

This material is protected by U.S. copyright law. Unauthorized reproduction is prohibited. To purchase quantity reprints, please e-mail reprints@ons.org or to request permission to reproduce multiple copies, please e-mail pubpermissions@ons.org.

Herbs or Natural Products That May Cause Cancer and Harm

Part Four of a Four-Part Series

Muriel J. Montbriand, PhD, RN

Purpose/Objectives: To provide evidence-based research information about 27 herbs and natural products that have the potential to cause cancer and harm.

Data Sources: Natural Medicines Comprehensive Database and Lawrence Review of Natural Products—Monograph System. Information about these herbs has been found in evidence-based studies cited in the references.

Data Synthesis: Early research shows that some herbs and natural products appear to have the potential to cause cancer and harm. Oncology nurses who receive this information can become resources for patients and other healthcare professionals.

Conclusions: Consumers and healthcare professionals are wise to weigh the benefits or risks and possibly limit or avoid the use of these products.

Implications for Nursing: The table and text in this article are presented as quick resources for healthcare professionals working in clinical oncology.

This review alerts consumers and healthcare professionals about herbs and natural products that have the potential to cause cancer and harm. Some herbs and natural products can be extremely poisonous or cause severe adverse reactions, which has been well documented by many authors (Bisset, 1994; Blumenthal et al., 1998; Brigden, 1995; Duke, 1987; Duke & Vasquez, 1994; Facts and Comparisons, 2001; Foster & Duke, 1990; Foster & Tyler, 1999; Leung & Foster, 1996). Preliminary research reviewed for this article indicates that 27 herbs and natural products have the potential to potentiate cancer and/or cause additional harm. Anecdotal and lay advertisement may stimulate interest in these products, attracting individuals who wish to protect themselves against cancer. These individuals may never have experienced cancer; however, all consumers should take note of these products, weigh the possible risks or benefits, and limit or avoid their use. The evidence-based information in this article will assist healthcare professionals to be better resources for consumers and patients.

Key Points . . .

- ▶ The 27 herbs and natural products discussed in this review may be poisonous or harmful and may cause cancer.
- ▶ Consumers should be aware of these herbs and natural products and avoid their use.
- ▶ Oncology nurses can become better resources for healthcare professionals and patients regarding herbs and natural products.

This is the fourth article in a four-part series dedicated to providing information about herbs and natural products for healthcare professionals in clinical oncology. The herbs and natural products discussed are those that may cause cancer and harm. The target group for this article is individuals who do not have cancer but are concerned about its development; however, all consumers may benefit from this information, taking note of these products and avoiding them when possible.

As indicated in previous articles in this series, some overlap in categories should be expected because early evidence, especially in vivo and in vitro evidence, often shows contrary results. For example, black tea was discussed in Part Two, where the emphasis was on its estrogenic properties and

Muriel J. Montbriand, PhD, RN, is an associate professor in the College of Nursing and a research associate in applied research/psychiatry in the College of Medicine at the University of Saskatchewan in Saskatoon, Canada. During this work, the author was a recipient of two Health Services Utilization and Research Commission, Socio-Health Grants, in Saskatoon. (Mention of specific products and opinions related to those products do not indicate or imply endorsement by the Oncology Nursing Forum or the Oncology Nursing Society.)

Digital Object Identifier: 10.1188/05.ONF.E20-E29

potential to enhance cancer growth. Black tea also contains tannins and could be (but is not) included in this article's discussion. Products that contain tannins are controversial in the literature; numerous studies and evaluations have indicated that tannins have carcinogenic and anticancer properties (Leung & Foster, 1996; McGuffin, Hobbs, Upton, & Goldberg, 1997). More instances of controversy appear in this article.

The names of herbs and natural products have been selected from listings in the Natural Medicines Comprehensive Database (2004) and Lawrence Review of Natural Products—Monograph System (Facts and Comparisons, 2001). Evidence about these herbs has been found in the studies cited in the references. Other products that potentiate cancer or harm may exist; however, this review includes only herbs and natural products recognized by the authors, professionals, or advisory boards of the resources noted.

The majority of the studies cited are *in vitro*, performed in glass on tissue from a living organism, or *in vivo*, performed on tissue not removed from a living organism (i.e., animal studies). Most studies have not advanced to clinical trials involving humans. The few human studies cited are preliminary clinical trials; therefore, although results may seem favorable or unfavorable, treat these findings with caution.

Neither the author nor publisher makes any medical claims for any of the herbs or natural products in this review or the table. This is informational literature. Note that some of the herbs described are deadly poisons and some are extremely dangerous.

Table 1 provides the names of herbs and natural products discussed in the text. Common names as well as brand names and manufacturers are included. Some products have numerous brand names, making a complete listing prohibitive. The number of brand names found is included in the table. When a brand name contains only one ingredient, it often bears the product's common name. Single-ingredient products are identified in the table. Other brands with numerous ingredients also are indicated. In the first three parts of this series, single-ingredient brands were recommended over multiple-ingredient brands; however, here, all brands that contain the herbs and natural products listed in this article should be avoided because of their potential to potentiate cancer growth or harm.

Products That May Potentiate Cancer Growth

Alpha hydroxy acid has the scientific names *hydroxysuccinic acid*, *monohydroxysuccinic acid (malic acid)*, *2-hydroxypropionic acid (lactic acid)*, *hydroxyacetic acid (glycolic acid)*, *dihydroxysuccinic acid (tartaric acid)*, and *gluconolactone*. Individuals self-medicate with alpha hydroxy acid to treat discomfort and pain associated with fibromyalgia (Russell, Michalek, Flechas, & Abraham, 1995). Reactions to alpha hydroxy acid are not associated with oral use but are related to topical applications to photo-damaged skin (Stiller et al., 1996) and dry skin (Kempers, Katz, Wildnauer, & Green, 1998; Wehr, Krochmal, Bagatell, & Ragsdale, 1986). Products containing this acid can cause increased sensitivity to the sun and ultraviolet light and can increase the danger of skin damage and skin cancer, especially with long-term use (Facts and Comparisons, 2001). Use of high concentrations of products containing alpha hydroxy acid can result in severe skin irrita-

tion, burning, and sloughing (Facts and Comparisons). For treatment of photo-aged skin, alpha hydroxy acid products in concentrations of 8% (Stiller et al.) typically are used, whereas Wehr et al. used 12% preparations.

Areca has the scientific name *Areca catechu* and is popularly known as betel nut. Areca sometimes is chewed for recreational purposes or used in self-medication for central nervous system stimulation (Gruenwald, Brendler, & Jaenicke, 1998). Sullivan, Allen, Otto, Tiobech, and Nero (2000) reported that this product has been used in Palau to treat schizophrenia; however, chewing areca nut is associated with oral cancer (VanWyk, 1997). In addition, excessive consumption of areca can cause convulsions and death (Facts and Comparisons, 2001). Chewing approximately 11 whole nuts per day is considered a typical dose when used therapeutically for treatment of schizophrenia (Sullivan et al.), but chewing and ingesting larger quantities of areca are considered unsafe.

