

ALTERNATIVE MEDICINE ALERT™

A Clinician's Guide to Alternative Therapies

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Ginger for Motion Sickness, Hyperemesis Gravidarum, Chemotherapy, and Anesthesia

By Jay Udani, MD, and Mary Hardy, MD

THE DISCOMFORT AND DISTURBANCE NAUSEA CAUSES CAN STRIKE all too predictably. Pleasure trips in cars or boats may be ruined by motion sickness. Hyperemesis gravidarum may characterize early pregnancy. Peri- and post-chemotherapy waves are unsettling. Anesthesia-induced nausea may complicate postoperative respiration and recovery.

Many classes of drugs are currently used to counter or prevent nausea. *Zingiber officinale*, or ginger, is a rhizome that has been used to prevent and treat nausea for centuries, and it might work as preventive or therapeutic adjunct or single agent in any of the settings noted above.

History/Tradition

Ginger is a perennial plant with thick underground stems called rhizomes, which are used for medical and culinary purposes. The aboveground stem can grow to heights of 24 feet.

Ginger is native to southern Asia, but is now cultivated extensively throughout the tropics. The very best quality ginger is grown in Jamaica, but more than 80% of the ginger imported to the United States is reported to come from China and India.¹

Medicinal use of ginger has been broadly documented in cultures as diverse as Indian, Chinese, Arabic, Greek, and Roman. It is cited in ancient Ayurvedic, Sanskrit, and Chinese texts as early as the fourth century B.C. for conditions such as stomachache, diarrhea, nausea, cholera, hemorrhage, and toothache.² Pythagoras is reputed to have used ginger as a digestive aid, and the first century Roman herbalist Discorides included ginger in his herbal text, which became the basis for much of the practice of medicine throughout the middle ages.³

In addition to its medicinal applications, ginger is also widely used as a spice in foods, beverages, candies, and liqueurs, and is also commonly used in many cosmetic products. The Chinese use fresh

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ginger in many dishes, not only for its spicy flavor and perfume, but also as a yang ingredient—to balance cooling (or yin) dishes. Five-spice powder and many curries contain dried ginger.

Pharmacology

The pharmacologically active components of ginger include an oleoresin and pungent “principles.” The oleoresin (5-8% of total matter) contains an essential aromatic oil (1-2%) consisting mainly of sequiterpene lactones, such as zingiberene. The pungent or hot “principles” are phenolic compounds, such as gingerols or shogaols. Shogaols, more pungent and more bitter, seem to form from gingerols mainly as a result of drying.¹ Ginger’s pungency is due to gingerol, and the aroma is due to ginger oil which contains 50 different constituents. Pungency and aroma are a good, quick way to gauge freshness. Most studies have used dried whole herb rather than fresh herb for practical reasons.

Ginger has many other pharmacologic effects, including antioxidant properties; inhibition of platelet aggregation; and modulation of prostaglandin, thromboxane, and leukotriene synthesis.

Mechanism of Action

Ginger’s mechanism of action for the prevention and treatment of nausea is not clear. Studies have shown increased gastric motility,² but not increased gastric

emptying.⁴ Ginger enhances salivary and gastric secretion, and has documented antispasmodic effects associated with its fat-soluble components, such as galanolactone, and its ability to antagonize serotonin receptor sites.² Unlike other antiemetics, ginger’s mechanism of action is not CNS-mediated.⁵

Clinical Studies

We conducted a systematic review of the literature using MEDLINE, PubMed, the Internet, and alternative medicine literature CD-ROMs using the keywords “ginger,” “nausea,” and “emesis.” There have been a series of studies examining ginger as an antiemetic. The clinical scenarios in these studies have been diverse and include post-anesthetic nausea, hyperemesis gravidarum, chemotherapy-induced nausea, motion sickness and seasickness.

At least four studies of ginger to reduce postoperative nausea and vomiting have been conducted, with conflicting results. All four are of women who had undergone laparoscopic gynecological procedures. The earliest study involved 60 women randomized to receive 1 g of ginger, 10 mg metoclopramide, or placebo.⁶ Women receiving both ginger and metoclopramide had significantly fewer episodes of nausea ($P < 0.05$) and less use of antiemetic after surgery ($P < 0.05$). There was no significant difference between the metoclopramide and ginger groups, and all three groups had identical side effect profiles. In 1993, an almost identical study was performed involving 120 women, with similar outcomes.⁷

In 1995, yet another study was performed with 108 women randomized to receive placebo, ginger 0.5 g, or ginger 1.0 g.⁸ All patients were premedicated with oral diazepam one hour prior to surgery. This study found an increase in incidence of moderate or severe nausea and vomiting in both groups taking ginger compared with placebo. In fact, the risk of nausea or vomiting increased with the higher ginger dose. The odds ratio for 0.5 g ginger for nausea was 1.39 and for vomiting was 1.55. This was the first negative study seen in this population.

