

Continuing Education for Pharmacists



Gossel

Thomas A. Gossel, R.Ph., Ph.D.
Professor Emeritus
Ohio Northern University
Ada, Ohio

J. Richard Wuest, R.Ph., PharmD
Professor Emeritus
University of Cincinnati
Cincinnati, Ohio



Wuest

Natural Products: Goldenseal, Gotu Kola, Grapeseed Extract, Green Tea

Goals. The goals of this lesson are to present information on the claims, mechanisms of action, typical dosages used and other items of interest on natural products and nutraceuticals alphabetically from goldenseal to green tea, and to provide background information for assisting others on their proper selection and use.

Objectives. At the conclusion of this lesson, successful participants should be able to:

1. exhibit knowledge of the claims, mechanisms of action and typical dosages for natural products and nutraceuticals presented;
2. select from a list, the synonyms for these products; and
3. demonstrate an understanding of information that can be used when discussing these products with consumers.

GOLDENSEAL

Goldenseal (*Hydrastis canadensis*), also known as eye balm, eye root, goldenroot, goldsiegel, ground raspberry, hydrastis, Indian dye, Indian plant, Indian tumeric, jaundice root, orange root, turmeric root, warnera, wild curcuma, yellow Indian paint, yellow paint, yellow

puccon, and yellow root, is an herb found in the midwestern areas of the United States along the Ohio river valley running up into the northeastern parts of the country. While it is indigenous to the U.S., it is now cultivated in many other areas of the world.

Goldenseal is a horizontal bright yellow plant with knotty and twisted rhizomes (creeping underground stems) out of which root fibers grow. These are the medicinal parts of the herb. They are harvested in the autumn, air dried and ground for use. The taste is very bitter and its odor is strong and disagreeable. The plant received its name from the goldenyellow scars on the rhizomes. When they are broken, the scars resemble the gold wax letter seals used in Colonial days. The coloration comes from the large amounts of the yellow alkaloid berberine, which is one of the constituents of goldenseal. Other bioactive components of goldenseal include canadine, canadine and hydrastine.

American Indians used goldenseal root as a diuretic, tonic, insect repellent, and for irritated and inflamed eyes. They also used it to treat arrow wounds and to make a yellow dye.

Today, goldenseal is used to treat the symptoms of the common cold, flu, whooping cough and other upper respiratory infections, chronic fatigue syndrome, colitis, constipation, diarrhea, dysmenorrhea and excessive menstrual flow, flatulence, gastritis, gonorrhoea, hay fever, hemorrhoids, jaundice, liver disease, loss of appetite, malaria, peptic ulcer disease, post-partum bleeding, urinary tract infections and vaginitis.

Topically, goldenseal is used as a mouthwash for sore gums and irritation of mucosal tissue. It is used on the skin for acne, eczema, infections, itching, rashes, seborrhea, ulcers and infections, including ringworm and herpes. In the eye, it is used for inflammation, conjunctivitis and redness. Goldenseal is used in the ears for earache and tinnitus.

In homeopathic medicine, goldenseal is used for treatment of bronchitis, digestive problems and irregular menstruation.

There is a traditional belief that goldenseal can be used to affect the outcome of urinalysis for illicit drugs by being ingested prior to testing or adding it to the urine sample after collection. It is reported to be commonly detected in

urinalysis in drug screening programs. This concept dates back to a novel, *Stringtown on the Pike*, written in the mid 1800s in which goldenseal bitters are mistaken for strychnine in a simple alkaloid test by an expert witness in a murder trial.

It is of some interest that the novel was one of several authored by a prominent pharmacist of his day, John Uri Lloyd. He was also a founder of the Cincinnati College of Pharmacy, cofounder of the American Pharmaceutical Association, the "Father of eclectic pharmacy" and developer of the extensive line of "Lloyd's Specifics." For historical perspective, eclectic pharmacy was the systematic collection and testing of substances (mostly herbs and plants) of potential medicinal value and selecting the best and most desirable for treating complaints and diseases. Eclectic pharmacy bridged the gap between leeches, strong laxatives and unproven remedies and today's scientific- and chemical-based therapeutic practice.

Proponents of the use of goldenseal claim that its components inhibit the growth of several microorganisms, including *Chlamydia trachomatis*, *Shigella dysenteriae*, *Salmonella paratyphi*, *Klebsiella*, *Mycobacterium tuberculosis* and *Helicobacter pylori*.