Aristolochia has the scientific names *Aristolochia serpentaria*, *Aristolochia reticulata*, and other *Aristolochia* species and commonly is called snakeroot or snakeweed. *Aristolochia* is used for self-medicating gastrointestinal and gallbladder colic (Gruenwald et al., 1998). This herb contains aristolochic acid, which is nephrotoxic and carcinogenic and is associated with cancers of the kidney, bladder, stomach, lung, and lymphoma in rodents. *Aristolochia* acid also is associated with cancers of the bladder, ureter, and renal pelvis in humans (Nortier et al., 2000). Nortier et al. reported more than 100 cases of nephropathy, referred to as "Chinese herb nephropathy," associated with use of this herb. Of these, 43 cases progressed to end-stage renal failure requiring dialysis or transplants. As a result, the U.S. Food and Drug Administration reported that this herb is unsafe (Natural Medicines Comprehensive Database, 2004). Lust (1974) warned of aristolochia's toxicity and indicated that those who wish to use this herb should do so only under the guidance of a healthcare professional.

Beer and alcoholic beverages: As well as being an appetite and digestive stimulant, beer is used medicinally to prevent many ailments such as cardiovascular disease, Alzheimer disease, cancer, gallstones, and kidney stones. Chronic ingestion of three or more alcoholic drinks per day can lead to physical dependence, malnutrition, amnesia, dementia, somnolence, cardiac myopathy, hepatotoxicity, and cirrhosis, among other conditions, as well as cancers of the mouth, esophagus, pharynx, larynx, and liver (Micromedex Inc., 2004; Thun et al., 1997). Traditionally, more than one alcoholic drink daily may increase mortality among women with breast cancer by as much as 30% (Thun et al.). One drink is equivalent to 4 oz (120 ml) of wine, 12 oz of beer, or 1 oz of spirits (Micromedex Inc.).

Beta-carotene has the same scientific name, *beta-carotene*. Notice this is not the same product as canthaxanthin (discussed in Part Three of this series) with the scientific names *4,4-diketo-beta-carotene* and *Beta,beta-carotene-4,4-dione*. Beta-carotene and canthaxanthin are two different chemical compositions; therefore, carefully scrutinize all scientific names. Individuals self-medicate with beta-carotene, a source of vitamin A (McEvoy, 1998), to decrease exercise-induced asthma (Cooper, Eldridge, & Peters, 1999) and prevent cancer (Cooper et al.; Omenn, 1998), cardiovascular disease, and age-related macular degeneration (Cooper et al.; Price & Fowkes, 1997). Smokers who take more than 20 mg of beta-

Table 1. Herbs and Natural Products That May Potentiate Cancer Growth and Harm: Common and Brand Names

Herb or Natural Product	Brand Name and Manufacturer or Other
Alpha hydroxy acid Other names: AHA, alpha-hydroxyethanoic acid, apple acid, citric acid, dihydroxysuccinic acid, gluconolactone, glycolic acid, hydroxyacetic acid, hydroxycaprylic acid, hydroxypropionic acid, hydroxysuccinic acid, lactic acid, malic acid, mixed fruit acid, monohydroxysuccinic acid, tartaric acid	#14 Colon (Systemic Formulas) ^b Chitosan Plus (Progressive Labs) ^b Lava (Universal Nutrition) ^b PMS Escape (Back Bay Scientific) ^b Firm Lotion (Mannatech) ^b Vascular Complete (Rexall-Sundown) ^b 123 brand names found
Areca Other names: areca nut, betel nut, betel quid, pinag, pinlag	No brand names found
Aristolochia Other names: birthwort, long birthwort, pelican flower, red river snakeroot, sangree root, sangrel, serpentaria, snakeroot, snakeweed, Texas snakeroot, Virginia serpentry, Virginia snakeroot	No brand names found
Beer and alcoholic beverages	Available in numerous varieties
Beta-carotene Other name: provitamin A	Beta Carotene (Puritan's Pride) ^a Beta Carotene (Olympian Labs) ^a Beta Carotene 5,000 IU Chewable (Jamieson) ^a Beta Carotene 10,000 IU (Jamieson) ^a Beta Carotene 25,000 IU (Jamieson) ^a Beta Carotene 25,000 IU With Vitamin C and E (Jamieson) ^b Brand names too numerous to count
Bishop's weed Other names: ajava seeds, ajowan, ajowan caraway, ajowan seed, ajowan], bishop's flower, bullwort, carium, flowering ammi, omum, yavani	No brand names found
Black and white pepper Other names: blanc poivre, kosho, pepe, pepper, pepper extract, pepper plant, peppercorn, pfeffer, pimenta, pimienta, piper, poivre, poivre noir	Advanced Formula (Biotech Corp.) ^b OcuPower (Nutraceutical Sciences Institute) ^b Super Prostate Formula (Physician's Choice) ^b 7 Day Smoke Away–Lung Saver (The Quit Smoking Co.) ^b 42 brand names found
Calcium Other names: bone meal, calcium acetate, calcium aspartate, calcium carbonate, calcium chelate, calcium chloride, calcium citrate, calcium citrate malate, calcium gluconate, calcium lactate, calcium lactogluconate, calcium orotate, calcium phosphate, di-calcium phosphate, heated oster shell-seaweed calcium, hydroxyapatite, oyster shell calcium, tricalcium phosphate	Calcium +D (Rexall-Sundown) ^b Calcium 500 mg (Rexall-Sundown) ^b Calcium 600 mg (Pro Health) ^b Calcium Oyster Shell 1,000 mg (Rexall-Sundown) ^b Brand names too numerous to count
Marjoram Other names: garden marjoram, gartenmajoran, knotted marjoram, majoran, majorana aetheroleum oil, majorana herb, marjolaine, meyorana, sweet marjoram	BLF #30 Head-X (Health Center for Better Living) ^b Liga-Pane (Nutri-Quest) ^b PMS Fort (Futurebiotics) ^b Sedivitax (Aboca USA, Inc.) ^b 6 brand names found
Methionine Other names: DL-methionine, DL methionine, L-methionine	Amino Acid 1,000 mg (Nature's Life) ^b Beef Liver 1,500 mg (Nature's Life) ^{b, c} Metabolol II (Champion Nutrition) ^b #150 Pro Nutro Protein (Systemic Formulas) ^{b, c} #408 CLNZ Toxin Chelator (Systemic Formulas) ^{b, c} 145 brand names found

(Continued on next page)

^a This herb or natural product is the only ingredient in this brand.

^b This brand name is an example of a product in which the herb or natural product is included along with other herbs and products. Monitor for all possible side effects of all ingredients in these products.

^c Safety of this product is a concern. The product contains animal material, possibly diseased animals that may harbor bovine spongiform encephalopathy (i.e., mad cow disease).

