
Common complementary and alternative therapies with potential use in dermatologic surgery: Risks and benefits

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Background: Ambulatory surgery patients often use complementary and alternative medicine (CAM) therapies. CAM therapies may create beneficial and detrimental perioperative conditions.

Objective: We sought to improve knowledge of CAM effects in dermatologic surgery, allowing dermatologists to potentially capitalize on therapeutic actions and to mitigate complications.

Methods: PubMed literature search of CAM therapies in dermatologic and surgical settings was performed. Common CAM therapies with possible effects on dermatologic surgery were selected. Beneficial and detrimental effects were reviewed.

Results: A myriad of products may be used perioperatively by the patient. Therapies appearing to have some evidence for potential benefit include bromelain, honey, propolis, arnica, vitamin C and bioflavonoids, chamomile, aloe vera gel, grape seed extract, zinc, turmeric, calendula, chlorella, lavender oil, and gotu kola. Potential complications vary according to product and include platelet inhibition, contact dermatitis and, in rare cases, systemic toxicity.

Limitations: This review focuses on CAM having significant published studies evaluating efficacy for wound healing, anti-inflammatory, antipurpuric, or perioperative-related use. Most published studies have been small and often have design flaws. The scope of CAM is large and not all therapies are discussed.

Conclusion: Selected CAM therapies have been reported to promote wound healing, reduce edema or purpura, and provide anti-inflammatory effects. Because of high rates of CAM use, surgeons should familiarize themselves with common uses, potential benefits, and complications. Further study of effects in the dermatologic surgery setting may improve the patient-doctor relationship and enhance outcomes. (J Am Acad Dermatol 2013;68:e127-35.)

Key words: arnica; bromelain; complementary and alternative medicine; dermatologic surgery; honey; propolis.

Complementary and alternative medicine (CAM) therapies are used to prevent or treat a variety of conditions, and for improvement of general health, by a high proportion of the population (estimated at 50%).¹ Annual visits to alternative practitioners have been estimated at 629 million, higher than the number of primary care visits. Rates of use are higher among college-educated persons and those with annual income

above \$35,000.^{1,2} Furthermore, growth is occurring at a rapid rate. Between 1990 and 1997, herbal medicine use increased 380%.³

A systematic review estimated the lifetime prevalence of CAM use among dermatology patients between 35% and 69%.⁴ Surgical patient surveys have shown similarly high rates of use. One survey of elective surgical outpatients found 51% took herbs, vitamins, supplements, or homeopathic medicines.⁵

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Funding sources: None.

Conflicts of interest: None declared.

Accepted for publication June 26, 2011.

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Published online September 5, 2011.

0190-9622/\$36.00

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doi:10.1016/j.jaad.2011.06.030

Twenty two to 32% percent of surgical patients were found in another two surveys to use alternative therapies.^{6,7} A study of 192 patients undergoing Mohs micrographic surgery reported 19% of patients used an alternative therapy.⁸

Reported effects of natural treatments have played an important role in medicine. The understanding that natural products can act as drugs, have therapeutic actions, and cause harmful effects are long-held observations. Several modern drugs, including digoxin (from foxglove), vinca alkaloids (from periwinkle), penicillin (from mold species), podophyllin, pyrethrin, and psoralen are derived from natural sources. In addition, phototherapy, photodynamic therapy, natural wound-healing treatments, and other therapies have been used for generations. Improved understanding of risks, benefits, and suggested uses of CAM treatments is likely to benefit both patients and physicians.

The scope of CAM is large.

Key definitions assist in understanding (Table I). What is defined as CAM is often subject to cultural context and often includes treatments without double-blind randomized controlled trials (RCT) or strong evidence to support medical use. However, many note that several current treatments also lack this evidence, and with generally poor financial support for study of nonpatentable natural treatments, lack of double-blind trials does not exclude the possibility of therapeutic effect.

