

# Continuing Education for Pharmacists

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## Natural Products: Burdock to Vitamin B-2

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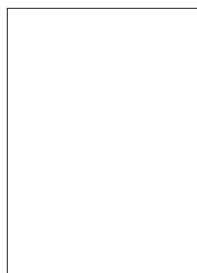
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**Goals.** The goals of this lesson are to present information on the claims, mechanisms of action, typical dosages used and other items of interest on natural products and nutraceuticals alphabetically from burdock to vitamin B-2, and to provide background information for assisting others on their proper selection and use.

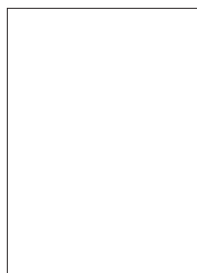
**Objectives.** At the conclusion of this lesson, successful participants should be able to:

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;
3. describe popular uses of the products discussed; and
4. identify sources for information on natural products.

This lesson is part of a series that presents an overview of the common uses, proposed mechanisms of action, typical dosage regimens and



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other information of interest on natural products and nutraceuticals. Products reviewed in this article are listed in Table 1.

The paramount difference between drugs and natural products was explained in the first article in this series. However, since natural products are a very controversial topic for some individuals, the authors restate that the information presented is neither a promotion of nor a condemnation against their use. It is merely an overview of what has been reported in both the public and scientific literature, and certainly not an in-depth treatise. Additional sources (websites) of information on natural products are provided in Table 2.

**Burdock** (*Arctium lappa*, *A. tomentosum*), also known as bardane, beggar's buttons, burr seed, clotbur, cockle buttons, cocklebur, fox's clote, great bur, happy major, hardock, harebur, lappa, love leaves, personata, philanthropium and thorny burr, grows in northern Asia, central Europe and North America. The fruit, seeds, leaves and roots of burdock have been used for centuries as decoctions and teas for a variety of disorders including anorexia nervosa, cancer, colds, constipation, cystitis, fever, gout,

rheumatism, stomach complaints, and sore throat. Burdock is also used as an aphrodisiac, blood purifier, diaphoretic (perspiration inducer), diuretic, and laxative.

Topically, it is used for a number of skin disorders including acne, carbuncles, dry skin, eczema, psoriasis, seborrhea of the scalp, and skin ulcers. Burdock is used as a flavoring agent for food in Europe and as a food in Asia.

Its constituent, arctiopicrin, is claimed to have antibacterial activity. However, no mechanism of action has been discovered for the traditional medical uses of burdock.

While no overt toxicities to burdock have been reported, an allergic reaction may occur in persons hypersensitive to chrysanthemums, daisies, marigolds, ragweed and other members of the *Asteraceae/Compositae* family of plants.

The typical dose of burdock is 3-6 grams of dried root three times a day. As a tea, 1-2 grams is steeped in 150mL of boiling water for five to 10 minutes and then strained. The dose of the liquid extract (1:1 in 25 percent alcohol) is 2-8 mL three times a day. The tincture (1:10 in 45 percent alcohol) is taken in a dose of 8-12 mL, also three times a day.

**Butcher's Broom** (*Ruscus aculeatus*) also known as box holly,

**Table 1**  
**Natural Products Covered**  
**in this Lesson**

Burdock  
Butcher's Broom  
Vitamin B-1  
Vitamin B-2

**Table 2**  
**Representative Sources for Information on Natural Products**

|   |                                      |
|---|--------------------------------------|
| American Botanical Council  | www.herbalgram.org                   |
| Facts and Comparisons   | www.factsandcomparisons.com          |
| Food and Drug Administration  | www.fda.gov ( <i>click on Food</i> ) |
| National Center for Complementary and Alternative Medicine of the National Institutes of Health | www.nccam.nih.gov                    |
| PDR for Herbal Remedies<br>PDR for Nutritional Supplements                                      | www.pdr.net                          |
| Pharmacist's Letter   | www.naturaldatabase.com              |

Jew's myrtle, knee holly, kneeholm, pettigree, and sweet broom, is a low-growing evergreen shrub widely distributed throughout the Middle East and Mediterranean area as well as the southern U.S. It is not the same as the broom herb covered earlier in this series.