The most recent study was done in 1998 and randomized 120 patients to placebo, droperidol, 1 g ginger po, or ginger plus droperidol.⁹ There were no significant differences in nausea or vomiting between the four treatment groups; in essence, droperidol and ginger showed no improvement over placebo. The side effect profiles for all four groups were also identical.

Investigators in the only randomized, double-blind, crossover trial of ginger for hyperemesis gravidarum gave patients 250 mg of ginger or placebo qid for four days, with a two-day washout period, and then four days of the other substance.¹⁰ Subjective measures of relief

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Please call **Leslie Coplin**, Managing Editor, at (404) 262-5534 between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

Merging Culinary with Medical: Ginger Gains Popularity

The sweet aroma of gingerbread evokes fond holiday memories for many people, but the current image of gingerbread people is very different from its historical forms. The cookie's name was derived from the ancient Greek custom of eating ginger wrapped in bread to minimize the discomfort caused by gluttonous feasts. And in medieval times, knights took hard round loaves flavored with ginger and honey when they headed off to battle.

Flavoring with ginger is no longer limited to the traditional gingerbread and spice cakes of years past. According to "Glorious Ginger," which appeared in the September 1998 *Vegetarian Times*, Americans consume about 38 million pounds of this pungent tuber every year. One of the world's most widely used spices, ginger is essential for Asian and Indian dishes. According to the September 1998 issue of *Prepared Foods*, during the past 10 years, U.S. chefs have been translating traditional Asian dishes for American tastes.

Penzeys Spice Catalog of Seasonings offers powdered, cracked, whole, or crystallized ginger at prices ranging from \$1.29 for a 1/4 cup plastic jar of powdered ginger to \$12.90

for a 1 pound bag of crystallized ginger. In addition to its traditional uses as a seasoning for curries, marinades, and stir-fry, ginger adds a nice flavor to chicken soup, sautéed vegetables, roasted chicken or pork, and grilled steak. The catalog's powdered China #1 Ginger, with its strong flavor and lemony overtones, is recommended for baking.

The November 1998 *Cooking Light* includes recipes for Pear Upside-Down Gingerbread Cake and Ginger-Chocolate Chip Biscotti, which is made with crystallized ginger, and a recipe for Ginger-Sweet Potato Pie with Cinnamon Meringue is featured in the November 1998 *Gourmet*.

In addition to adding a sweet, peppery flavor to many dishes, medicinal uses of ginger date back 5,000 years. The July 1998 issue of *Better Homes and Gardens* says that ginger contains cancer-fighting antioxidants, reduces blood clots, may lower cholesterol, and appears to enhance insulin. Ginger's other possible health benefits include easing headaches, quieting coughs, stimulating circulation, soothing sore muscles, and aiding digestion, according to the *Vegetarian Times* article.

Prevention's Healing Herbs labeled ginger as an "herbal chameleon" because it's available in so many forms—fresh ginger, capsules, tea, candied, and ginger ale, a long-time remedy for the flu and other stomach ailments. ■

were significantly greater with ginger (70.4%, $P = 0.003$). Objective measures backed these findings significantly as well ($P = 0.035$).

Only one study evaluating ginger for nausea associated with chemotherapy was found: a case series of 11 patients undergoing 8-MOP photopheresis for cutaneous T cell lymphoma who had a history of chemotherapy-induced nausea.¹¹ In this non-randomized, non-blinded protocol, patients were given 1590 mg of ginger 30 minutes prior to chemotherapy administration. A nonsignificant reduction in nausea was seen on the nausea scale (a non-validated scale) compared with historical controls.

Multiple studies have been performed using ginger to prevent motion sickness. Three randomized, controlled trials of experimentally induced motion sickness have been performed, two of which showed no effect of ginger on prevention or treatment of motion sickness.^{5,12} The third study compared 1 g of ginger to 100 mg dimenhydramine or placebo, each given one-half hour prior to experimentation using a revolving chair.¹³ The ginger group tolerated the revolving chair significantly better than the dimenhydramine or placebo groups.

The one trial of ginger for the treatment of seasickness was a double-blind, randomized, placebo-controlled study of 80 naval cadets on rough high seas voy-

ages.¹⁴ Cadets who complained of seasickness were given 1 g of ginger or placebo every hour for four hours. Ginger significantly reduced seasickness measured by vomiting and cold sweats ($P < 0.05$). Ginger tended to reduce nausea and vertigo, but not significantly.

Formulation

Standardized preparations are not necessarily recommended because the clinical studies to date have not used them. There is currently no consensus regarding to which constituents to standardize. Given the nature and severity of the illness being treated, i.e., a self-limited condition, clinical response is an adequate endpoint and the need for highly standardized product is not critical.