There are a variety of reasons patients use CAM. CAM use could be expected given limitations of conventional medicine, including expense, difficulty and inconvenience of access, side effects, toxicities, and incomplete efficacy. The most common natural products used in the 2007 US National Health Interview Survey were fish oil/omega 3, glucosamine, echinacea, flaxseed oil, ginseng, combination herbal pills, ginkgo biloba, chondroitin, garlic, and coenzyme Q10.²

The US government currently regulates drugs by monitoring quality, marketing, dosing, and indication guidelines. The inability to patent unaltered commonly available treatments may result in a lack of extensive research of the treatments, with the treatments sometimes being derided.⁹ The Dietary

Supplement Health and Education Act of 1994 categorized natural and alternative therapies as “supplements” (not “drugs”), thereby exempting most CAM therapies from several safety, efficacy, and other regulations, and leading to poor industry regulation with difficulty identifying high-quality sources, reliable concentrations, assurance of unadulterated substances, and advice on effects

and dosing from a trusted source.³ When using CAM, products adhering to good manufacturing practice are recommended to improve quality and standardization.¹⁰ Homeopathic agents are considered over-the-counter drugs, and are therefore considered generally safe. A limited number of double-blind studies exist, with some showing effect greater than placebo.^{11,12}

In Germany, the governmental Commission E has evaluated evidence, efficacy, and indications for use of 300 herbal products.¹³ This widely available review has improved understanding and

provided a common basis for discussion. In the United States, a branch of the National Institutes of Health, the National Center for Complementary and Alternative Medicine, has a number of reports and fact sheets on therapies for reference, and has been formed to “explore complementary and alternative healing practices in the context of rigorous science, train complementary and alternative medicine researchers, and disseminate authoritative information to the public and professionals.”¹⁴ Patients and physicians should be directed toward reputable sources of scientific information (Table II).

PERIOPERATIVE INSTRUCTION AND DISCUSSION

Perioperative CAM management is summarized in Table III. The effect of CAM in the perioperative setting can be significant. It is in the interest of both patient and physician to be comfortable discussing treatments, and to be familiar with common beneficial and detrimental effects. Open nonjudgmental discussion is critical to maximizing outcomes. CAM disclosure rates by patients are generally far from 100%, ranging from 30% to 47%.¹⁵ Verbal questioning for specific CAM categories may result in a more accurate history.³ Clear recommendations should be

CAPSULE SUMMARY

- Commonly available complementary and alternative medicine therapies with potential use in the perioperative dermatologic surgery setting are reviewed, including reported beneficial and detrimental effects.
- Definitions, regulatory practices, and scientific sources of information are discussed.
- Improved knowledge and familiarity with relevant complementary and alternative medicine therapies promotes an improved dermatologic surgeon-patient relationship and may allow surgeons to capitalize on therapeutic actions and to mitigate complications.

Table I. Complementary and alternative medicine definitions

Term	Definition
Complementary	Adjunctive; used together with conventional (prescribed or physician-recommended) therapy
Alternative	Used in place of traditional or physician-recommended therapy
Integrative	Combines CAM treatment having evidence of safety and efficacy with conventional medicine
Holistic	School of medicine that promotes health of the "whole" person in mind, body, and spirit
Homeopathy	School of medicine based on principle of similars and law of minimum dose; considered OTC drugs by FDA
Traditional Chinese medicine	Health as balance between complementary forces of yin and yang; methods include acupuncture, acupressure, herbology, dietary recommendations
Ayurvedic medicine	Seeks to restore health by balancing 3 forces (doshas) of body through healthful lifestyle (emphasizing diet and exercise) and natural healing techniques

CAM, Complementary and alternative medicine; FDA, Food and Drug Administration; OTC, over the counter.

made regarding which therapies to continue and discontinue. Therapies with a less desirable risk-benefit ratio or unclear effects should be discontinued. The American Society of Anesthesiologists recommends herbal medicines be discontinued at least 2 weeks preoperatively.¹⁶ Common CAM agents that increase bleeding risk are detailed in Table IV. Although discontinuation is recommended, one should also consider the possibility of negative effects or changes to be guarded against after discontinuation,³ for example stopping a medication that potentiated the effect of warfarin may lead to a decreased international normalized ratio. There remains a need for the development of formal guidelines regarding discontinuation of specific natural products before surgery.¹⁵

ORAL AGENTS WITH POTENTIAL USE IN DERMATOLOGIC SURGERY

Bromelain

Bromelain, a protease enzyme mixture from pineapple, has been reported to have anti-inflammatory, antiedema, antithrombotic, fibrinolytic, and anticancer properties.¹⁷ Bromelain is taken orally and

considered safe up to 2000 mg daily for years. Reported side effects have been mild and of low incidence; in 12 placebo-controlled studies one showed a 1.8% incidence of side effects including diarrhea, nausea, gastric disorder, and allergic reaction.¹⁸

