warfarin interferes with the ability of vitamin K to form the vitamin K-dependent coagulation factors II, VII, IX, and X, as well as the anticoagulant proteins C and S.^{xii xiii} Achieving

optimal therapeutic concentrations requires close monitoring; multiple challenges make it difficult to maintain stable prothrombin international normalized ratios (PT-INR). Many factors alter INR's, including pharmacogenomic expression of enzyme activities affecting drug metabolism, dietary vitamin K intake, other medications, patient age, the presence of comorbid diseases, and herbs.^{xiv xv} Coumarins appear ubiquitously in green plants, though some herbs antagonize vitamin K more strongly than others.^{xvi} Lists of herbs have drawn concern; popular plants in veterinary products include angelica, arnica, bromelain, chamomile, corydalis yanhuso, danshen, devil's claw, fenugreek, feverfew, garlic, ginger, ginseng, green tea, licorice, meadowsweet, papain, passionflower, red clover, reishi mushroom, skullcap, turmeric, and willow bark.^{xvii} Although ginseng appears here, the term "ginseng" actually refers to several species, each with different amounts anticoagulant compounds.^{xviii} Paradoxical effects are also possible; one study showed that American ginseng actually *reduced* warfarin's anticoagulant effect.^{xix}

Avoiding surprises

It may a week to restore normal hemostasis after stopping garlic, 1.5 days after ginkgo, and 24 hours after ginseng.^{xx} It seems prudent, therefore, for veterinary patients to refrain from anticoagulant herbs at least several days before elective surgery.

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