All food forms of ginger can be used, but dried capsules are preferable. Candied ginger is usually not dried well enough to be therapeutic, and the pickled and candied forms have not been tested formally. The liquid sources of ginger (ginger ale or ginger tea) generally have such low concentrations of ginger that large quantities of liquid are required to consume adequate amounts of ginger.

When buying ginger tablets or capsules, look for the amount of ginger in each capsule, and look for a lot number and expiration date. Although some products

are standardized, the smell and taste of ginger are better guides to freshness and therefore, by extension, efficacy.

A botanical monograph on ginger has recently been approved by the United States Pharmacopeia for inclusion in the national formulary.¹⁵

Dose

The usual dosage for preventing motion sickness is 1 g (tablets or capsules) of dried powdered gingerroot given orally one-half hour prior to voyage.¹⁶ Ginger is less effective when given to a patient who is already nauseated.

Adverse Effects

The use of ginger in pregnancy for hyperemesis gravidarum is controversial among botanical experts. Ginger's effect on testosterone binding and on thromboxane synthetase activity warrant pause in recommending ginger for pregnant women.¹⁷

The risk of bleeding is slight, but real. Concerns about ginger increasing bleeding were not supported by a study of patients undergoing a laparoscopic gynecological procedure who showed no difference in intraoperative or postoperative bleeding complications.⁷

In the only study of hyperemesis gravidarum, fetal loss rate was not reported, but it is not clear whether investigators kept track of this variable at all.¹⁰ Two leading authoritative sources categorize ginger as "not to be used during pregnancy."^{18,19} An editor's note in the German Commission E monographs opines that there are no data to support this admonition,¹⁹ but the caution is based upon two Japanese studies^{20,21} in the 1980s showing in vitro mutagenic properties of isolated ginger compounds.¹⁹ An earlier study showed ginger to possess anti-mutagenic activity.²²

There are no conclusive data about ginger in pregnancy, and so caution and prudence must prevail.

Ginger is also not recommended for patients with gallstones as ginger is a cholagogue and increases the flow of bile.¹⁸ In addition, large doses of ginger have been known to cause heartburn.¹⁶

Recommendation

Ginger is an ancient spice that has documented antiemetic effects in post-anesthesia, hyperemesis gravidarum, chemotherapy, and seasickness. The data are not conclusive in any setting, but it is reasonable to use a trial of ginger for the prevention of postoperative nausea, motion sickness, and seasickness. Despite common food and folk use, physicians should not recommend ginger for nausea during pregnancy. The caution becomes a warning if the pregnant patient has a history of bleeding

disorders or miscarriage. The data on ginger for the prevention and treatment of chemotherapy-induced nausea are too poor to draw conclusions.

For patients who wish to try it, we recommend 1 g of ginger 30 minutes prior to an activity that may induce motion sickness or seasickness, as well as prior to surgery, assuming the patient is allowed to take medications po. ❖

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Ginkgo Biloba for Attention and Memory Disorders

By Mady Hornig, MD

GINKGO BILOBA EXTRACTS HAVE EMERGED RECENTLY as part of the “herbal armamentarium.” This broad group of natural remedies has enticed people who never before would have entered a health food store to flock in for putative, antiaging miracles.

Ginkgo has been touted as an effective antioxidant, with presumed ability to provide protection against damage induced by free radicals. In addition, it is thought to improve many disorders related to circulatory problems, including peripheral and cerebral vascular disease. There is increasing interest in the efficacy of ginkgo extracts for the treatment of even mild, age-related deficits in memory, vigilance, and attention.¹

The German Commission E notes that ginkgo is approved for symptomatic treatment of deficits in mem-

ory impairment, concentration difficulties, and depression from organic brain disease. My own clinical experience with adult attention deficit/hyperactivity disorder (AD/HD) patients who have taken ginkgo formulations, either as monotherapy or in conjunction with psychostimulants, indicates modest to marked improvement in vigilance capacity in this population.

History

Since 2800 B.C. extracts of the fan-shaped, bilobed leaves, the fruits, and the seeds of the ancient *Ginkgo biloba* tree have been used as part of Chinese herbal therapies to combat age-related symptoms and asthma. A remnant of the prehistoric era that is believed to be more than 200 million years old, the ginkgo tree is used to produce EGb 761, the most widely prescribed botanical extract in Germany, where it is used for cognitive and circulatory disorders.

Culture

The expansion of the aged population in the United States and concerns about memory loss and preventing dementia have led to an increased interest in memory-boosting, antiaging agents. Heightened desire to improve performance in a wide variety of arenas, ranging from the workplace to the bedroom, has paralleled the consumer’s increased interest in natural remedies to enhance everything from cognitive to social to sexual functioning. Ginkgo extracts are now included in a number of popular “memory boosting” preparations that are easily available at local supermarkets.