Table 1. Herbs and Natural Products That May Potentiate Cancer Growth and Harm: Common and Brand Names (Continued)

Herb or Natural Product	Brand Name and Manufacturer or Other
Omega-6 fatty acids Other names: N-6, N-6 EFAs, N-6 essential fatty acids, omega 6, omega-6, omega-6 oils, polyunsaturated fatty acids, PUFAs	The Missing Link: Master Nutrient Formula (Designing Health, Inc.) ^b Our Daily Fish (Functional Products) ^b Ultimate Oil (Nature's Secret) ^b #132 FLX Vegetable Omega-3 Flax Seed Oil (Systemic Formulas) ^b 19 brand names found
Pau d'arco Other names: ipe, ipe roxo, ipes, Lapacho, Lapacho colorado, Lapacho morado, pau de arco, purple lapacho, red lapacho, taheebo, taheebo tea, trumpet bush	Amazon A-F (Raintree Nutrition, Inc.) ^b Amazon Prostate Support (Raintree Nutrition, Inc.) ^b Pau D'Arco (Source Naturals) ^b Pau d'Arco-Black Walnut Virtue (Blessed Herbs) ^b 51 brand names found
Sassafras Other names: ague tree, cinnamon wood, common sassafras, kuntze saloop, sassafraz, saxifraz	BLF #47 Rest Ease Ingredients (Health Center for Better Living) ^b T-CAN (Dial Herbs) ^b 5 brand names found
Shark liver oil Other names: basking shark liver oil, deep sea shark liver oil, dog fish liver oil, shark liver, shark oil	Shark Oil (Futurebiotics) ^b 2 brand names found
St. John's wort Other names: amber, amber touch-and-heal, demon chaser, fuga daemonum, goatweed, hardhay, hypereikon, hyperici herba, hypericum, Johns wort, klamath weed, millepertuis, rosin rose, Saint Johns wort, tipton weed	St. John's Wort (Gala Herbs) ^a St. John's Wort (Metabolic Response Modifiers) ^a St. John's Wort (Swanson) ^a Appleheart St. John's Wort (Appleheart) ^b Bio St. John's (Pharmanex) ^b St. John's Wort (Jamieson) ^b St. John's Wort (Celestial Seasonings) ^b 168 brand names found
Tannin: American chestnut No other names	No brand names found
Tannin: bistort Other names: adderwort, dragonwort, Easter giant, Easter mangiant, oderwort, osterick, patience dock, red legs, snakeweed, sweet dock	T-MSLE (Dial Herbs) ^b 1 brand name found
Tannin: black walnut Other names: nogal Americano, nogueira-preta, noyer noir, schwarze walnuss	Fingerprinted Black Walnut Hulls, GNC Herbal Plus (GNC) ^b Fresh Green Black Walnut Wormwood Complex (Now) ^b 39 brand names found
Tannin: coffee Other names: café, coffea, espresso, java, mocha	Numerous brand names
Tannin: English walnut Other names: fructus cortex, juglans, juglandis, juglandis folium, walnussblät-ter, walnussfrüchtschalen, walnut	Clear Skin (PhytoPharmica) ^b (a homeopathic product) 4 brand names found
Tannin: Mormon tea Other names: Brigham tea, desert tea, popotillo, teamster's tea, squaw tea	Brigham Tea (Nature's Way) ^b HAS Original Formula (Nature's Way) ^b Yucca-AR Formula (Nature's Way) ^b 10 brand names found
Tannin: oak bark Other names: common oak, durmast oak, eichenrinde, English oak, pedunculate oak, quercus cortex, sessile oak, stave oak, stone oak, tanner's bark, tanner's oak	C&F Formula (Dial Herbs) ^b Psoriacin (Dr. Clayton's Naturals) ^b 9 brand names found

(Continued on next page)

^a This herb or natural product is the only ingredient in this brand.

^b This brand name is an example of a product in which the herb or natural product is included along with other herbs and products. Monitor for all possible side effects of all ingredients in these products.

^c Safety of this product is a concern. The product contains animal material, possibly diseased animals that may harbor bovine spongiform encephalopathy (i.e., mad cow disease).

Table 1. Herbs and Natural Products That May Potentiate Cancer Growth and Harm: Common and Brand Names (Continued)

Herb or Natural Product	Brand Name and Manufacturer or Other
Tannin: pomegranate Other names: granada, grenadler, shi liu gen pi, shi liu pi	Midlife Care (Health Factor) ^b Optein (Solgar) ^b Estrolean Fat Burner Supreme (Bodyonics, Ltd.) ^b 8 brand names found
Tannin: quillaia Other names: China bark, murillo bark, Panama bark, soapbark, soap tree	MSM Rejuvenator (Progressive Labs) ^b 1 brand name found
Tannin: sorrel Other names: acedera com n, azed-brava, garden sorrel, sorrel dock, sour dock, wiesensauerampfer	Quanterra Sinus Defense (Pfizer) ^b SinuComp (PhytoPharmica) ^b 3 brand names found
Tannin: willow bark Other names: basket willow, bay willow, brittle willow, crack willow, Daphne willow, knackweide, laurel willow, lorbeerweide, osler rouge, pupurweide, purple osler willow, reifweide, salicis cortex, silberweide, violet willow, weidenrinde, white willow, white willow bark	White Willow Bark Extract (Nature's Way) ^a Pain-Less (Herbalist) ^b Herbal Pain and Fever Relief (Holista) ^b 129 brand names found
Tannin: witch hazel Other names: hazel, hmamelis, snapping tobacco wood, spotted elder, winter bloom, witchazel	Atri-Verm (Atrium Inc.) ^b Body Guard (Jamieson) ^b Circusome (Jamieson) ^b 16 brand names found

^a This herb or natural product is the only ingredient in this brand.

^b This brand name is an example of a product in which the herb or natural product is included along with other herbs and products. Monitor for all possible side effects of all ingredients in these products.

^c Safety of this product is a concern. The product contains animal material, possibly diseased animals that may harbor bovine spongiform encephalopathy (i.e., mad cow disease).

carotene have a significantly higher risk of developing lung or prostate cancer ("The Effect of Vitamin E and Beta Carotene," 1994; Heinonen et al., 1998; Omenn; Omenn et al., 1996; Pryor, Stahl, & Rock, 2000). Premenopausal women who consume five or more servings of fruit or vegetables rich in beta-carotene appear to have a lower risk of breast cancer (Zhang et al., 1999). Adverse effects for high usage of this product include a yellow or orange pigmentation of the skin (McEvoy) and liver damage (Health and Welfare Canada, 1990; Montbriand, 1994). Natural Medicines Comprehensive Database (2004) indicated that the Institute of Medicine reviewed beta-carotene but did not provide a recommended daily intake, citing lack of sufficient evidence. Health and Welfare Canada has not revised its recommended daily dosages since 1990 and has not provided a recommended dose for beta-carotene.