Bromelain provides anti-inflammatory effects through nuclear factor kappa beta and Cox-2 inhibition. Under conditions of immune stimulation tumor necrosis factor- α , interferon- γ , and transforming growth factor- β levels were reduced by bromelain. Bromelain appears to reduce edema; the effect has been greater than aspirin.¹⁸ Bromelain has also been reported to potentiate antibiotic effects by enhancing tissue permeability.¹⁹ In one study of patients with infections not responsive to antibiotics alone, 22 of 23 responded with addition of bromelain.¹⁸ Limited studies have been conducted on reported anticancer properties; papillomas in mice treated topically showed reduced tumor formation and increased apoptosis.¹⁷ Bromelain reduces platelet aggregation and activation.^{17,20} Traditionally recommended perioperative dosing is 500 mg 3 times daily between meals beginning the day of surgery and continuing for 8 days.

Arnica

Arnica, most commonly *Arnica montana*, is used for anti-inflammatory and antipurpuric effects. Oral arnica in amounts greater than that commonly found in foods or in homeopathic formulations has been strongly discouraged as a result of severe health risks, including coma, hypertension, renal toxicity, cardiotoxicity, muscle paralysis, and death, and is unsafe for pregnant women.²¹ Homeopathic doses are safe, however the concentration is so low that the possibility of effect has been questioned.²² Topical preparations should be limited to closed skin. The German E commission has approved only external use.²³

Several compounds in arnica provide anti-inflammatory activity including sesquiterpene lactones helenalin and chamissonolid that are potent inhibitors of nuclear factor kappa beta.^{24,25} A limited number of positive studies exist. Oral arnica reduced ecchymosis slightly after rhytidectomy²⁶; decreased pain after carpal tunnel surgery²⁷ and tonsillectomy¹¹; and combined with *Bellis perennis* was better able to maintain postpartum hemoglobin,¹² reduced edema and ecchymosis after rhinoplasty,²⁸ and was equivalent to diclofenac after hallux valgus surgery for wound irritation and mobility.²⁹

Several negative studies also exist. After carpal tunnel surgery arnica did not show reduction in pain or bruising,³⁰ and no difference was found after

Table II. Sources of information on complementary and alternative medicine

National Center for Complementary and Alternative Medicine (NCCAM)	http://nccam.nih.gov
Office of Dietary Supplements, National Institutes of Health	http://ods.od.nih.gov
Office of Cancer Complementary and Alternative Medicine, National Cancer Institute	http://www.cancer.gov/cam/
German Commission E Databases	Blumenthal et al ¹³ International Bibliographic Information on Dietary Supplements, PubMed, NCCAM Clearinghouse
University- and medical center–based World Wide Web resources	Columbia University Center for Complementary and Alternative Medicine (http://www.rosenthal.hs.columbia.edu/) MD Anderson Cancer Center Complementary/Integrative Medicine Education Resources (http://www.mdanderson.org/education-and-research/resources-for-professionals/clinical-tools-and-resources/cimer/index.html) Memorial Sloan-Kettering Cancer Center Integrative Medicine Service http://www.mskcc.org/mskcc/html/11570.cfm
Office reference guides	Peirce A. The American Pharmaceutical Association Practical Guide to Natural Medicines. New York: HarperCollins, 1999. Miller L. Herbal Medicinals: A Clinician's Guide. New York: Informa Healthcare, 1999.

pulse dye laser bruising^{19,31} or in hematoma formation after vein stripping.³² Systematic review of 8 placebo-controlled trials concluded there were a number of methodological flaws in each, and that there remained insufficient evidence to support an effect greater than placebo.³³

It appears from review there is currently little evidence for reduction of purpura. One must be mindful of serious risks of nonhomeopathic oral formulations and of topical use on broken skin.²¹ Antiedema and anti-inflammatory effects may be better supported. Traditional oral dosing is 2 capsules 30C potency homeopathic arnica 2 to 6 hours before surgery and then 4 times daily up to 5 days postoperatively, discontinued when pain, swelling, and discoloration resolve. Topical arnica may be applied twice daily on closed skin. Arnica inhibits platelet aggregation.³⁴ Contact dermatitis has been reported. As a protected species in some regions, *Arnica* is recommended to be purchased from reputable sources.¹