Pharmacokinetics

Ginkgo biloba extracts contain a variety of flavonoids, terpenoids, and phenolic acids. The pharmacokinetic profile is dependent upon the relative concentrations of the different components in the specific preparation. Bioavailability of EGb 761 appears to be high. The German Commission E notes that only extracts with an herb-to-extract ratio in the range of 35:1 to 67:1 are acceptable.

Mechanism of Action

Ginkgo extracts have a wide range of potential effects that relate to the large number of active components. Actual effects vary according to the relative concentrations of each of these components. Proposed mechanisms of action similarly cover a broad spectrum, ranging from prevention of oxidative stress from free radicals or hypoxia to alterations in peripheral and central neurotransmitter systems.

The antioxidant potential of ginkgo constituents is

demonstrated by their ability to down-regulate mediators of free radical-induced damage, such as superoxide dismutase, lipid peroxide products, and phospholipids;² inhibit products of hypoxia-induced membrane breakdown, including choline-containing phospholipids;³ antagonize the anticoagulant effects of platelet activating factor;⁴ and improve vascular relaxation, through inhibition of nitric oxide.^{5,6} Together, these effects work to improve cerebral blood flow.

Ginkgo's capacity to alter neurotransmission and provide neuroprotection derives from at least four animal-model mechanisms. One, ginkgo induces significant decreases in glucose utilization in brain areas mediating somatosensory processing and vigilance as well as vestibular mechanisms. These mechanisms (frontoparietal somatosensory cortex, nucleus accumbens, cerebellar cortex, and pons of the rat)⁷ are consistent both with ginkgo's ability to improve attention and its efficacy in tinnitus and vertigo. Two, ginkgo reduces the number of adrenal peripheral benzodiazepine receptors, thereby altering cholesterol transport-inhibiting, stress-related corticosteroid secretion.⁸ Three, EGb 761 ginkgo extract protects against age-related changes in hippocampus.⁹ And four, ginkgo extracts are reversible inhibitors of monoamine oxidase A and B subspecies.¹⁰

Clinical Studies

Few controlled studies on the cognitive-enhancing effects of ginkgo have been performed in humans, despite its popularity. A randomized, double-blind, placebo-controlled study in mildly to severely demented patients with Alzheimer's disease or multi-infarct dementia showed stabilization or improvement of cognitive performance and social functioning after six to 12 months of treatment with EGb 761 ginkgo extract (120 mg/d).¹¹ For a detailed review, see *Alt Med Alert* 1998;1:23-24.

In subjects with age-associated memory impairment, automatic information processing was improved after both acute and chronic (57 days) ginkgo biloba extract administration.¹² Assessment of memory processing was based on reaction time in electrophysiologic testing (P300 evoked potential).

Much of the extensive German literature on ginkgo, most done over 8-12 weeks with 120-160 mg/d is not statistically rigorous. There have been no controlled studies in AD/HD or depression.

Animal Studies

Studies in animal models provide encouraging results with respect to cognitive and neuroprotective effects of ginkgo extracts. Improvements in learning are seen in

both adult and aged mice, correlated with improved histologic appearance of the hippocampus.¹³ Chronic administration of EGb 761 is also associated with improved learning and memory in rats (and with greater longevity).¹⁴

Adverse Effects

In general, toxicity is very low. In a large, placebo-controlled dementia study, there was no significant difference in the placebo and the EGb 761 group with respect to reports of adverse effects, although gastrointestinal complaints occurred twice as often in the treated group as compared to the control group.¹¹ In combination with other platelet inhibitors, such as aspirin, spontaneous bleeding into the anterior chamber of the eye has been reported.¹⁵ Spontaneous subdural hematomas have also been reported.¹⁶ Until further studies are performed, patients on aspirin or anticoagulants should avoid ginkgo.

Table		
Sample Ginkgo Biloba Prices		
Brand	Formulation	Price/Count
Nature's Resource	40 mg (24% leaf extract)	\$9.79/50 capsules
Kroger	40 mg (50:1)	\$5.99/36 tablets
Pharmaton Ginkoba	40 mg (50:1)	\$14.99/36 tablets
Sundown Herbals	400 mg (leaf extract)	\$4.95/100 capsules
One-A-Day Memory*	60 mg (leaf extract)	\$8.99/30 tablets
Lichtwer Pharma Ginkai	50 mg (50:1)	\$7.99/30 tablets
*also contains vitamins B ₆ , B ₁₂ , and choline		