Berberine is reported to have choleric (bile-stimulatory), hypotensive, antisecretory and sedative effects. Detractors of its use report that the alkaloids of goldenseal are poorly absorbed when given orally and might not reach adequate concentrations in the body to produce significant pharmacologic activity. Conversely, proponents of the use of goldenseal state that the fact they are detectable in urine attests to their absorption and systemic activity.

When taken orally in appropriate doses for short-term use in adults, goldenseal appears to be safe. However, very high doses may rarely cause nausea, anxiety, depression, seizures and paralysis. Goldenseal is contraindicated for use

during pregnancy and lactation. Berberine reportedly crosses the placenta and may harm the fetus. Kernicterus has developed in newborn infants exposed to goldenseal. It also can be excreted in breast milk.

The traditional dose of goldenseal is 250 to 500 mg of extract (standardized to 5 percent hydrastine three times a day. Also, 500 mg to 1 gram of dried rhizome three times a day has been used.

GOTU KOLA

Gotu kola (*Centella asiatica*, *C. coriacea*), also known as brahmabuti, brahma-manduki, centella, centellase, divya, hydrocotyle, idrocotyle, Indian Pennywort, Indian water navelwort, khulakhudi, madecassol, mandukaparni, manduk parani, mandukig, marsh penny, talepetrako, thick-leaved pennywort, tsubo-kusa, tungchian and white rot, is a slender creeping plant that grows in swampy areas of India and Sri Lanka, southern China, Madagascar, South Africa, the southern U.S., Mexico, Columbia, Venezuela, eastern South America and the South Sea Islands.

The medicinal portions of gotu kola are the dried above ground parts, the fresh and dried leaves, and its stem. Highly used in Indian and Chinese medicine, the plant is harvested throughout the year and dried in the sun.

People take gotu kola to reduce anxiety, depression and fatigue; to improve intelligence and memory; to enhance circulation, decrease edema and treat varicose veins; as an aphrodisiac as well as a contraceptive; and to increase longevity. It has been used to treat symptoms of the common cold and the flu, abdominal pain, anemia, asthma, cholera, diabetes, dysentery, diarrhea, epilepsy, gastric and peptic ulcers, gastritis, hepatitis, indigestion, jaundice, leprosy, pleurisy, peripheral artery disease, sunstroke, tonsillitis, shingles and urinary tract infections. Topically, gotu kola is used for wound healing and to reduce scarring.

In homeopathic medicine,

gotu kola is used for skin diseases associated with itching and swelling, and to reduce inflammation of the uterus.

Gotu kola has several constituents that are thought to have pharmacologic activity. These include asiatic acid, madecassic acid, asiaticosides A and B, various essential oils, flavonoids and flavone derivatives. There is evidence, but not conclusive proof, that gotu kola might bind with cholecystokinin in the intestine and GABA receptors in the central nervous system. Cholecystokinin is a hormone liberated by the intestinal mucosa on contact with entering gastric contents. It stimulates the gallbladder and the secretion of pancreatic juices. This would provide gastrointestinal and digestive effects.

GABA (gamma aminobutyric acid) is the principle inhibitory neurotransmitter in the central nervous system. If gotu kola does significantly bind with GABA receptors, this could provide antianxiety, sedative, analgesic and anticonvulsant activity. There are proponents of its use who believe that gotu kola might protect neurons in the brain from beta-amyloid (the substance thought to destroy neurons in the hippocampus, which leads to memory loss) toxicity and thus have a role in treating patients with Alzheimer's dementia.

There are reports suggesting that constituents of gotu kola seem to speed up wound healing, have anti-inflammatory effect, improve connective tissue remodeling by increasing fibroblast (cells in connective tissue that form collagen) activity, increasing epithelial cell turnover and decreasing capillary permeability.

It has been proposed that gotu kola might increase the collagen content within arterial plaque. Since plaque with low collagen content are structurally weak and linked to an increased risk of rupture and embolism, gotu kola might help stabilize arterial plaque. Proponents further state that there is preliminary evidence that it may have a

strengthening effect on the gastric mucosal lining and suppress free radical damage, thus providing useful preventative and therapeutic effects on gastrointestinal ulcers.

