



# Continuing Education for Pharmacists

Volume XXIII, No. 11

## Natural Products: Choline to Coenzyme Q10

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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 choline to coenzyme Q10, 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. identify 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. describe popular uses of products discussed.

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



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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 lesson in this series. However, since natural products are a controversial topic for some people, 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. Some of these websites require subscription.

**CHOLINE**, also known as bilineurine, intrachol, lipotropic factor and trimethylethanolamine, is an essential nutrient widely distributed in food. Major sources include beans, cauliflower, egg yolks, fish, iceberg lettuce, liver, muscle meats, nuts and soya.

Choline is involved in many roles in the body, the major three of which are: as a precursor for acetylcholine; as a precursor for phosphatidyl choline (associated with lecithin activity); and as a methyl donor in metabolic reactions.

Choline is an essential com-

ponent of many biological membranes and plasma lipoproteins. It is a lipotropic agent that mobilizes lipids and removes excess fat from the liver. Choline is essential for the synthesis of acetylcholine, one of the major neurotransmitters in the brain and throughout the body. Since adequate acetylcholine levels in the brain are believed to be a protectant against certain types of dementias, including Alzheimer's disease, there are proponents for the use of choline for these conditions. Proof of effectiveness has not been obtained.

While choline can be biosynthesized in the body, this does not appear to be adequate to continuously meet the demand for the nutrient. An association between insufficient dietary intake of choline and a deficiency state (fatty infiltration of the liver) in rats was first reported in 1955. It is now known that sufficient choline, folic acid, methionine and vitamin B-12 are needed to prevent deposition of fat in the liver of humans. Choline is used as a supplement in infant formulas and as a dietary supplement for adults.

Choline is claimed to be useful for the treatment of asthma, chronic hepatitis, cirrhosis of the liver,

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

Choline
Chondroitin sulfate
Chromium
Cinnamon
Clove
Coenzyme Q10





**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 PDR for Nutritional Supplements	www.pdr.net
Pharmacist's Letter	www.naturaldatabase.com

complex partial seizures, high cholesterol, depression, dementias (including Alzheimer's disease), memory loss, schizophrenia, Huntington's chorea and Tourette's disease. It is also used to delay fatigue associated with endurance sports.

Choline is not approved by FDA as a therapeutic agent for any of these conditions. It does have orphan drug status for intravenous injection in TPN (total parenteral nutrition) therapy in patients with hepatic steatosis (fatty degeneration of the liver).

Before the FDA's massive review of prescription drugs for safety and effectiveness (i.e., the DESI review that began in the early 1970s), choline-containing products were available for treating post-surgical abdominal distention (e.g., Ilopan Choline) and for treating asthma (e.g., choline theophyllinate or oxtriphylline/Choledyl). However, none of these met the test of effectiveness and all were removed from the market.

Adverse effects with large doses of choline include gastrointestinal distress, nausea, vomiting, diarrhea and increased sweating. Some individuals experience a "fishy" body odor after taking large doses of choline.

The DRI (Dietary Reference Intake) established for choline by the National Institute of Medicine is 550 mg daily for adult males and

lactating women, 450 mg for pregnant women, and 425 mg for other adult females. For infants, children and adolescents, the DRI ranges from 125 to 200 mg daily depending on age. The average American diet reportedly supplies 200 to 600 mg of choline daily.

**CHONDROITIN SULFATE**, also known as chondroitin sulfuric acid, chronsurid, galactosaminoglycuronoglycan sulfate and stratum, is a biologic polymer that serves as the flexible connecting matrix between protein filaments in cartilage. Commercial products are derived from natural sources including bovine cartilage, shark cartilage and pork ears/snouts, or it is manufactured synthetically.

Chondroitin sulfate is used to treat osteoarthritis, osteoporosis, hyperlipidemia, and ischemic heart disease.

When purified forms of chondroitin sulfate were first extracted from animal cartilage in the early 1960s, it was suggested that if enough were available in the cells (chondrocytes) that synthesize proteoglycans (one of the substances that forms the matrix of cartilage), the healing process would be accelerated.

There are many proponents for the use of chondroitin sulfate in treating osteoarthritis. They state that the articular cartilage found between joints such as the fingers,

knees and hips contains from 65 to 80 percent water plus collagen and proteoglycans. This allows for smooth, easy and painless movement. Chondrocytes that produce new collagen and proteoglycans are also present.

One of the building blocks for the above two substances is chondroitin, which attracts water into proteoglycan molecules. This not only serves as a shock absorber for cartilage, but also pulls in nutrients as well. There is no direct blood flow to chondrocytes; they must derive their nutrition from synovial fluid.

With repeated wear of joint tissue, chondrocyte function is disrupted, altering the matrix of cartilage, causing breakdown, pain, stiffness and inflammation. The theory behind the use of chondroitin sulfate is that with proper supplementation, chondrocytes may be able to replace proteoglycans, enhance repair of degeneration and reduce inflammation. However, at the time of writing this lesson, proof of efficacy for chondroitin to significantly improve osteoarthritis or its symptoms is not sufficient to obtain FDA approval. Proof of efficacy for the other claimed benefits of chondroitin are lacking as well.