Bishop's weed has the scientific names *Ammi majus* and *Ammi visnaga*. Individuals self-medicate with bishop's weed for digestive disorders, asthma, angina, and kidney stones. Bishop's weed also is used as a diuretic (Chevallier, 2000). Bishop's weed can cause skin malignancies in patients predisposed to cancer (Fetrow & Avila, 1999). This herb can cause photosensitivity, contact dermatitis, and allergic reactions, as well as nausea, vomiting, and headache when taken orally (Natural Medicines Comprehensive Database, 2004). No reliable information speaks for this herb's safety. In addition, no commercial brands containing bishop's weed have been found; therefore, users may be collecting this herb in the wild. No typical dose has been reported.

Black pepper has the scientific name *Piper nigrum*, which refers to black and white peppers. Individuals self-medicate

(orally) with pepper to treat gastric, bronchial, and cancer conditions (Leung & Foster, 1996). Early evidence indicates that black pepper may protect against colon cancer (Nalini, Sabitha, Viswanathan, & Menon, 1998). Conversely, Singh and Rao (1993) found that black pepper induces the enzymes that cause liver tumors (el-Mofty, Khudoley, & Shwaireb, 1991). Aspiration of large amounts of black pepper has caused deaths (Cohle et al., 1988; Sheahan, Page, Kemper, & Suarez, 1988). Typical doses range from 300–600 mg or as much as 1.5 g per day (Gruenwald et al., 1998); 0.25 tsp is equivalent to 1.25 g dry weight. Treat this herb with caution.

Calcium has the same scientific name, as well as *Ca*. People self-medicate with calcium to treat hypocalcemia, osteoporosis, rickets, premenstrual syndrome, and leg cramps and to reduce susceptibility to colorectal cancer (Natural Medicines Comprehensive Database, 2004). Epidemiologic research shows that high intake of dietary calcium tends to increase the risk of prostate cancer (Chan et al., 1998). Gastrointestinal irritation, belching, and flatulence have been reported as adverse effects associated with high oral calcium intake (Martindale, 1999). The recommended daily intake for individuals 19 years and older is 1,200–1,300 mg (Yates, Schlicker, & Sutor, 1998). The recommended doses can be taken with confidence, but higher doses put an individual at risk.

Marjoram has the scientific name *Origanum majorana*, which is synonymous with *Majorana hortensis*. Individuals self-medicate with marjoram to treat coughs and colds as well as gall bladder and gastrointestinal conditions (Natural Medicines Comprehensive Database, 2004). The marjoram flower, leaf, and oil contain arbutin and hydroxyquinone.

The latter seems to have the potential to cause cancer (Blumenthal et al., 1998). According to Gruenwald et al. (1998), a typical dose of marjoram is 1–2 C of tea, prepared by steeping 1–2 tsp of the flower or leaf in 250 ml of boiling water for five minutes.

Methionine has the scientific name *L-2-amino-4-(methylthio)butyric acid*. Individuals self-medicate with methionine to support their liver function and prevent liver damage in acetaminophen poisoning (Vale, Meredith, & Goulding, 1981). Found in meat, fish, and dairy products, methionine is a sulfur-containing essential amino acid (Martindale, 1999). With high intake of methionine, salt, and nitrite in the diet, the risk of gastric cancer increases (La Vecchia, Negri, Franceschi, & Decarli, 1997). Manufacturers' packages may give typical doses, but other than the amount in food, extra doses of methionine are considered possibly unsafe (Natural Medicines Comprehensive Database, 2004). Methionine should be used only for medical emergencies (e.g., acetaminophen poisoning) by healthcare professionals (Vale et al.)

Omega-6 fatty acids, with the scientific name *omega-6 polyunsaturated fatty acids*, are found in vegetable oils. Do not confuse this product with the omega-3 fatty acids that are found in fish oils. Not only are the properties of the two fatty acids different, they also compete metabolically: Omega-6 fatty acids inhibit the incorporation of omega-3 fatty acid into tissue lipids (Hwang et al., 1997). Although omega-3 fatty acids in fish oil seem to have anticancer properties, preliminary in vivo and in vitro research indicates that omega-6 fatty acids may play a role in the development of breast cancer (Godley, 1995). Other scholars speculate that omega-6 fatty acids may prevent breast and prostate cancers (Rose, 1996). Individuals self-medicate with omega-6 fatty acids to prevent heart disease, lower cholesterol, and reduce cancer risk (Natural Medicines Comprehensive Database, 2004). Omega-3 and omega-6 frequently are found in the same products. Until the potential for metabolic competition has been researched further, individuals should weigh the potential risks of taking these supplements. No typical dose has been provided.

Pau d'arco has the scientific names *Lapacho colorado*; *Tabebuia avellanadae*, which is synonymous with *Tabebuia impetiginosa*; and *Tabebuia heptaphylla*. Pau d'arco commonly is known as taheebo. People self-medicate with pau d'arco to treat cancer, *Candida*, and viral and parasitic infections (Natural Medicines Comprehensive Database, 2004). Anticancer activities have been noted, particularly in the treatment of sarcomas, but studies have been discontinued because, in testing, no more than 30 mcg of lapachol (the active constituent) could be reached per 1 ml of plasma without causing extreme toxicity (Duke, 1987; Facts and Comparisons, 2001; Foster & Tyler, 1999). High doses cause severe nausea, vomiting, diarrhea, dizziness, anemia, and risk of hemorrhage (Duke; Facts and Comparisons; Foster & Tyler). Although no evidence suggests that pau d'arco has the potential to cause cancer, it has been included in this discussion because this product often is taken to treat or prevent cancer. However, pau d'arco can cause serious harm. Significant evidence of the toxicity of this herb has been amassed; therefore, pau d'arco should be used with extreme caution (Natural Medicines Comprehensive Database). Some manufacturers warn that their products should be taken for no more than seven days, but they do not offer

a rationale for limited use nor do they give an indication of toxicity. Avoidance of this herb is prudent.

Sassafras has the scientific names *Sassafras ablidum*, which is synonymous with *Sassafras officinale*, and *Sassafras varifolium*. Individuals self-medicate with sassafras believe it is a tonic or blood purifier (Tyler, 1994). Preliminary evidence shows that sassafras root bark and oil contain safrole and related components that are carcinogenic, causing liver cancers in experimental animals (Duke, 1987; Ellenhorn, 1997; McGuffin et al., 1997; Newall, Anderson, & Phillipson, 1996; Tyler, 1993). Sassafras, in large amounts or with chronic use, can cause hallucinations lasting for several days (Newall et al.), tremors, vomiting, dilated pupils, hypertension, tachycardia, stupor, collapse (Facts and Comparisons, 2001), abortion, paralysis, liver cancer, and death (Facts and Comparisons; Newall et al.). In addition, a few drops of sassafras oil can be fatal to children (Newall et al.). No typical dose has been recorded (Natural Medicines Comprehensive Database, 2004).