*R. aculeatus* has been used in folk medicine for over 2000 years, but received its common name in Europe where butchers tied its stiff twigs together and used it to clear their cutting boards. The portions of the plant used in herbal medicine are the rhizome (above ground root system) and underground roots.

Long used as a diuretic and laxative, in the 1950s it was discovered that extracts of the rhizomes of butcher's broom could cause vasoconstriction and might be useful in treating circulatory disorders. Substances in the extracts include steroidal saponins (ruscogenin and neoruscogenin), which are direct stimulators of alpha-adrenergic receptors in the peripheral blood vessels.

Butcher's broom gained increased popularity during the 1970s for use as an anti-inflammatory agent, and for the prevention of atherosclerosis and venous insufficiency. It is claimed that the herb reduces pooling of fluid in the legs (edema) and has a protectant effect on capillaries, venous endothelium and smooth muscle. It is also used for supportive therapy for leg

cramps, peripheral vascular disease, and the itching and burning of hemorrhoids.

The typical dose of butcher's broom is equivalent to 7-11 mg of total ruscogenin/neoruscogenin in the form of standardized commercially available capsules, ointments and suppositories.

**Vitamin B-1** (thiamine), also known as antiberiberi factor, antineuritic factor, aneurine, anurine, thiamin and thiaminium, can be synthesized by a number of species of plants. In mammals, intestinal bacteria can produce it, but most mammals, including humans, are dependent on dietary intake to sustain life.

Inadequate ingestion of vitamin B-1 can lead to its deficiency state, beriberi. This condition, first recognized in China 3500 years ago, is considered to be the earliest documented nutritional deficiency disorder. However, it was not until the early 20th century that thiamine was isolated and proof established that it was, indeed, a cure for beriberi.

The term beriberi is derived from an Asian dialect (Sinhalese) and means extreme weakness. Beriberi was very common in persons whose diets consisted principally of highly polished rice. While milling produces a more appealing looking rice, it removes

the husk, which contains most of the vitamin B-1.

Vitamin B-1 deficiency leads to mental symptoms including depression, irritability, failure to concentrate, and memory defects. Subjective and objective changes in the peripheral nervous system have been encountered including tenderness of the calf muscles, partial anesthesia, muscle weakness (particularly of the lower limbs), as well as reduced or absent reflexes. Electrocardiographic recordings show developing cardiomyopathy. Additional complaints include weakness, loss of weight, anorexia, and gastric upset.

Vitamin B-1 deficiency is also associated with alcoholism. It can occur in some forms of malnutrition, parenteral nutrition when adequate amounts of vitamin B-1 are not injected, malabsorption syndromes, excessive carbohydrate ingestion, acute infections, and thyrotoxicosis. Drugs that reportedly lead to vitamin B-1 depletion include long-term use of loop diuretics and phenytoin.

The early warning signs of vitamin B-1 deficiency include anorexia, vomiting, easy fatigue, weight loss, nystagmus (rapid, involuntary movement of the eyeballs), peripheral pain, irregular heart beat, and shortness of breath on exertion. In the extreme phase of the deficiency, muscle wasting, cardiac enlargement and circulatory failure are characteristic.

Vitamin B-1 deficiency may arise either directly as a result of low intake of the vitamin or from disproportionate carbohydrate ingestion. During pregnancy, increased utilization of vitamin B-1 may cause a deficiency which can be aggravated by loss of appetite and vomiting which, in turn, leads to even less food intake. Diseases such as chronic ulcerative colitis and sprue that interfere with absorption may also produce deficiency states, even when dietary intake is adequate.

While severe beriberi is relatively uncommon in the world

today, minor degrees of deficiency that cause listlessness, apprehension, anorexia and fatigue still occur. Manual dexterity may be lost and sufferers become irritable, confused and inattentive to details.

Vitamin B-1 is rapidly and actively absorbed from the small intestine. Within the body it is transformed by phosphorylation with incorporation of two molecules of phosphoric acid to become the active coenzyme, thiamine diphosphate. This reaction can take place in most tissues but is prevalent in liver cells.

Small amounts of the phosphorylated form occur in all animal cells, but the body cannot store significant amounts of the free vitamin. Dephosphorylation can occur in the kidney (and probably other organs), and excess quantities of free vitamin are excreted in urine. Therefore, supplies must be replenished daily. During active diuresis, large amounts of vitamin B-1 can be lost. Smaller amounts are excreted in sweat.