Taken in recommended doses, gotu kola is usually well-tolerated. However, there are reports of gastrointestinal upset and nausea. Rarely, hepatotoxicity has been associated with its use. When used topically, gotu kola can rarely cause allergic contact dermatitis.

The typical oral dose of gotu kola is 60 mg of its extract two to three times a day. One percent creams have been used topically for wound healing.

GRAPSEED EXTRACT

Grapeseed (*Vitis vinifera*), also known as activin, calzin, enocianina, European wine grape, flame grape, leucoanthocyanin, muskat, oligomeric proanthocyanidins, oligomeric procyanidins, OPC, PCOs, petite sirah, proanthodyn, procyanidolic oligomers and sultanas, is indigenous to southern Europe and western Asia. However, it is cultivated in most temperate regions of the world.

The medicinal portions of grape plants are considered to be the leaves, fruit and flowers. Grapeseed extract, the most used and studied portion, is generally obtained as a by-product of wine production.

Although wine has been a beverage ingested by humans for millennia, the use of grapeseed extract for medicinal purposes is a relatively recent event. Its popularity increased in the Western World with the French using it to treat venous and capillary disorders such as retinopathies, venous insufficiency and vascular fragility. This has been reported to be the result of what has been called the French Paradox. The observation has been made that even though the French have a high dietary intake of fatty foods, this is not associated with a higher occurrence of atherosclerosis and other cardiovascular diseases seen elsewhere in Europe and North America. Allegedly, this is due to their

high intake of wine and wine by-products.

Grapeseed extract is used in folk medicine for preventing cardiovascular diseases, atherosclerosis, cerebral and myocardial infarction, hemorrhoids, hypertension, peripheral vascular disease and varicose veins. It is also used for the complications of diabetes, such as neuropathy; allergic rhinitis; age-related macular degeneration, poor night vision; to improve wound healing; and to prevent dental cavities, cirrhosis of the liver, cancer and the breakdown of collagen.

The therapeutic activity of grapeseed extract is attributed to its component proanthocyanidins, which are members of a group of compounds called flavonoids. These substances are claimed to have a wide variety of effects, including antioxidant, vasodilatory, antilipoperoxidant activity and antiplatelet aggregation properties, all of which would be helpful in treating heart disease.

Proanthocyanidins are responsible for producing the red color of grapes. The red varieties of grapes reportedly provide greater antioxidant activity than the white or blush categories, with red wines containing approximately 10 times more proanthocyanidins than white wines.

Other flavonoid constituents of grapeseed extract include catechin, kaempferol (aka kaempferol), myricetin and quercetin. Catechin reportedly can inhibit low-density lipoprotein oxidation, and the others have antioxidant activity as well. Catechins might inhibit allergen-induced histamine release from mast cells.

Flavonoids also appear to decrease superoxide production, increase nitric acid release from platelets and increase the levels of antioxidants, such as alphatocopherol (vitamin E) from storage in the body. Claims are made that grapeseed proanthocyanidins may produce greater protection against reactive oxygen species, free-radical induced

lipid peroxidation and DNA damage than combinations of vitamin C and vitamin E, with or without beta-carotene (vitamin A).

Grapeseed extract is well tolerated, with no adverse events reported at a higher level of occurrence than those seen with placebo.

The typical dose of grapeseed extract for treating chronic venous insufficiency using commercially available products is 75 to 300 mg daily for three weeks followed by maintenance doses of 40 to 80 mg daily. For cardiovascular protective effects, 150 to 300 mg of proanthocyanidins from grapeseed extract is suggested.

GREEN TEA

Green tea (*Camellia sinensis*, *C. thea*, *C. theifera*, *Thea bohea*, *T. sinensis*, *T. viridis*), also known as Chinese tea, epigallo catechin gallate, and Japanese tea, is a large evergreen shrub native to eastern Asia. Although originally cultivated in China, the tea plant is now grown in extensive amounts for commercial purposes in Argentina, India, Indonesia, Japan, Kenya, Malawi, Pakistan, Sri Lanka and Turkey.

The tea plant has leathery, dark green leaves and fragrant, white flowers. The dried, cured leaves of green tea have reportedly been used medicinally for more than 5,000 years to promote digestion, improve mental faculties, decrease flatulence and regulate body temperature.