Shark liver oil has the scientific names *Cetorhinus maximus*, *Centroporus squamosus*, and *Squalus acanthias*. Individuals self-medicate with shark liver oil to treat leukemia and other cancers (Facts and Comparisons, 2001; Hasle & Rose, 1991). Animal studies demonstrate that shark liver oil has antiangiogenesis properties in certain cancers, including cutaneous lesions, kidney cancer, and urinary bladder cancer (Skopinska-Rozewska et al., 1999). Other research disputes these findings (Hasle & Rose). Aspiration of shark liver oil has resulted in lipoid pneumonia (Asnis, Saltzman, & Melchert, 1993; Lee, Im, Song, Seo, & Lim, 1999; Lee, Lee, et al., 1999). No typical dose has been reported (Natural Medicines Comprehensive Database, 2004).

St. John's wort has the scientific name *Hypericum perforatum*. Individuals self-medicate with St. John's wort for many mood disturbances, such as anxiety and depression. A component of St. John's wort, hyperforin, seems to inhibit growth of a variety of cancer cells (Schempp et al., 2002). However, St. John's wort also interferes with numerous prescription drugs such as calcium channel blockers, antifungals, glucocorticoids, cisapride, alfentanil, fentanyl, losartan, fluoxetine, midazolam, omeprazole, ondansetron, fexofenadine, and chemotherapeutic agents (e.g., etoposide, paclitaxel, vinblastine, vincristine, vindesine), making therapy less effective (Henderson, Yue, Bergquist, Gerden, & Arlett, 2002; Hennessy et al., 2002; Roby, Anderson, Kantor, Dryer, & Burstein, 2000; Schulz, 2001; Wang et al., 2001). St. John's wort was banned in France because of the numerous drug-herb interactions, and Canada, Japan, and the United Kingdom are implementing cautionary information on product labels (Richter, 2000). The typical dose for depression is 300 mg three times a day (Kim, Streltzer, & Goebert, 1999). St. John's wort is included in this alert review not because it directly causes cancer (although it may precipitate cancer growth through its interactions) but because of its cancer connection, public popularity, and potential to cause harm.

Tannin-Containing Preparations

Tannins, whether gallic acid or catechin, exhibit carcinogenic and anticarcinogenic properties (Leung & Foster, 1996; McGuffin et al., 1997). More recent research still demonstrates

these ambiguities (Chen, Chang, & Lin, 2003; Fujiki et al., 2003; Krajka-Kuzniak & Baer-Dubowska, 2003; Labieniec & Gabryelak, 2003; Marienfeld, Tadlock, Yamagiwa, & Patel, 2003). All of the following herbs have high tannin concentrations, and regular consumption increases the risk of esophageal or nasal cancer (Leung & Foster; McGuffin et al.). This list is not all inclusive.

American chestnut has the scientific names *Castanea dentata* and *Castanea americana*. Individuals self-medicate with American chestnut to treat respiratory ailments or for its sedative or tonic activity (Natural Medicines Comprehensive Database, 2004). Typically, this herb is taken as tea prepared with 1 tsp of leaves and bark (Weiner & Weiner, 1994).

Bistort has the scientific name *Polygonum bistorta* and is used to self-medicate for digestive disorders, particularly diarrhea (Natural Medicines Comprehensive Database, 2004). This herb usually is taken orally as an infusion made of the powdered rhizome and root. Ointments and extracts made with the powdered root are used topically (Gruenwald et al., 1998).

Black walnut has the scientific name *Juglans nigra* and is used to treat diphtheria, leukemia, and syphilis (Duke, 1987). Natural Medicines Comprehensive Database (2004) did not report any adverse reactions for black walnut and indicated that the typical oral dose of black walnut hull is 1,000 mg three times daily.

Coffee has the scientific name *Coffea arabica*. Coffee intake may increase the risk of breast cancer in obese women and ovarian cancer for all women; it also increases the risk of pancreatic cancer (McGuffin et al., 1997; Tyler, 1993, 1994). Drinking one liter or more of strong unfiltered coffee per day can increase total cholesterol levels by 10%. Coffee also is known to increase low-density lipoprotein cholesterol levels and triglycerides (Gruenwald et al., 1998; McGuffin et al.; Schulz, Hansel, & Tyler, 1998). Tyler (1993) suggested that a safe intake of caffeine is no more than 250 mg per day (about two-and-a-half cups of boiled coffee or four cups of instant coffee).

English walnut has the scientific name *Juglans regia*. Black walnut has resulted in tongue cancer and lip leukoplakia (Blumenthal et al., 1998), and mutagenic effects have been found in animal studies (McGuffin et al., 1997). The hull of the English walnut is thought to contain the constituent juglone, which has a carcinogenic effect. The hull is used topically for skin diseases; however, the amount of juglone in the hull varies. The leaf portion is probably safe if used for a short period of time (Natural Medicines Comprehensive Database, 2004). A typical dose of oral English walnut leaf is 1.5 g in a cup of tea three times daily (Bisset, 1994). In self-medication, English walnut fruit is used to lower cholesterol, the hull is used to treat gastrointestinal inflammation, and the leaf is used to treat diarrhea (Blumenthal et al.).

Mormon tea has the scientific name *Ephedra nevadensis*. Mormon tea and a product called ephedra often are confused. Ephedra or Ma Huang, which has the scientific name *Ephedra sinica*, is considered an unsafe herb (McGuffin et al., 1997). Mormon tea does not contain ephedrine (a component of *Ephedra sinica*) and therefore is alkaloid-free and lacks the potential therapeutic and toxic effects of ephedra (McGuffin et al.). Other than tannin, no adverse reactions to Mormon tea have been recorded (Natural Medicines Comprehensive Database, 2004). Mormon tea is prepared by steeping dried

branches of this herb in 150 ml of boiling water for 5–10 minutes (Fetrow & Avila, 1999).

Oak bark has the scientific names *Quercus robur*, *Quercus petraea*, and *Quercus alba*. Individuals self-medicate with this herb to treat diarrhea (Blumenthal et al., 1998), colds, or loss of appetite (Gruenwald et al., 1998). Oak bark contains 8%–12% tannins. Adverse reactions include gastrointestinal disturbances, kidney damage, and liver necrosis. A typical dose is one cup of a tea prepared from oak bark as much as three times a day for a maximum of three to four days (Bisset, 1994).

Pomegranate has the scientific name *Punica granatum*. The fruit rind of pomegranate contains as much as 28% tannins. People generally self-medicate with this product to treat diarrhea, dysentery, tapeworms, or opportunistic intestinal worms (Gruenwald et al., 1998). Overdoses of pomegranate cause strychnine-like effects (i.e., heightened reflex arousal that can escalate to paralysis). Doses in excess of 80 g are known to cause vomiting, bloody emesis, dizziness, chills, vision disorders, collapse, and possible death from respiratory failure (Gruenwald et al.). No typical dosage has been reported (Natural Medicines Comprehensive Database, 2004).

Quillaia has the scientific name *Quillaja saponaria*. People self-medicate with quillaia to treat colds (Natural Medicines Comprehensive Database, 2004). Many adverse effects are associated with ingestion of large amounts of quillaia: liver damage, diarrhea, respiratory failure, stomach pain, convulsions, coma (Duke, 1987; McGuffin et al., 1997) red blood cell hemolysis (Duke; Leung & Foster, 1996), and renal failure (McGuffin et al.). Duke indicated that the *Quillaja saponin* sapotoxin is very poisonous; digitalis is recommended as an antidote. No typical dosage has been listed in Natural Medicines Comprehensive Database; however, Bisset (1994) reported that a typical single dose is 0.2 g chopped and steeped as tea. One teaspoon is approximately 2.3 g.