Drug Interactions

Because of ginkgo's reversible monoamine oxidase inhibitory capacity, the potential for interactions with other agents that affect monoamine neurotransmitters (e.g., antidepressants) is not known. Given the potential for serotonin syndrome, caution should be used when coadministering these agents. There is also the remote possibility of hypertensive crisis if ginkgo is used in very high dosage or if the extract preparation has a particularly high concentration of the monoamine oxidase inhibiting component and if the patient also ingests food with a high concentration of tyramine (cheeses, red wine) or sympathomimetic agents. Interactions with other platelet inhibitors have been reported. (*See Adverse Effects.*)

Formulation

The EGb 761 formulation of ginkgo biloba extract is the most popular, and contains flavonoids, terpenoids

(including the ginkgolides and bilobalide), and organic acids. It is standardized to 24% flavone glycosides and 6% terpenelactones. Currently, it is not clear whether specific preparations of ginkgo have greater overall efficacy or if they might be more effective for specific conditions. Differential efficacy of the various components of different ginkgo extracts is only now being explored. There are also no data regarding differential efficacy or toxicity of formulations containing other “memory boosters,” such as phosphatidyl serine or B complex vitamins.

Dosage

Dosage of the EGb 761 preparation is typically 120 mg/d, although studies with Alzheimer’s patients, such as the one by Le Bars and colleagues, suggest that 240 mg/d is a more effective dosage. It is sometimes divided into three daily doses, but based on the most popular extract formulation, EGb 761, once-daily dosing appears to be adequate for many conditions, including cognitive disorders such as Alzheimer’s disease.

Conclusion

Ginkgo biloba extracts appear to be effective in modulating reactions to inflammatory and oxidative stress and in regulating neurotransmission, with preliminary evidence of beneficial effects in disorders of attention, learning and memory, including age-associated memory impairment, AD/HD, and Alzheimer’s disease. The precise mechanism of action is unclear, but evidence suggests a capacity to avert free radical-induced damage through inhibition of membrane breakdown, protection against age-related hippocampal degeneration, and effects on monoamine transmission. Side effects such as bleeding are uncommon and appear to be associated with platelet inhibitory effects of ginkgo extracts.

Recommendation

Given the absence of alternatives and the relatively low toxicity, therapeutic trials are clearly warranted in Alzheimer’s disease. The data from the Le Bars group indicate that long-term therapy is likely to be helpful in either preventing further deterioration or in inducing improvement. For younger patients with AD/HD, traditional therapies should be pursued first, with continued patient surveillance at least every three months. Ginkgo should not be coadministered with anticoagulants. ❖

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Calendula Preparations to Treat Cutaneous Infections

By Vance Dietz, MD, MPH, TM

SCRATCHES, BRUISES, AND MINOR CUTS! MOST PARENTS have had to deal with them for their children and themselves. Since Ambroise Pare substituted egg whites for boiling water to treat war wounds in the 16th century, the search for wound healing compounds has been ongoing and it will continue.¹ Many unguents are available to prevent or treat infection. In addition, nature has provided numerous anti-inflammatory and antiviral herbs that have been used through the years. One of the most common of these is derived from *Calendula officinalis*, the marigold.

History of Calendula

Calendula officinalis, also called pot marigold or simply calendula, originated in the Mediterranean and is a member of the aster or daisy family. An annual, calendula's flowers bloom in the summer. Since medieval times this remarkably hardy herb has been grown in gardens, where it will sprout in poor soil, stone piles, and similar areas. Although its flowers are also bright orange and yellow, calendula should not be confused with the common garden marigold (*Tagetes sp.*).

Folklore

Calendula has been widely used as an anti-inflammatory and as a remedy for skin infections, burns, and numerous other conditions. It is a folk remedy for warts and, when combined with milk, for cancer.² Calendula is said to be good for bee stings when rubbed on the skin. It is said to be effective as an "analgesic, anthelmintic, anti-spasmodic, astringent, bactericide, carminative, ... diaphoretic, diuretic ... laxative, stimulant..."² In addition, the "tincture of flowers has been used to heal amenorrhea, bruises, cholera, cramps, syphilis, tuberculosis, ulcers, and wounds." When boiled together with honey and ground ivy, calendula is said to stop the spread of cancers or ulcers, although this remains unproven. In addition, powder from the plant's petals is used like saffron to season and color seafood, chowders, soups, stews, sauces, and more.