It is no news bulletin to state that other than water, tea is the most widely ingested beverage around the world, with the exception of the United States, where coffee has become the most popular beverage. Elsewhere, tea is used at meals, ceremonies, celebrations and relaxation time. What is not generally known is that the three major types of tea, black, green and oolong, do not differ in the species of plant on which the leaves grow. Rather, the difference is in the way the leaves are processed after they are harvested.

Black and oolong tea are produced by fermenting and

oxidizing the young tea leaves. Black tea is fully fermented and oolong tea is partially fermented. Green tea is produced by steaming fresh leaves at high temperatures. This inactivates the oxidizing enzyme components, leaving the polyphenol flavonoid content intact (i.e., catechin, epicatechin, epigallocatechin, and gallic catechin). Green tea has approximately six times the antioxidant activity as the other two types. All three types of tea contain similar amounts of caffeine, theobromine, theophylline and tannins until they are commercially processed.

Green tea is taken to improve alertness and cognitive performance. The CNS stimulant effect of green tea is due to its caffeine content, which averages 2 to 4 percent, or 10 to 80 mg per cup, depending on how much tea is used and how long it is brewed.

It is also used as a diuretic; in combination with other herbs for appetite suppression; and to treat diarrhea, stomach disorders, vomiting and headache. It has also been used to reduce the risk of breast, colon, gastric, lung, prostate and skin cancer, and to treat solid tumor cancers. Other uses include treating cardiovascular disease, chronic fatigue syndrome and Crohn's disease, diabetes, hypertension, kidney stones, migraine, and Parkinson's disease.

Topically, green tea has been used as a wash to soothe sunburn, as a poultice for "bags" under the eyes, as a compress for tired eyes and headaches, and to stop bleeding from the socket after tooth extraction.

In homeopathic medicine, green tea is used to treat agitation, cardiac and circulatory conditions, depression, headache and stomach complaints. In Indian medicine, green tea preparations are used for cardiac pain, diarrhea, loss of appetite and migraine. In Chinese medicine, green tea is used to treat diarrhea resulting from digestive problems, malaria, migraine and nausea. It has also been used in China as a cancer preventative.

There is little doubt that in most people, consumption of green tea (and any other caffeinated beverage) will increase mental alertness and improve cognitive performance. There is evidence that combining caffeine-containing beverages with glucose as "energy" drinks may improve mental performance better than placebo or either caffeine or glucose alone.

There is some, but inconclusive, evidence that drinking green tea may reduce the risk of bladder, esophageal, gastric and pancreatic cancer, as well as breast and ovarian cancer recurrence. Drinking green tea on a daily basis seems to lower cholesterol and triglyceride levels, as well as the risk of hypertension, and to help prevent or delay the onset of Parkinson's disease. But, none of the studies reporting these effects meet the rigorous standards needed for FDA approval of such claims.

There is insufficient reliable evidence that consuming green tea lowers the risk of developing diabetes, lung cancer, ischemic heart disease and death after myocardial infarction, or that it is useful for weight reduction in obese individuals.

Other pharmacologic activities attributed to caffeine include increased release of dopamine; decreased airway resistance along with stimulation of respiration; decreased gamma aminobutyric acid (GABA) and serotonin signaling; positive inotropic and chronotropic effects on the heart; elevation of both diastolic and systolic blood pressure (but not in chronic users); and a diuretic effect.

The proposed mechanism of action of the polyphenol flavonoids contained in green tea include an antimutagenic effect that may protect DNA, inhibit tumor cell proliferation, cause cell cycle arrest and cancer cell death. Animal research suggests these components may do this via reactive oxygen species formation and mitochondrial depolarization.

Polyphenol flavonoids are

claimed to reduce cellular adhesiveness of bacteria associated with dental disease. Further claims are made that they prevent skin damage and cancer caused by ultraviolet radiation by means of their antioxidant effect.

Although some individuals cannot tolerate green tea and those with conditions adversely affected by caffeine should avoid it, there is a lack of reports of clinical toxicity from daily consumption of moderate amounts of green tea. However, there are reports of excessive CNS stimulation (such as dizziness, insomnia, agitation, restlessness, tremors, fatigue, confusion), nausea, vomiting, abdominal bloating and pain, upset stomach, flatulence and diarrhea resulting from ingestion of large amounts of green tea or high doses of green tea extract, equivalent to five or more liters of tea per day.