Vitamin B-1 is an important factor in carbohydrate metabolism. It enables pyruvate to enter the Krebs Cycle to produce energy. Without vitamin B-1, there could be no energy production. It aids oxidative decarboxylation reactions (removal of carbon dioxide and carboxyl groups) when pyruvic acid is converted to acetyl coenzyme A in the Krebs Cycle, which is the primary pathway for energy production in the body. It also helps convert blood glucose into biological energy by aiding carbohydrate metabolism.

In deficiencies, blood pyruvate levels rise steeply, and often blood lactate levels as well. It has not yet been determined whether the central nervous system effects of vitamin B-1 deficiency are caused by these high levels, or by other actions.

Vitamin B-1 is necessary for synthesis of acetylcholine in nerve cell membranes, and it helps maintain nerve tissue, nerve function, and nerve impulse

transmission. It is required for maintaining the function of muscles, especially the heart. Vitamin B-1 is involved in the conversion of fatty acids into hormones, such as cortisol, testosterone and progesterone, and for converting amino acids into proteins and enzymes.

The U.S. Department of Agriculture estimates that as many as 80 percent of Americans do not ingest adequate amounts of vitamin B-1 in their diet. Chronic dieting and eating highly processed foods are considered to be contributory to the problem. Additionally, cooking destroys vitamin B-1, and since it is water soluble, some is lost to the water used to cook food.

Vitamin B-1 is contained in nearly all foods, but usually in low concentrations. The richest sources are whole grain cereals, brewer's yeast, legumes, nuts and organ meats.

The proven therapeutic use for vitamin B-1 is the prevention and treatment of beriberi and other symptoms of deficiency. Since vitamin B-1 deficiency can be involved in the etiology of peripheral neuritis, it is used to treat neuritis due to other causes. Vitamin B-1 is also used for poor appetite, ulcerative colitis, chronic diarrhea, gastrointestinal disorders, diabetic neuropathy, heart disease, alcoholism, and stress.

The vitamin has been successfully used to prevent Wernicke's encephalopathy, a potentially fatal disorder that occurs in some individuals who consume large amounts of alcohol. Symptoms of this disorder include double vision, mental confusion, muscle weakness and difficulty in walking. Untreated, this can advance to permanent brain damage and memory impairment.

There is a lack of proven evidence of effectiveness for vitamin B-1 when used for maintaining a positive mental attitude, enhancing learning ability, reducing memory loss, increasing energy, repelling insects; and treating canker sores,

indigestion, vision problems and motion sickness. As can be seen, some of these uses are an extension of symptoms caused by vitamin B-1 deficiency.

The typical dose of vitamin B-1 as a dietary supplement in adults is 1-2 mg per day. For mild deficiency syndromes, the usual dose is 5-30 mg daily. Up to 300 mg daily is used for severe deficiencies.

**Vitamin B-2** (riboflavin) was thought to be an essential dietary need as early as 1897 when a water soluble pigment with a peculiar yellow-green fluorescence in milk whey was discovered. It wasn't until 1932, however, that the substance was definitely identified as being a vitamin; and 1935 before it was chemically identified and synthesized.

Vitamin B-2, in its pure form, is a yellow, fluorescent pigment with a slight odor. When excreted, it is the vitamin that gives urine a characteristic bright yellow coloration.

Vitamin B-2 is an essential nutrient for humans and plays a key role in the production of energy. It is the precursor of flavin mononucleotide (riboflavin monophosphate, FMN) and flavin adenine dinucleotide (FAD). FMN and FAD are cofactors for a group of protein enzymes (flavoenzymes).

Flavoenzymes catalyze an extensive range of oxidative and reductive biochemical reactions. They are crucial elements in cellular respiration and many other components of health. In cellular respiration, FAD and FMN act as intermediary hydrogen acceptors in the mitochondrial electron transport chain, taking on hydrogen ions derived from food, and passing electrons on to the cytochrome system. All oxidative metabolism is dependent on an adequate supply of vitamin B-2.

The body's requirement for vitamin B-2 is related not so much to total caloric intake, as it is to body size, metabolic rate, and rate of growth, all of which are related to

protein intake. The lower the protein intake, the more vitamin B-2 is excreted and lost. Studies indicate that tissue stores of riboflavin are not maintained when the dietary intake of this vitamin is less than 1 mg daily, and 1.3 mg or more daily is necessary to maintain tissue reserves.