Mechanism of Action

Calendula's mechanism of action in wound healing is not completely clear. The main compounds of calendula flower extracts include triterpenoids and flavonoids,

especially flavonol glycosides.³ Among the triterpenoids, the faradiol monoester appears to be most related to calendula's anti-inflammatory activity.⁴ However, laboratory studies demonstrate an anti-inflammatory effect of more than one compound in the plant.⁴⁻⁸ Bactericidal activity against *Staphylococcus aureus* has also been reported.⁹

Animal Studies

Della Loggia et al assessed the ability of a CO₂-induced extract of calendula containing triterpenes to reduce inflammation in mice using the croton oil ear test. In this induced otodermatitis test,⁴ the irritant croton oil was injected on the inner surface of the ear canal. Varying doses of calendula extract were applied topically to the same areas. Controls received only the irritant. Small plugs were placed in each ear and after six hours the plugs were removed. The difference in weight between the two plugs was taken as a measure of the edematous response.

The authors also conducted the experiment using indomethacin in place of the calendula extract. Both the CO₂ extracts and the triterpenes fractions were found to reduce the edema when compared with the controls ($P < 0.01$). In addition, a dose-dependent response to both types of extracts was observed. The extracts were shown to inhibit edema to a greater degree than seen in mice treated with indomethacin. The authors demonstrated that the faradiol monoester content in the CO₂ extract was the best index of its anti-inflammatory activity.

Zitterl-Eglseer and colleagues also assessed the anti-inflammatory activity of calendula using the croton oil-induced test.⁶ The authors demonstrated a statistically significant reduction in edema in mice treated with a calendula preparation as compared to the controls. The anti-inflammatory effect of calendula in animals has been studied using other established laboratory models of artificially induced inflammation, including the tetradecanoylphorbol-13-acetate (TPA) induced inflammatory test⁷ and the carrageenin-induced inflammatory test.⁸ In both studies, the calendula preparation demonstrated an anti-inflammatory effect similar to that of the commercially approved medication indomethacin and, in Belgium, acetylsalicylate de lysine.

Clinical Studies

Although numerous laboratory-based studies on the anti-inflammatory effect of calendula were found, few studies have been conducted in humans. French researchers assessed the ability of calendula ointment to promote healing in second- and third-degree burns.¹⁰

Calendula was compared to pure vaseline and a commercial proteolytic ointment indicated in the management of burns. Approximately 50 people with second- or third-degree burns were treated for 12 days in each group. Assessment of success was conducted at eight and 12 days and was defined as the absence of an eschar or local infection. In total, 70% of the calendula group were classified as successes compared to 66% of those treated with the commercial product ($P > 0.05$) and only 54% of those receiving vaseline ($P = 0.05$). In addition, 35% of those treated with the calendula ointment denied an adverse effect and 60% denied pain, but only 10% of those treated with the commercial product denied any adverse effects ($P < 0.05$) and 21% denied any pain ($P < 0.05$).

In Brazil, Neto et al also demonstrated the ability of calendula to promote burn healing. They studied the impact of calendula and a combination of calendula and barbatimao (derived from *Stryphnodendron barbadetiman*) on three groups: individuals with burns (both sunburns and domestic burns, such as hot oil); with varicose ulcers; and with cuts and dermatitis.¹¹ The authors stated that all individuals had been treated by conventional therapy without success. Each group had 5-8 patients. Fifteen individuals with burns who were treated with

calendula alone or in combination with barbatimao reportedly had complete healing within 2-6 days. Of the 12 individuals treated with a calendula preparation for varicose ulcers, eight reported complete healing within 30 days. Finally, seven of the 11 individuals with cuts or chronic dermatitis reportedly were healed within 10 days. Thus, calendula appeared to have greater efficacy in the management of burns than when used for ulcers, cuts or dermatitis.

Kartikayan et al compared the effect of calendula cream in a homeopathic preparation to antibiotic topical ointment for trophic ulcers in leprosy patients.¹² After 3-4 weeks, patients using calendula ointment showed a 30-40% reduction in depth and diameter of the ulcers and the absence of any secondary infections. Although the authors did not comment on the outcome of those treated with an antibiotic ointment, they did point out that, in general, trophic ulcers do not heal without immobilization of the affected extremity. None of the patients in the study had affected extremities immobilized.

Extracts of calendula combined with other herbal preparations were also shown to accelerate healing of artificially induced skin abrasions in five healthy subjects.¹³ Compared to controls, the preparation accelerated healing by an average of 3.4 days.

Calendula Useful in Garden, Kitchen, and First Aid Kit

When creating a dramatic landscape, nothing can compare to the vivid yellows and oranges calendula brings to a garden. But this popular garden flower does more than add brilliant color — it can be found in recipes, first aid ointments, and aromatic essential oils.

Named calendula by ancient Romans after it bloomed on the first day or “calends” of every month, for years this herb was associated with the sun and believed to open at sunrise and close at sunset. Although its symbolic meaning is hopelessness and grief, ancient Greeks and Arabs valued this herb for its edible qualities. In fact, its common name, pot marigold, derived from the plant’s use as an herb added to the cooking pot.

