

brain tissue and improves cerebral metabolism. O<sub>2</sub> utilization in the brain may be improved and age-related changes in the animal hippocampus may be prevented.

- Additional studies indicate that ginkgo reversibly inhibits MAO-A and MAO-B, inhibits

acetylcholinesterase, and decreases adrenal benzodiazepine receptors.

- Studies have shown that coadministration of warfarin with GBE or ginkgolide B (a platelet activating factor antagonist) influenced blood coagulation parameters. Ginkgo and its extracts

were shown not to affect the clearance of warfarin enantiomers, suggesting that the herb does not significantly influence CYP1A2, CYP3A4, or CYP2C9 activity.

Assessment Points			
System	Effect	Assessment by Hx	PE
HEENT	Increased ocular blood flow	Bleeding	Mucosal bleeding
CV	Vasodilation		BP/HR
HEME	Inhibition of platelet aggregation	Bleeding, bruising	Mucosal bleeding Petechiae
GI	N/V, diarrhea		
CNS	Increased cerebral blood flow Headache	Headache	
DERM	Contact dermatitis	Exposure	Rash

**Key References:** Jiang X, Williams KM, Liauw WS, et al.: Effect of ginkgo and ginger on the pharmacokinetics and pharmacodynamics of warfarin in healthy subjects, *Br J Clin Pharmacol* 59(4):425–432, 2005; Yeh KY, Pu HF, Kaphle K, et al.: *Ginkgo biloba* extract enhances male copulatory behavior and reduces serum prolactin levels in rats, *Horm Behav* 53(1):225–231, 2008 (epub 2007); Marcilhac A, Dakine N, Bourhim N, et al.: Effect of chronic administration of *Ginkgo biloba* extract or Ginkgolide on the hypothalamic-pituitary-adrenal axis in the rat, *Life Sci* 62(25):2329–2340, 1998.

### Perioperative Implications

#### Preoperative Concerns

- Outside of potentially increased risk of bleeding, periop concern with ginkgo intake revolves around drug interactions.
- Minimal data on effects in pregnancy, breastfeeding, and pediatrics.
- Many pts do not account for alternative medicines when asked for medication lists by their physician.
- Inhibition of platelet aggregation can result in significant intraop bleeding; thus ginkgo should be D/C at least 36 h before elective surgery.

#### Monitoring

- Routine

#### Airway

- Avoid nasal intubation to minimize intranasal bleed.

#### Preinduction/Induction

- Avoid excessive hypotension with induction agents because ginkgo's subtle vasodilatory effects can further decrease BP; effects on the adrenal receptors minimize a normal stress response. Hence prolonged and excessive hypotension can jeopardize perfusion of vital organs.

#### Maintenance

- Side effects can be amplified with concomitant use of interacting drugs. Such concerns include bleeding, hypotension, seizures, sedation, serotonin syndrome, and cholinergic crisis.

#### Extubation

- No known concerns

#### Postoperative Period

- Avoid administering classes of drugs that may interact with ginkgo and potentiate its effects, as previously mentioned.

#### Novel Therapies

- Can improve cerebral oxygen supply, decrease cerebral oxygen extraction rate and consumption, reduce cerebral oxygen metabolic rate, and maintain balance of cerebral oxygen supply and demand in elderly pt with preexisting cerebral ischemia.
- May ameliorate neuropathic pain by scavenging reactive oxygen species, contribute to hypersensitivity neuropathic pain.

## Ginseng

James G. Hilliard | Jeffery R. Kirsch

### Uses

- Ginseng has been used for more than 2000 y in Chinese herbal medicine for a variety of proposed health benefits.
- Used as an adaptogen, it is believed to increase the body's resistance to stress and fatigue.
- Known to have antistress, antifatigue, antiviral, antifungal, antineoplastic, neuroprotective, and antihyperglycemic effects

### Perioperative Risks

- Ginseng blocks morphine in a non-opioid-dependent manner.
- Ginseng has the ability to lower postprandial blood glucose in both pts with diabetes type 2 and nondiabetic pts.
- Ginseng may promote bleeding in surgical pts. Ginsenosides (the active ingredients) in American ginseng have been shown to inhibit platelet aggregation. Studies in lab rats show prolongation of the coagulation time of thrombin and activated partial thromboplastin. One study suggests that the antiplatelet activity of panaxynol, a constituent of ginseng, may be irreversible in humans. Given these findings, it may be prudent to recommend that pts discontinue ginseng use at least 7 d prior to surgery.

### Worry About

- Reduced efficacy of opioids and unpredictable dosing requirements of analgesics.
- The development of hypoglycemia, especially in diabetic pts taking insulin or oral antihyperglycemic agents.
- May have additive effects when used with corticosteroids and may intensify the side effects of corticosteroids.
- May lead to development of headache, tremors, and manic episodes when used in pts receiving MAO inhibitors such as phenelzine.
- Interferes with the pharmacodynamics and drug-level monitoring of pts taking digoxin and may increase digoxin levels.
- May increase the risk of surgical bleeding owing to its antiplatelet effects and inhibition of the coagulation cascade.
- May have estrogen-like effects and should be avoided in pregnant or breastfeeding women and in children. Avoid the use of ginseng in pts with hormone-sensitive conditions, such as breast cancer, uterine cancer, or endometriosis.
- Consumption can increase and/or decrease BP. Caution should be used in those with hypertension or hypotension.