Sorrel has the scientific name *Rumex acetosa*. Sorrel contains 7%–15% tannins (Leung & Foster, 1996). Individuals often self-medicate with sorrel to treat colds (Gruenwald et al., 1998). Adverse reactions include diarrhea, nausea, polyuria (Facts and Comparisons, 2001), and dermatitis (Newall et al., 1996). Oxalic acid is a poisonous constituent of sorrel that has a corrosive effect on the digestive tract and can lead to oxalic crystals in the kidneys, blood vessels, heart, lungs, and liver, as well as hypercalcemia (Ellenhorn, 1997). Clinical trials studying sorrel in the treatment of acute and chronic sinusitis used Quanterra Sinus Defense Sinupret® (Bionorica, Kerschensteinerstrasse, Germany) tablets, three times daily for as much as two weeks (Marz, Ismail, & Popp, 1999; Neubauer & Marz, 1994; Schulz et al., 1998). Sinupret contains 29 mg of sorrel, in addition to other herbs such as gentian, elder flower, European vervain, and primrose.

Willow bark has the scientific names *Salix alba*, *Salix purpurea*, and *Salix fragilis*. Willow bark constituents include flavonoids, tannins, and salicylates. Attention usually is given to salicylates that are in very low concentrations in most willow bark. Willow bark often is used as a self-medication to treat colds, headaches, and joint pain (Bisset, 1994). Gastrointestinal disturbances and kidney and liver damage are possible adverse effects, perhaps related to the tannin content (McGuffin et al., 1997).

Achieving medicinal quantities of salicylates greater than 1% from willow bark is difficult. Salicylates usually are extracted with very hot water (Facts and Comparisons, 2001; Tyler, 1993). Tyler (1993) indicated that the volume of liquid needed to extract a therapeutic salicylate dose from most willow bark is an overwhelming 38 gallons. Using superior willow bark, 1.5 gallons of willow bark tea per day would need to be ingested to obtain pain relief, equivalent to 4.5 g of aspirin, approximately the daily dose for a person treated with rheumatoid arthritis (Robbers & Tyler, 1999). On the basis of these quantities of liquid, using willow bark may be less convenient than taking aspirin, which does not contain tannin.

Witch hazel has the scientific name *Hamamelis virginiana*. The astringent and hemostatic properties of witch hazel are attributed to tannin constituents in the plant (Newall et al., 1996). Individuals orally self-medicate with witch hazel to treat diarrhea, tuberculosis, colds, and fever (Natural Medicines Comprehensive Database, 2004). Oral intake of witch hazel can cause stomach irritation and, in rare cases, liver damage (Bisset, 1994). Tannins can cause nausea, vomiting, and possible bowel impactions with regular intake of 1 g of this herb (Facts and Comparisons, 2001). The typical dose of 2 g of dried leaves taken three times daily or as a tea (Newall et al.) seems high considering the side effects following ingestion of 1 g (Facts and Comparisons).

Conclusions and Implications

This review of 27 herbs and natural products offers an alert to consumers and healthcare professionals. Although many natural products and herbs have the potential to be poisonous or harmful, the herbs reviewed here have the added potential to cause cancer. Two herbs, pau d'arco and St. John's wort, are included because they have enormous

popularity among consumers but also have an enormous potential to be dangerous.

No brand names were found for some of the herbs listed in Table 1 (e.g., aristolochia, areca, bishop's weed). In addition, the typical doses for American chestnut, bistort, English walnut, marjoram, Mormon tea, oak bark, and quillaia are instructions for making a tea. This instruction may lead some individuals to believe that concoctions can be made by finding these herbs in the wild or purchasing them in their natural state. Inclusion of these instructions for making teas is for information only—these are harmful herbs. Weigh the risks and benefits carefully before embarking on any health regimens that include their use.

The list of herbs that contain tannins is not all inclusive. This section of the review serves as an alert for the possible harmful and cancer growth properties of tannin. Read all labels carefully on natural products and herbals. If a label contains any of the products listed in Table 1 of this review, decrease your dose to the safe recommended amount or, in many cases, avoid that product or herb.

The focus of these four review articles has been herbs or natural products that cause or protect against cancer. Healthcare professionals are encouraged to use the tables in these reviews as quick references and the text for additional information. With this information, oncology nurses have an opportunity to be better resources for their patients and healthcare colleagues.

The author gratefully acknowledges the continuing support of Carl D'Arcy, PhD, director of applied research/psychiatry at the University of Saskatchewan in Saskatoon, Canada.

Author Contact: Muriel J. Montbriand, PhD, RN, can be reached at montbriand@skyway.usask.ca, with copy to editor at rose_mary@earthlink.net.

References

- Asnis, D.S., Saltzman, H.P., & Melchert, A. (1993). Shark oil pneumonia. An overlooked entity. *Chest*, 103, 976–977.
- Bisset, N.G. (Ed.). (1994). *Max Wichtl herbal drugs and phytopharmaceuticals. A handbook for practice on a scientific basis*. London: Medpharm Scientific Publishers Stuttgart.
- Blumenthal, M., Busse, W.R., Goldberg, A., Gruenwald, J., Hall, T., Riggins, C.W., et al. (Eds.). (1998). *The complete German commission E monographs: Therapeutic guide to herbal medicines* (S. Klein, Trans.). Boston: American Botanical Council.
- Brigden, M.L. (1995). Unproven (questionable) cancer therapies. *Western Journal of Medicine*, 163, 463–469.
- Chan, J.M., Giovannucci, E., Andersson, S.O., Yuen, J., Adami, H.O., & Wolk, A. (1998). Dairy products, calcium, phosphorous, vitamin D, and risk of prostate cancer. *Cancer Causes and Control*, 9, 559–566.
- Chen, W.J., Chang, C.Y., & Lin, J.K. (2003). Induction of G1 phase arrest in MCF human breast cancer cells by pentagalloylglucose through the down-regulation of CDK4 and CDK2 activities and up-regulation of the CDK inhibitors p27(Kip) and p21(Cip). *Biochemical Pharmacology*, 65, 1777–1785.
- Chevallier, A. (2000). *Natural health encyclopedia of herbal medicine* (2nd ed.). New York: DK.
- Cohle, S.D., Trestrail, J.D., III, Graham, M.A., Oxley, D.W., Walp, B., & Jachimczyk, J. (1988). Fatal pepper aspiration. *American Journal of Diseases of Children*, 142, 633–636.
- Cooper, D.A., Eldridge, A.L., & Peters, J.C. (1999). Dietary carotenoids and certain cancers, heart disease, and age-related macular degeneration: A review of recent research. *Nutrition Reviews*, 57, 201–214.
- Duke, J.A. (1987). *CRC handbook of medicinal herbs* (5th ed.). Boca Raton, FL: CRC Press.
- Duke, J.A., & Vasquez, R. (1994). *Amazonian ethnobotanical dictionary*. Boca Raton, FL: CRC Press.
- The effect of vitamin E and beta carotene on the incidence of lung and other cancers in male smokers. Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. (1994). *New England Journal of Medicine*, 330, 1029–1035.
- Ellenhorn, M.J. (1997). *Ellenhorn's medical toxicology: Diagnoses and treatment of human poisoning* (2nd ed.). Baltimore: Williams and Wilkins.
- el-Mofly, M.M., Khudoley, V.V., & Shwaireb, M.H. (1991). Carcinogenic effect of force-feeding an extract of black pepper (*Piper nigrum*) in Egyptian toads (*Bufo regularis*). *Oncology*, 48, 347–350.
- Facts and Comparisons. (2001). *The Lawrence review of natural products—monograph system*. St. Louis, MO: Wolters Kluwer.
- Fetrow, C.W., & Avila, J.R. (1999). *Professional's handbook of complementary and alternative medicines*. Springhouse, PA: Springhouse.
- Foster, S., & Duke, J.A. (1990). *A field guide to medicinal plants: Eastern and Central North America* (Vol. 40). Boston: Houghton Mifflin.
- Foster, S., & Tyler, V.E. (1999). *Tyler's honest herbal* (4th ed.). Binghamton, NY: Haworth Herbal Press.
- Fujiki, H., Sukanuma, M., Kurusu, M., Okabe, S., Imayoshi, Y., Taniguchi, S., et al. (2003). New TNF-alpha releasing inhibitors as cancer preventive agents from traditional herbal medicine and combination cancer prevention study with EGCG and sulindac or tamoxifen. *Mutation Research*, 523–524, 119–125.