Historically, both flowers and leaves were added to vegetable stews, and pickled marigolds were once part of the normal diet, according to *The Classic Herb Cookbook*. Today the petals’ musky aroma and tangy, lightly bitter flavor make them popular additions to soups, salads, fish and egg dishes.

Dried calendula petals have long been used in Europe as a “poor man’s saffron” to color rice. *Reader’s Digest’s 1001*

Hints and Tips for Your Garden suggests folding calendula into butter or cream cheese for a colorful, flavorful bread and cracker spread.

In addition to its culinary uses, calendula has many medicinal and cosmetic uses. Calendula petals can be used as a hair rinse, a fabric dye, and a bright addition to potpourri. Tea made from infusing 3 teaspoons of petals in 8 ounces of water may soothe canker sores. According to *The Complete Book of Herbs*, calendula tea also may offer relief from internal spasms and gastric disorders, and a poultice made from the flowers is a natural first aid for burns and stings. The April 1998 issue of *Nutrition Science News* includes calendula in a list of essential ingredients for sunscreen that offers good protection. People suffering from sunburn may want to note the advice given in the May 1998 issue of *Better Nutrition*, in which the author says calendula is the best herb known for relieving sunburn pain.

The *Better Nutrition* article also states that before antibiotics were available, physicians used calendula to prevent gangrene and hasten wound healing. Civil War medics made many references to calendula in their writings, and one 19th century doctor reportedly recommended calendula compresses for healing bullet wounds in the American West. ■

Adverse Effects

No adverse effects of calendula ointment were found in the literature. However, a case of severe allergy to calendula tea was reported from Russia. Individuals allergic to other members of the aster family, such as ragweed, should exercise caution when ingesting calendula.

Drug Interaction

No drug interactions have been reported.

Formulation

Calendula extract generally is prepared from the flower as a tincture, lotion, or cream that usually is applied directly or as a cool compress. Calendula tea preparations have been gargled or taken internally to treat oral and gastric ulceration. Calendula is also prepared and available as a homeopathic remedy, fluid extract, and oil.

Dosage

Herbal ointments are often used 3-4 times a day. Commission E lists the calendula flower as an approved substance in ointments equivalent to 2-5 g of crude drug in 100 g of ointment. The calendula herb, comprised of an extract of the whole plant, is not approved.

Conclusion

Medicinal preparations of calendula have been used since medieval times. Calendula has a strong history as a folk remedy for skin infections, particularly in Europe. Numerous laboratory-based studies have demonstrated a significant anti-inflammatory effect of calendula extracts on induced inflammation in mice. Data from human studies are limited and the studies conducted were not rigorous. Nevertheless, they suggest that calendula can promote the healing of burns and that it has an anti-inflammatory effect.

Recommendation

When questioned by their patients about the use of calendula, clinicians could advise that laboratory studies using animal models suggest an anti-inflammatory effect. Although clinical studies are limited in number and in scope, they do suggest a benefit of using calendula to treat and manage skin inflammation, particularly

burns. Clinicians can also feel confident that the use of calendula preparations is safe. ❖

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In Future Issues:

Selenium for Cancer Prevention
Acupuncture for Narcotic Addiction
Garlic for Boosting Immunity

With Comments from John La Puma, MD, FACP

Homeopathic Remedy for Vertigo

Source: Weiser M, et al. Homeopathic vs. conventional treatment of vertigo: a randomized double-blind controlled clinical study. *Arch Otolaryngol Head Neck Surg* 1998; 124:879-885.

To compare the efficacy and safety of a homeopathic remedy against betahistine hydrochloride (active control) in the treatment of patients with vertigo of various origins in a confirmative equivalence trial, we randomized a total of 119 patients from 15 general practice study centers.

Both homeopathic and conventional treatments showed a clinically relevant reduction in the mean frequency, duration and intensity of the vertigo attacks. The therapeutic equivalence of the homeopathic remedy and betahistine was established statistically. Both remedies reduced the frequency, duration and intensity of vertigo attacks during a 6-week treatment period. Also, vertigo-specific complaints were significantly reduced in both treatment groups.

■ Comment

Fortunately, peripheral vertigo is usually self-limited. Unfortunately, physicians usually have little to offer beyond antihistamines and antiemetics.

These German investigators at a contract research organization recruited, randomized, treated, and observed patients with acute or chronic (>6 months) vertigo who had at least three attacks the week before the study. They used identically tasting and looking liquid placebos 15 gtt tid plus either the homeopathic remedy or betahistine (18 mg/d) for 42 days. They measured quality of life using the validated Medical Outcome Study-Short Form 36, and self-reported frequency, duration, and intensity of vertigo. The subjects were assessed on days 1, 3, 7, 14, 28, and 42.