Zinc

Zinc 15 to 30 mg daily is used to aid in wound healing. Toxicity occurs at doses above 50 mg daily. Adverse effects of oral zinc include abdominal pain, nausea, vomiting, and diarrhea.³⁵ Topical formulations may aid in wounds and inflammatory conditions; zinc oxide has shown the greatest efficacy.³⁶ Zinc plays key roles in each phase of wound healing and has anti-inflammatory effects.³⁶ Topical zinc has enhanced re-epithelialization in animals regardless

of nutritional zinc status,³⁵ perhaps mediated through integrin and matrix metalloproteinase activation that enhances keratinocyte migration.³⁵ Zinc-deficient rats have delayed re-epithelialization and decreased scar strength.³⁶ Whether zinc enhances wound healing in human beings is unclear for nondeficient individuals. Individuals predisposed to low zinc may benefit, including those with malnutrition, liver disease, inflammatory bowel disease, stress, trauma, skin diseases, and chronic wounds.³⁵ Topical zinc oxide has mild antibacterial effects, particularly against *Staphylococcus aureus*.³⁵

Turmeric

Turmeric, an Asian spice, appears to have anti-cancer, anti-inflammatory, antioxidant, antiviral, antifungal and pro-wound-healing effects.³⁷ The spice is used freely in food, and toxicity is very rare. Dosing up to 8000 mg daily for 3 months showed no adverse effects.³⁷ In animals, topical turmeric hastened healing of acute wounds,³⁸⁻⁴¹ even in radiated skin.⁴² Curcumin-treated human keratinocytes showed increased cell migration,⁴³ and curcumin protected keratinocytes and fibroblasts against injury from hydrogen peroxide.⁴⁴

Vitamin C and bioflavonoids

These are often recommended to improve wound healing. Two RCTs found improvements in mechanical strength of wounds after excisions.⁴⁵ Although few intervention studies exist for wounds, vitamin C is considered safe, anti-inflammatory, and important

Table III. Perioperative complementary and alternative medicine management

Medication and social history
 Specific written and verbal inquiry of CAM category use
 Open discussion with patient regarding perceived and known risks and benefits
 Consult scientific sources regarding therapies patient wishes to use during perioperative period
 Recommend discontinuation of therapies with negative or poorly understood risk-benefit ratio 2 wk before surgery
 Consider monitoring for adverse events or changes after discontinuation (eg, change in INR)
 Make recommendations for when CAM therapies can be restarted
 Consider reporting of attributable adverse events to health agencies (Center for Food Safety and Applied Nutrition, FDA, make report at <http://vm.cfsan.fda.gov/~dms/supplmnt.html>) and in literature

CAM, Complementary and alternative medicine; FDA, Food and Drug Administration; INR, international normalized ratio.

for collagen formation. Common dosing is 1000 mg vitamin C twice daily with 500 mg bioflavonoid complex beginning 1 week preoperatively and continuing 1 month postoperatively. Excess vitamin C causes diarrhea.

Grape seed extract (*Vitis vinifera*, or pycnogenol)

Grape seed extract is used for strengthening vessels and preventing bruising. Common dosing is 50 to 300 mg daily perioperatively. The extract increases wound contraction and closure speed in mice, vascular endothelial growth factor and tenascin levels in the wound edge, and connective tissue deposition.¹⁹

TOPICAL AGENTS WITH POTENTIAL USE IN DERMATOLOGIC SURGERY

Honey

Honey is a mixture produced by bees consisting of water, sugar, saccharides, catalase, glucose oxidase, amino acids, and antioxidants. The sugar solution draws exudate promoting a moist environment, and the low pH inhibits bacterial growth. Honey provides a barrier effect, leading to speculation it might provide infection prophylaxis. On wounds, medical use preparations (CE marked and irradiated) are recommended to avoid fungal spore contamination. Although honey is considered safe, it is prudent to conservatively avoid use in patients with bee product or bee sting allergy.⁴⁶ A Cochrane review evaluated 19 trials⁴⁷; honey was concluded to reduce time to healing in acute wounds (partial