- Godley, P.A. (1995). Essential fatty acid consumption and risk of breast cancer. *Breast Cancer Research and Treatment*, 35, 91–95.
- Gruenewald, J., Brendler, T., & Jaenicke, C. (Eds.). (1998). *PDR® for herbal medicines*. Montvale, NJ: Thomson Healthcare.
- Hasle, H., & Rose, C. (1991). [Shark liver oil (alkoxyglycerol) and cancer treatment]. *Ugeskr Laeger*, 153, 343–346.
- Health and Welfare Canada. (1990). *Nutrition recommendations*. Ottawa, Canada: Canadian Government Publishing Centre.
- Heinonen, O.P., Albanes, D., Virtamo, J., Taylor, P.R., Huttunen, J.K., Hartman, A.M., et al. (1998). Prostate cancer and supplementation with alpha-tocopherol and beta-carotene: Incidence and mortality in a controlled trial. *Journal of the National Cancer Institute*, 90, 440–446.
- Henderson, L., Yue, Q.Y., Bergquist, C., Gerden, B., & Arlett, P. (2002). St John's wort (Hypericum perforatum): Drug interactions and clinical outcomes. *British Journal of Clinical Pharmacology*, 54, 349–356.
- Hennessy, M., Kelleher, D., Spiers, J.P., Barry, M., Kavanagh, P., Back, D., et al. (2002). St Johns wort increases expression of P-glycoprotein: Implications for drug interactions. *British Journal of Clinical Pharmacology*, 53, 75–82.
- Hwang, D.H., Chanmugam, P.S., Ryan, D.H., Boudreau, M.D., Windhauser, M.M., Tulley, R.T., et al. (1997). Does vegetable oil attenuate the beneficial effects of fish oil in reducing risk factors for cardiovascular disease? *American Journal of Clinical Nutrition*, 66, 89–96.
- Kempers, S., Katz, H.I., Wildnauer, R., & Green, B. (1998). An evaluation of the effect of an alpha hydroxy acid-blend skin cream in the cosmetic improvement of symptoms of moderate to severe xerosis, epidermolytic hyperkeratosis and ichthyosis. *Cutis*, 61, 347–350.
- Kim, H.L., Streltzer, J., & Goebert, D. (1999). St. John's wort for depression: A meta analysis of well-defined clinical trials. *Journal of Nervous and Mental Disease*, 187, 532–538.
- Krajka-Kuzniak, V., & Baer-Dubowska, W. (2003). The effects of tannic acid on cytochrome P450 and phase II enzymes in mouse liver and kidney. *Toxicology Letters*, 143, 209–216.
- Labieniec, M., & Gabryelak, T. (2003). Effects of tannins on Chinese hamster cell line B14. *Mutation Research*, 539, 127–135.
- La Vecchia, C., Negri, E., Franceschi, S., & Decarli, A. (1997). Case-control study on influence of methionine, nitrite, and salt on gastric carcinogenesis in northern Italy. *Nutrition and Cancer*, 27, 65–68.
- Lee, J.S., Im, J.G., Song, K.S., Seo, J.B., & Lim, T.H. (1999). Exogenous lipid pneumonia: High-resolution CT findings. *European Radiology*, 9, 287–291.
- Lee, J.Y., Lee, K.S., Kim, T.S., Yoon, H.K., Han, B.K., Han, J., et al. (1999). Squalene-induced extrinsic lipid pneumonia: Serial radiologic findings in nine patients. *Journal of Computer Assisted Tomography*, 23, 730–735.
- Leung, A.Y., & Foster, S. (1996). *Encyclopedia of common natural ingredients used in food, drugs, and cosmetics* (2nd ed.). New York: John Wiley and Sons.
- Lust, J. (1974). *The herb book*. New York: Bantam Books.
- Marienfild, C., Tadlock, L., Yamagiwa, Y., & Patel, T. (2003). Inhibition of cholangiocarcinoma growth by tannic acid. *Hepatology*, 37, 1097–1104.
- Martindale, W. (1999). *Martindale: The extra pharmacopoeia* (32nd ed.). London: Pharmaceutical Press.
- Marz, R.W., Ismail, C., & Popp, M.A. (1999). [Profile and effectiveness of a phytogenic combination preparation for the treatment of sinusitis.] *Wiener Medizinische Wochenschrift*, 149, 202–208.
- McEvoy, G.K. (Ed.). (1998). *AHFS drug information*. Bethesda, MD: American Society of Health-System Pharmacists.
- McGuffin, M., Hobbs, C., Upton, R., & Goldberg, A. (1997). *American Herbal Products Association's botanical safety handbook*. Boca Raton, FL: CRC Press.
- Micromedex Inc. (2004). *Micromedex healthcare series*. Englewood, CO: Author.
- Montbriand, M.J. (1994). An overview of alternate therapies chosen by patients with cancer. *Oncology Nursing Forum*, 21, 1547–1554.
- Nalini, N., Sabitha, K., Viswanathan, P., & Menon, V.P. (1998). Influence of spices on the bacterial (enzyme) activity in experimental colon cancer. *Journal of Ethnopharmacology*, 62, 15–24.
- Natural Medicines Comprehensive Database. (2004). Therapeutic Research Faculty National database [Data file]. Available at <http://www.naturaldata.com>
- Neubauer, N., & Marz, R.W. (1994). Placebo-controlled, randomized double-blind clinical trial with Sinupret sugar coated tablets on the basis of a therapy with antibiotics and decongestant nasal drops in acute sinusitis. *Phytomedicine*, 1, 177–181.
- Newall, C.A., Anderson, L.A., & Phillipson, J.D. (1996). *Herbal medicines: A guide for health care professionals*. London: Pharmaceutical Press.
- Nortier, J.L., Martinez, M.C., Schmeiser, H.H., Arlt, V.M., Bieler, C.A., Petein, M., et al. (2000). Urothelial carcinoma associated with the use of a Chinese herb (Aristolochia fangchi). *New England Journal of Medicine*, 342, 1686–1692.
- Omenn, G.S. (1998). Chemoprevention of lung cancer: The rise and demise of beta-carotene. *Annual Review of Public Health*, 19, 73–99.
- Omenn, G.S., Goodman, G.E., Thornquist, M.D., Balmes, J., Cullen, M.R., Glass, A., et al. (1996). Risk factors for lung cancer and for intervention effects in CARET, the beta-carotene and retinol efficacy trial. *Journal of the National Cancer Institute*, 88, 1550–1559.
- Price, J.F., & Fowkes, F.G. (1997). Antioxidant vitamins in the prevention of cardiovascular disease. The epidemiological evidence. *European Heart Journal*, 18, 719–727.
- Pryor, W.A., Stahl, W., & Rock, C.L. (2000). Beta carotene: From biochemistry to clinical trials. *Nutrition Reviews*, 58(2, Pt. 1), 39–53.
- Richter, O. (2000). Several countries issue restrictions on St. John's wort. *Richter's Herbletter* 7/30/00. Retrieved March 7, 2002, from <http://www.richters.com>
- Robbers, J.E., & Tyler, V.E. (1999). *Tyler's herbs of choice: The therapeutic use of phytomedicinals*. New York: Haworth Herbal Press.
- Roby, C.A., Anderson, G.D., Kantor, E., Dryer, D.A., & Burstein, A.H. (2000). St. John's wort: Effect on CYP3A4 activity. *Clinical Pharmacology and Therapeutics*, 67, 451–457.
- Rose, D.P. (1996). The mechanistic rationale in support of dietary cancer prevention. *Preventive Medicine*, 25, 34–37.
- Russell, I.J., Michalek, J.E., Flechas, J.D., & Abraham, G.E. (1995). Treatment of fibromyalgia syndrome with super malic: A randomized, double blind, placebo controlled, crossover pilot study. *Journal of Rheumatology*, 22, 953–958.
- Schempp, C.M., Kirkin, V., Simon-Haarhaus, B., Kersten, A., Kiss, J., Termeer, C.C., et al. (2002). Inhibition of tumour cell growth by hyperforin, a novel anticancer drug from St. John's wort that acts by induction of apoptosis. *Oncogene*, 21, 1242–1250.
- Schulz, V. (2001). Incidence and clinical relevance of the interactions and side effects of Hypericum preparations. *Phytomedicine*, 8, 152–160.
- Schulz, V., Hansel, R., & Tyler, V.E. (1998). *Rational phytotherapy: A physician's guide to herbal medicine* (3rd ed.) (T.C. Telger, Trans.). Berlin, Germany: Springer.
- Sheahan, K., Page, D.V., Kemper, T., & Suarez, R. (1988). Childhood sudden death secondary to accidental aspiration of black pepper. *American Journal of Forensic Medicine and Pathology*, 9, 51–53.
- Singh, A., & Rao, A.R. (1993). Evaluation of the modulatory influence of black pepper (*Piper nigrum*, L.) on the hepatic detoxication system. *Cancer Letters*, 72, 5–9.
- Skopinska-Rozewska, E., Krotkiewski, M., Sommer, E., Rogala, E., Filewska, M., Bialas-Chromiec, B., et al. (1999). Inhibitory effect of shark liver oil on cutaneous angiogenesis induced in Balb/c mice by syngeneic sarcoma L-1, human urinary bladder and human kidney tumour cells. *Oncology Reports*, 6, 1341–1344.
- Stiller, M.J., Bartolone, J., Stern, R., Smith, S., Kollias, N., Gillies, R., et al. (1996). Topical 8% glycolic acid and 8% L-lactic acid creams for the treatment of photodamaged skin. A double-blind, vehicle-controlled clinical trial. *Archives of Dermatology*, 132, 631–636.
- Sullivan, R.J., Allen, J.S., Otto, C., Tiobech, J., & Nero, K. (2000). Effects of chewing betel nut (*Areca catechu*) on the symptoms of people with schizophrenia in Palau, Micronesia. *British Journal of Psychiatry*, 177, 174–178.
- Thun, M.J., Peto, R., Lopez, A.D., Monaco, J.H., Henley, S.J., Heath, C.W., Jr., et al. (1997). Alcohol consumption and mortality among middle-