Vitamin B-2 is also part of glutathione reductase, an important enzyme that helps provide antioxidant protection to the eyes and is claimed to reduce the risk for cataract formation. FMN and FAD are involved in fatty acid synthesis, deamination of amino acids, and conversion of pyruvic acid into acetyl coenzyme A. It aids conversion of carbohydrates to adenosine triphosphate (ATP) in the production of energy. Vitamin B-2 is necessary for growth and reproduction and the healthy growth of skin, hair and nails.

Vitamin B-2 deficiency (ariboflavinosis) primarily affects the skin, eyes and mucous membranes. Early symptoms may be nonspecific and related to the oral area or to vision. Soreness and burning of the lips, mouth, and tongue are common complaints. These are usually accompanied by discomfort in eating and swallowing. Telltale symptoms include photophobia, increased tearing, burning and itching of the eyes, visual fatigue, spasms of the eyelids, and loss of visual acuity that cannot be accounted for by refractive error. The sensation of "grittiness" under the eyelids is a common complaint.

Lesions of the lips begin with pallor and maceration at the angles of the lips and facial skin or with dryness, redness, or tissue sloughing along the line of closure of the mouth. Ulceration occurs in severe deficiency. At the angles of the lips and face, transverse ulcers appear, which may extend outward for several centimeters. Lesions at this area of the lips have been designated "cheilosis." Those at angles of the mouth are referred to as "angular stomatitis."

There is some dispute about the tongue signs of vitamin B-2 deficiency, particularly in the ability to distinguish between the inflammation (i.e., glossitis) of this deficiency versus that of vitamin B-3 (niacin) deficiency. In the real world, deficiency of vitamin B-2 and vitamin B-3 often coexist.

Dermatitis due to vitamin B-2 deficiency begins most often in the nasolabial fold (the area between the nose and upper lip) and is scaly and oily in character. Similar lesions may appear around the eyes and on the ears. Dermatitis involving dry, itchy, scaly skin (seborrheic dermatitis) and scaling eczema of the face and genitals can occur. In severe, long-term vitamin B-2 deficiency, damage to nerve tissue can cause depression and hysteria.

The eye lesions of ariboflavinosis (decreased vitamin B-2 levels) have been the subject of much investigation that remains a matter of controversy. A characteristic vascularization of the cornea has been described in which layers of capillaries proliferate and extend into the superficial layers of the cornea to form tiers and loops. This tissue is normally devoid of blood vessels and is supplied with nutrition by tears.

Corneal vascularization due to vitamin B-2 deficiency occurs in the entire circumference of the cornea and is nearly always bilateral. It interferes with vision and may lead to corneal opacities.

Vitamin B-2 is heat stable, but because it is water soluble, substantial amounts can be lost when food is cooked in water. Since it exists in the germ and bran of grains, milling and processing of grains result in substantial loss.

The U.S. Department of Agriculture has estimated that nearly 35 percent of Americans obtain less than the daily recommended dietary allowance (RDA) of vitamin B-2. Individuals at greatest risk for vitamin B-2 deficiency are alcoholics, the elderly, and premature infants.

Untreated persons with hypothyroidism are also at risk, since levothyroxine regulates flavin kinase, which is needed for synthesis of the FAD-containing enzyme, erythrocyte glutathione reductase. Thyroid supplementation corrects this problem.

Vitamin B-2 is absorbed in the upper part of the small intestine and absorption is maximized (approximately four-fold) when taken with food. Its conversion to active coenzymes takes place in most cells of the body, but is especially high in the small intestine, heart, liver and kidney.

The best sources of vitamin B-2 are liver, milk and other dairy products. Moderate amounts are found in meats, green vegetables, eggs, avocados, mushrooms, and fish, especially salmon and tuna.

The proven therapeutic use for vitamin B-2 is the prevention and treatment of ariboflavinosis and other symptoms of deficiency. It is also claimed to be useful in preventing cataracts from forming, anemia, burning feet, and hair loss. Claims are made that it prevents eczema, migraine and cardiac tissue damage following ischemia (e.g., in angina and after a myocardial infarction).

Adult dietary supplement doses for vitamin B-2 range from 1 to 4 mg daily. The adult dose for treating riboflavin deficiency is 5 to 30 mg daily in divided doses.