Table IV. Common complementary and alternative medicine agents with effects on coagulation^{3,20}

Agent	Mechanism
Borage seed oil	Contains alpha-linoleic acid, which inhibits platelet aggregation
Bromelain	Inhibits platelet aggregation
Clove	Inhibits platelet aggregation
Coumarin-containing compounds (angelica root, arnica, anise, asafoetida, alfalfa, bilberry, capsicum, celery, chamomile, Dang gui, fenugreek, goldenseal, horse chestnut, horseradish, licorice, lovage, parsley, passionflower, quassia, red clover, rue)	Vitamin K antagonists (inhibit hepatic synthesis of vitamin K-dependent coagulation factors II, VII, IX, X, and proteins C and S; potentiates effect of warfarin)
Dan shen	Inhibits platelet aggregation
Vitamin E (tocopherol)	Inhibits platelet aggregation and adhesion
Fish oil	Inhibits platelet aggregation and adhesion
Feverfew	Inhibits platelet aggregation
Garlic	Inhibits platelet aggregation
Ginger	Inhibits platelet function
Ginkgo	Inhibits platelet-activating factor
Ginseng	Inhibits platelet aggregation
Green tea	Inhibits platelet aggregation
Huang qi	Inhibits platelet aggregation
Kava Kava	Inhibits platelet aggregation
Onion	Inhibits platelet aggregation
Salicylic acids (meadowsweet, poplar, willow bark)	Inhibits platelet synthesis of thromboxane A2, thereby inhibiting platelet aggregation
Turmeric	Inhibits platelet aggregation
<i>Vitex agnuscastus</i>	Inhibits platelet aggregation

thickness burns) compared with various conventional dressings. Honey therefore acts as a moist dressing and may be a substitute or addition to ointment or conventional dressing in selected patients.

Propolis

Another agent produced by honeybees is propolis. It also has antibacterial effects, including against anaerobes. It has been used to treat mucositis and may act similarly to silver sulfadiazine on burns. A component, caffeic acid phenethyl ester, improved skin flap survival in rats; the effect was hypothesized as a result of antioxidant effects protective against

Table V. Common complementary and alternative medicine therapies with potential use in dermatologic surgery

Therapy	Description	Reported benefits	Reported risks
Oral agents			
Bromelain	Pineapple enzyme mixture	Anti-inflammatory Antiedema Potentiation of antibiotic effect Antitumor	Generally considered safe up to 2000 mg daily for years Low rate: GI distress, allergy Antiplatelet
Arnica	Arnica flower (usually <i>Arnica montana</i> , oral or topical)	Antipurpura Anti-inflammatory Analgesic effects	Homeopathic doses or topical use on intact skin considered safe, other use has risk of severe systemic toxicity Antiplatelet
Vitamin C	Common vitamin, found in citrus fruits (oral or topical)	Support collagen stability in wounds and vessels Anti-inflammatory	Considered safe water-soluble vitamin, diarrhea at high doses
Grape seed extract	<i>Vitis vinifera</i> , pycnogenol	Increased VEGF expression Decreased closure time Antiedema Anti-inflammatory	Possible contact dermatitis P450 inhibitor Antiplatelet
Zinc	Mineral; zinc sulfate (oral), zinc oxide (topical)	Enhanced wound healing in animals and in zinc-deficient human beings Mild antibacterial	High doses may produce abdominal pain, nausea/vomiting, or diarrhea
Topical agents			
Honey	Complex mixture produced by bee	Moist dressing Antibacterial Barrier effect Anti-inflammatory	Fungal spores (nonmedical grade) Unlikely allergy
Propolis	Mixture produced by bee	Promotes re-epithelialization May provide antioxidant benefits to flaps	Possible irritation or allergy
Chamomile	Flower (topical or oral)	Anti-inflammatory Improves healing time in animals	Possible contact dermatitis Antiplatelet
Aloe	<i>Aloe barbadensis</i> plant gel (topical or oral)	Anti-inflammatory Promotes re-epithelialization Antipruritic Decreased ischemia Increased perfusion	Possible contact dermatitis Antiplatelet
Turmeric	Spice from Asia	Anticancer; anti-inflammatory; antioxidant Enhanced wound healing in animals and in vitro studies	Generally very safe; no toxicity seen at 8000 mg daily for 3 mo
Calendula	Medicinal plant	Limited data suggesting increased rate of wound re-epithelialization	Possible contact dermatitis
Chlorella	Algae mixture	Limited data in rats suggest reduced wound size and scar formation	Little data to support risks with topical use
Lavender oil	Essential oil of lavender plant	May reduce wound erythema	May have cytotoxic effects on fibroblasts
Gotu Kola	Medicinal plant; <i>Centella asiatica</i>	Increased rate of re-epithelialization and wound contracture in rats	Contact dermatitis reported