- aged and elderly U.S. adults. *New England Journal of Medicine*, 337, 1705–1714.
- Tyler, V.E. (1993). *The honest herbal: A sensible guide to the use of herbs and related remedies* (3rd ed.). Binghamton, NY: Pharmaceutical Products Press.
- Tyler, V.E. (1994). *Herbs of choice: The therapeutic use of phytomedicinals*. Binghamton, NY: Pharmaceutical Products Press.
- Vale, J.A., Meredith, T.J., & Goulding, R. (1981). Treatment of acetaminophen poisoning. The use of oral methionine. *Archives of Internal Medicine*, 141, 394–396.
- VanWyk, C.W. (1997). Oral submucous fibrosis. The South African experience. *Indian Journal of Dental Research*, 8, 39–45.
- Wang, Z., Gorski, J.C., Hamman, M.A., Huang, S.M., Lesko, L.J., & Hall, S.D. (2001). The effects of St. John's wort (*Hypericum perforatum*) on human cytochrome P450 activity. *Clinical Pharmacology and Therapeutics*, 70, 317–326.
- Wehr, R., Krochmal, L., Bagatell, F., & Ragsdale, W. (1986). A controlled two-center study of lactate 12 percent lotion and a petroleum-based creme in patients with xerosis. *Cutis*, 37, 205–207, 209.
- Weiner, M.A., & Weiner, J.A. (1994). *Herbs that heal: Prescription for herbal healing*. Mill Valley, CA: Quantum Books.
- Yates, A.A., Schlicker, S.A., & Sutor, C.W. (1998). Dietary reference intakes: The new basis for recommendations for calcium and related nutrients, B vitamins, and choline. *Journal of American Dietetic Association*, 98, 699–706.
- Zhang, S., Hunter, D.J., Forman, M.R., Rosner, B.A., Speizer, F.E., Colditz, G.A., et al. (1999). Dietary carotenoids and vitamins A, C, and E and risk of breast cancer. *Journal of the National Cancer Institute*, 91, 547–556. 