The authors state that betahistine (2-

pyridine) stimulates H1 and H2 cerebral receptors, resulting in vasodilation, and that it is (in Germany) the current treatment of choice for vertigo. Meclizine HCl is often given in the United States for the same indication. The homeopathic preparation tested included ambra grisea DE6, anamirta cocculus D4, conium maculatum D3, and petroleum rectificatum D8.

Data on 105 patients were analyzed: 29 men and 76 women, mean age early 50s, 23% with abnormal findings, half with vestibular vertigo or vasomotor vertigo, and half with unknown diagnoses. Most (70%) in both treatment groups were being treated for the first time, with symptoms generally less than two months.

Both preparations reduced direct vertigo symptoms, intensity of vertigo during exercises, and vertigo-associated symptoms. Frequency of attacks fell to barely once daily from 4-6 times daily; duration of attacks was halved; intensity was cut by 2/3. No significant differences in physical or mental health or tolerability of the agents were observed between the treatment groups.

Problems with this trial include lack of a real placebo control (adding a placebo to each of the two interventional arms is curious, though the authors claim it would be unethical not to offer one of the two treatments given); uncertain etiology of vertigo; an uncertain rate of spontaneous, unrelated improvement; and the relationship of the demonstrated improvement to the person-to-person contact offered six times in six weeks. No mechanism was postulated for the effectiveness of the homeopathic remedy.

Recommendation

Taking this homeopathic preparation—or any homeopathic preparation—is unlikely to do serious harm. But proof of the ability to diminish symptoms that can be expected to fade awaits a better and placebo-controlled trial. ❖

Stricter Supplement Labeling Rules Needed: FDA

Source: Rheinstein PH, Tsai VW.

Keeping abreast of new drug approvals and labeling changes. *Am Fam Physician* 1998; 58:995-998.

On April 29, 1998, the FDA proposed a rule that would define criteria for the structure and function claims permitted by the Dietary Supplement Health and Education Act of 1994 (DSHEA) and the disease claims prohibited by it. Permissible claims include “promotes regularity,” “helps maintain cardiovascular health,” or “supports the immune system.” Prohibited disease claims include “protects against cancer,” “antiseptic,” “lowers cholesterol,” and “reduces nausea associated with chemotherapy.” Adverse events associated with dietary supplements should be reported to MedWatch at www.fda.gov/Med-Watch.

■ Comment

Currently, supplements are sold without government screening. Consumers must rely on companies' good names, on the assurances of brand names, or on the recommendations of friends or relatives. There is no guarantee that supplements contain what the label says they do because there are no federally required standards for their composition. Major pharmaceutical firms are entering the market and are likely to add quality improvement and perhaps standardization to the field.

Recommendation

The proposed DSHEA rule is a start—a stricter rule would be better. Standardized preparations from German companies are probably most reliable, until public standards and high quality make themselves known. Given their activity, some supplements should be reclassified as medications. ❖

32. Which of the following mechanisms is responsible for ginger's antiemetic activity?

- CNS depression
- Increased gastric motility
- Increased gastric emptying
- None of the above

33. Therapeutic doses of ginger are considered safe in pregnancy.

- True
- False

34. Ginger appears to prevent and/or treat nausea in all of the following situations *except*:

- seasickness.
- anesthesia-induced nausea.
- food poisoning.
- chemotherapy-induced nausea.

35. The German Commission E monographs state ginkgo is approved for treating all of the following *except*:

- memory impairment.
- concentration difficulties.
- depression from organic brain disease.
- adult attention deficit/hyperactivity disorder.

36. Which of the following is not true?

- Ginkgo induces significant increases in glucose utilization in brain areas mediating somatosensory processing and vigilance as well as vestibular mechanisms.
- Ginkgo reduces the number of adrenal peripheral benzodiazepine receptors, thereby altering cholesterol transport-inhibiting, stress-related corticosteroid secretion.
- EGb 761 (ginkgo extract) protects against age-related changes in hippocampus.
- Ginkgo extracts are reversible inhibitors of monoamine oxidase A and B subspecies.

37. What should you recommend for a home medicine chest of non-toxic skin creams?

- Neosporin and topical steroid creams are common useful ointments. Herbal and homeopathic preparations are, in general, not advisable.
- Neosporin, topical steroid creams and calendula cream are safe and useful ointments.
- Many preparations of calendula cream are sold but there is no evidence that they are effective.
- None of the above.

38. A mother asks about the use of calendula cream for her child. She states she understands that more studies may be done.

What is an appropriate response?

- Some studies suggest that calendula contains compounds that can reduce inflammation in mice in lab experiments.
- The use of calendula is folk medicine with no good evidence to suggest that it is useful.
- There are too many health risks associated with the use of calendula for injury treatment.
- Numerous cases of contact dermatitis have been reported with herbal creams such as calendula.



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