GI, Gastrointestinal; VEGF, vascular endothelial growth factor.

reperfusion injury.¹⁹ Propolis has also aided in healing herpetic erosions.¹⁹ Propolis may be considered as a topical treatment on erosions or wounds to facilitate re-epithelialization and protect against infection. Recommended dosing is 1 to 3 mL topical tincture daily until healed. Oral capsule dosing is

frequently 500 to 1000 mg daily (Lauri Grossman, DC, CCH, RSHom (NA), written communication, April 20, 2010). As with honey, it may be conservatively avoided in patients with bee product allergy. There may rarely be skin itching or redness noted.

Chamomile

Topical chamomile (*Matricaria recutita*) significantly decreased surface areas of wounds, and improved healing time in animals.^{1,48,49} Human studies are needed to further evaluate a potential benefit in surgical wound healing.

Aloe vera

Aloe vera is a mixture of beta-sitosterol, an angiogenic factor, salicylic acid, magnesium lactate, and other compounds. Aloe has been reported to improve re-epithelialization of surgical wounds, provide anti-inflammatory effects, and possibly increase dermal perfusion to decrease ischemia.¹ In an RCT of patients after hemorrhoidectomy, aloe reduced pain, decreased analgesic requirements, and increased wound healing ($P < .001$).⁵⁰ In rats, aloe gel hastened healing of dermal wounds,⁵¹ and a human postdermabrasion patient showed reduction in edema and faster healing in aloe-treated skin.⁵² Dermatitis after postdermabrasion application has been reported.⁵³

Calendula

Limited data have been published; one study showed improved wound healing after application of hypericum/calendula extract. In animals, surgical wounds displayed faster re-epithelialization after topical treatment^{54,55} and fibroblasts increased proliferation and migration.⁵⁶

Chlorella vulgaris

Chlorella, a green algae compound containing minerals, vitamins, and chlorophyll, used as a topical dressing in rats, reduced wound size and scar formation compared with control and sodium alginate dressings.⁵⁷ Further studies evaluating efficacy in wound healing have not been reported in PubMed.

Lavender oil

Limited data exist evaluating lavender for treatment of wounds. A rat wound model showed no effect of topical lavender,⁵⁸ and an RCT of episiotomy wounds showed reduced erythema with topical lavender compared with povidone-iodine.⁵⁹ One study found lavender oil and components linalyl acetate and linalool to be cytotoxic to endothelial cells and fibroblasts.⁶⁰

Gotu kola (*Centella asiatica*)

The plant gotu kola is used in food in Asia. Rat wounds treated with topical extract showed increased rates of re-epithelialization and contraction, and attenuated dexamethasone-induced delay in healing ($P < .001$).⁶¹⁻⁶⁴ The extract increased collagen and fibronectin in human fibroblast culture.⁶⁵

There has been a report of contact dermatitis to a component, madecassol.⁶⁶

CONCLUSIONS

Evidence of effects of natural, botanical, and other CAM therapies remains insufficient for recommendations on many fronts. Even for agents studied in several trials, a lack of standardization of concentrations, administration routes, and doses prevents clear conclusions. Given high rates of patient use, wide availability, potentially reduced costs, notable laboratory findings, and potential benefits, further study is recommended. A role for CAM therapies even as placebo use should not be discredited in aiding selected patients, especially as complementary or combined therapy. Thorough review of the literature and guidance of governmental research agencies when planning studies is likely to assist in gathering more reliable future evidence. Consideration may be given to these agents (Table V) in the therapeutic armamentarium for selected patients undergoing dermatologic surgery, and open discussion with patients regarding possible risks and benefits is recommended for the best possible dermatologic surgery outcomes.

We gratefully acknowledge Priya Thakker, MD, for her contributions to editing and improving the manuscript.

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