### Overview

- *Ginseng* refers to several species of the genus *Panax* and comprises a family of plants (American ginseng, Asian ginseng, Chinese ginseng, Korean red ginseng, *Panax ginseng*; *Panax* spp., including *P. ginseng* C.C. Meyer, and *P. quinquefolius* L., excluding *Eleutherococcus senticosus*).
- Dietary supplements are typically derived from American ginseng (*Panax quinquefolius*) or Asian ginseng.
- Siberian ginseng (*Eleutherococcus senticosus*) is a different genus and does not contain the ingredients believed to be active in the two forms used in supplements.
- Ginseng can be taken as fresh or dried roots, extracts, solutions, capsules, tablets, sodas, and teas; also used as a cosmetic agent.

### Drug Class/Mechanism of Action/Usual Dose

- The active ingredients in American ginseng are panaxosides (saponin glycosides). The active ingredients in Asian ginseng are ginsenosides (triterpenoid glycosides).
- Most of the pharmacologic actions of ginseng are attributed to the ginsenosides belonging to a group of compounds known as *steroidal saponins*.

**Drug Effects**

System	Effect	Test
CV	Tachycardia, palpitations, Htn with other cardiac stimulants, edema	HR, BP
HEME	Decreases effectiveness of warfarin, inhibits coagulation cascade	INR, PT, PTT
NEURO	Excessive use: Somnolence, hypertonia, nervousness, and excitability mania in pts on phenelzine Reduces analgesic effect of morphine	
ENDO	Hypoglycemia	Blood glucose
GYN	Mastalgia, postmenopausal bleeding	Hct

**Key References:** Volger BK, Pittler MH, Ernst E: The efficacy of ginseng: a systematic review of randomized clinical trials, *Eur J Clin Pharmacol* 55(8):567–575, 1999; Tokuyama S, Takahashi M: Pharmacological and physiological effects of ginseng on actions induced by opioids and psychostimulants, *Japan J Pharm* 117(3):195–201, 2001.

**Perioperative Implications****Preoperative Concerns**

- Check coagulation studies; monitor blood glucose.

**Monitoring**

- Standard

**Induction**

- Increased amounts of opioids may be required to blunt adrenergic response to intubation.

**Airway**

- No specific concerns

**Postoperative Concerns**

- Monitor blood glucose level, monitor for signs of excessive postop bleeding.
- Increased amounts of opioids may be required to manage postop pain.

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**Glucosamine Sulfate**

Bridget Perrin Pulos

**Uses**

- For pain associated with OA, particularly of the knee
- IBD
- Other inflammatory disorders, such as rheumatoid arthritis, psoriasis
- Possible benefits for wound healing and prevention of migraines

**Perioperative Risks**

- No convincing evidence of increased periop risk owing to glucosamine therapy
- No known significant interactions with commonly administered anesthetic drugs

**Worry About**

- Potential increase in INR in pts on warfarin who initiate glucosamine therapy, or increase glucosamine dose

**Overview**

- Available without a prescription in North America.
- Classified as a food additive, not regulated by the USA FDA, made from crustacean skeletons.
- As monotherapy, little consistent evidence of therapeutic effect.
- Often used in combination with other drug supplements, such as chondroitin.
- In combination with chondroitin, may prolong the time to total knee replacement in those with severe OA.
- Side-effect profile is indistinguishable from placebo and better than that of NSAIDs.
- High oral bioavailability with substantial first-pass metabolism, freely diffusible with a 28- to 58-h half-life.

**Drug Class/Mechanism of Action/Usual Dose**

- Glucosamine is a component of the extracellular matrix of articular cartilage, found naturally in the body.
- Recommended oral dose is 1500 mg/d or 500 mg 3 times per d.
- Precise mechanism of action of glucosamine is unknown; thought to aid in cartilage repair, normalize cartilage metab, and have mild anti-inflammatory properties.

**Assessment Points**

System	Effect	Test
HEME	May potentiate warfarin or increase risk of bleeding when taken with other drugs that increase risk of bleeding	PT/INR if pt is on warfarin
ENDO	No consistent effect	Glucose if otherwise indicated

**Key References:** Fransen M, Agaliotis M, Nairn L, et al.: Glucosamine and chondroitin for knee osteoarthritis: a double blind randomized placebo-controlled clinical trial evaluating single and combination regimens, *Ann Rheum Dis* 74(5):851–858, 2015; Altman RD: Glucosamine therapy for knee osteoarthritis: pharmacokinetic considerations, *Expert Rev Clin Pharmacol* 2(4):359–371, 2009.

**Perioperative Implications**

- Glucosamine therapy has no significant periop or anesthetic implications. No need to interrupt therapy

for a surgical procedure, no reason to modify an anesthetic plan due to glucosamine, and there is no urgency with regard to restarting therapy postop.

**Glycine**

Alan David Kaye | Rachel J. Kaye | Mark R. Jones

**Uses**

- Inhibitory neurotransmitter in the brain stem and spinal cord.
- Glycine and GABA receptors may mediate the effects of inhaled anesthetics.

- A nonessential amino acid sold as a natural sugar substitute, a sedative, and an antacid; used to promote muscle growth and decrease Sx of BPH; also as a polyphenol and an antipsychotic.
- Glycine 1.5% used as a nonhemolytic irrigation solution during TURP.

- Antagonists of glycine binding to NMDA receptor complex are used as anticonvulsants.
- Attempts to use glycine and other NMDA agonists in schizophrenia have had little success.
- Intrathecal glycine is not different from placebo in the treatment of complex regional pain syndrome.