Large doses of caffeine can also cause massive catecholamine release leading to irregular heartbeat, metabolic acidosis, hyperglycemia and ketosis, headache, anxiety, ringing in the ears, hypokalemia, respiratory distress and chest pain. Having reported all this, it should be pointed out that the daily consumption of moderate amounts of green tea seems to cause no health problems.

The typical doses of green tea vary significantly, ranging up to 10 cups per day. The commonly used dose consumed for medicinal purposes in tea-drinking nations is around three cups per day using one teaspoonful of powdered tea in eight ounces of boiling water. This would provide 240 to 320 mg of polyphenol flavonoids.

The content of this lesson was developed by the Ohio Pharmacists Foundation, UPN: 129-999-09-002-H01-P. Participants should not seek credit for duplicate content.

Continuing Education for Pharmacists

Quiz

Natural Products: Goldenseal, Gotu Kola, Grapeseed Extract, Green Tea

1. All of the following are synonyms for goldenseal EXCEPT:

- a. centella.
- b. ground raspberry.
- c. hydrastis.
- d. Indian tumeric.

2. The coloration of goldenseal comes from its large content of the alkaloid:

- a. atropine.
- b. berberine.
- c. hydrastis.
- d. Indian tumeric.

3. The systematic collection and testing of plants of potential medicinal value and selecting the best for treating complaints is called:

- a. organic pharmacy.
- b. naturopathic pharmacy.
- c. homeopathic pharmacy.
- d. eclectic pharmacy.

4. The medicinal portions of gotu kola include all of the following EXCEPT the:

- a. fresh leaves.
- b. stems.
- c. roots.
- d. dried leaves.

5. There is evidence, but not conclusive proof, that gotu kola might bind with which of the following substances in the body?

- a. Pepsinogen
- b. Intrinsic factor
- c. Hydrochloric acid
- d. Cholecystokinin

6. The popularity of using grapeseed extract increased in the Western World with the French using it to treat all of the following ailments EXCEPT:

- a. retinopathies.
- b. sleep disorders.
- c. vascular fragility.
- d. venous insufficiency.

7. Proanthocyanidins are members of a group of compounds called:

- a. alkaloids.
- b. cyanides.
- c. flavonoids.
- d. prostaglandins.

8. The three major types of tea (black, green, oolong) come from:

- a. the same species of tea plant.
- b. two different species of tea plant.
- c. three different species of tea plant.
- d. more than a dozen different species of teaplant.

9. Which type of tea has the greatest antioxidant activity compared to the other two types?

- a. Black
- b. Green
- c. Oolong

10. One of the pharmacologic activities attributed to caffeine includes increased release of:

- a. serotonin.
- b. gamma aminobutyric acid.
- c. dopamine.
- d. acetylcholine.



The Georgia Pharmacy Association is accredited by the Accreditation Council for

Pharmacy Education as a provider of continuing pharmacy education.

Natural Products: Goldenseal, Gotu Kola, Grapeseed Extract, Green Tea

Volume XXVI, No. 10

GPhA Code J09-02

Program Number: 142-999-09-002-H01-P

CE Hours: 1.5 (0.15 CEUs)

Release Date: 2/5/2009

Expiration: 10/15/2011

1. Select one correct answer per question and circle the appropriate letter below using blue or black ink (no red ink or pencil).
2. Members submit \$4, Non-members must include \$10 to cover the cost of grading and issuing statements of credit. Please send check or money order only. Note: GPhA Members will receive priority in processing CE. Statements of credit for GPhA members will be mailed within four weeks of receipt of the course quiz.

- | | |
|------------|-------------|
| 1. A B C D | 6. A B C D |
| 2. A B C D | 7. A B C D |
| 3. A B C D | 8. A B C D |
| 4. A B C D | 9. A B C |
| 5. A B C D | 10. A B C D |

Mail completed quiz to: GPhA, 50 Lenox Pointe NE, Atlanta, GA 30324

A passing grade of 70% is required for each examination. A person who fails the exam may resubmit the quiz only once at no additional charge.

Please check here if you are indicating a change of address _____ Phone # _____

Name _____ License Number(s) and State(s) _____

Address _____

City _____ State _____ Zip _____

How long did this program take to complete? _____