Chondroitin sulfate can cause upset stomach, nausea, diarrhea and constipation. It does not appear to cause significant systemic adverse reactions.

The typical dose of chondroitin sulfate for treating osteoarthritis is 200 to 400 mg two or three times a day, often in conjunction with glucosamine and/or magnesium ascorbate.

**CHROMIUM** is believed to be an essential trace mineral in human nutrition. There is evidence that it plays an important role in proper carbohydrate metabolism. Chromium is part of glucose tolerance factor, an essential activator of insulin-mediated reactions.

It was first discovered in the 1950s that chromium is necessary for the maintenance of normal

glucose tolerance in rats. Subsequently, it was found that patients receiving long-term total parenteral nutrition without chromium supplementation developed glucose intolerance, peripheral neuropathy and weight loss. These symptoms ended when the patients were given intravenous chromium chloride. FDA has approved the intravenous administration of chromium chloride supplements in patients on long-term TPN.

While chromium chloride is used for parenteral supplementation, very little is absorbed when inorganic salts are ingested orally. Therefore, organic compounds, such as chromium picolinate, which are much better absorbed, are used in commercial supplements.

Chromium is found in relatively high amounts in many foods, such as beer, black pepper, brewer's yeast, brown sugar, cereals, cheese, coffee, meat products, mushrooms, tea, whole grains and wine. Fruits, vegetables and refined foods are not considered to be good sources.

Chromium supplements are used for weight loss, glycemic control in diabetes, for treating corticosteroid-induced hyperglycemia, lowering elevated LDL levels, increasing HDL cholesterol levels in men taking beta-blockers and to enhance athletic performance.

Potential of insulin is the theory behind chromium's use in glucose regulation. Proposed mechanisms involve increasing insulin binding to receptors, increasing the number of insulin receptors and increasing insulin receptor activity. These, in turn, would lead to increased insulin proficiency and improved glycemic control.

Another suggested mechanism is that chromium may decrease hepatic extraction of insulin and improve glucose tolerance. These theories are based on rat studies, not clinical trials in humans.

The American Diabetes Association has stated that, "chromium supplementation has no known benefit in patients who are not

chromium deficient." The Federal Trade Commission has declared that claims about chromium boosting athletic performance, building muscle and promoting weight loss are unsubstantiated and deceptive.

The forms of chromium (trivalent compounds) found in foods show little or no toxicity. Acute oral ingestion of high amounts of chromium salts in supplements may lead to irritation of the gastrointestinal tract, nausea, vomiting, ulcers and circulatory shock.

Excessive ingestion of chromium picolinate has reportedly caused rhabdomyolysis (breakdown of muscle causing pain and weakness), formation of pustules on the skin, inflammation of interstitial tissue in nephrons, anemia, thrombocytopenia, liver dysfunction and renal failure.

The typical dose of oral chromium picolinate for reducing serum triglycerides in patients with type 2 diabetes is 200 mcg three times a day. The same dosing is recommended for increasing serum HDL levels in males taking beta-blockers. For reversing corticosteroid-induced hyperglycemia or preventing a worsening of pre-existing diabetes, 400 mcg once daily or 200 mcg three times a day has been used.

**CINNAMON** (*Cinnamomum verum*, *Cinnamomum zeylanicum*), also known as Batavia cassia, Batavia cinnamon, Ceylon cinnamon, Panang cinnamon, Saigon cassia and Saigon cinnamon, is native to Sri Lanka, southeastern India and Indonesia. With the colonization of the Western Hemisphere, the plant was brought to South America and the West Indies for cultivation.

While it is used primarily as a spice and flavoring agent, historically, cinnamon has been used to treat gastrointestinal upset and dysmenorrhea. The essential oil of cinnamon plants has been used as an anthelmintic, antidiarrheal,

antiflatulent, antimicrobial and antispasmodic. It is also used for the treatment of symptoms of the common cold and influenza.

In the pharmaceutical, food and cosmetic industries, cinnamon is used in gargles, mouthwashes, toothpastes, liniments, lotions, candy, gum, detergents, soap and many other products. There are no FDA-approved therapeutic uses for cinnamon in the U.S., but the German Commission E has approved its use for loss of appetite and gastric upset.

While no overt adverse effects have been reported from the use of cinnamon, its essential oil can irritate mucous membranes and skin. Allergic reactions are also possible.

The typical dose for cinnamon is one cup of tea, prepared by placing one-half to one gram of the bark in 150 ml of boiling water and steeping for five to 10 minutes. The tea is strained and ingested three times a day.

**CLOVE** (*Eugenia caryophyllata*, *Syzygium aromaticum*), also known as caryophyllus and oil of clove, is indigenous to the Molucca Islands of Indonesia. It is cultivated in warm climates such as Africa, South America and Polynesia. The dried buds, stems and leaves produce clove oil. The dried flower buds are used to obtain clove spice.

Clove is one of the better known herbs, and has a long history of culinary and medicinal use. Traditionally, clove has been used as an expectorant, and to alleviate diarrhea, flatulence, halitosis and nausea.

Its essential oil continues to be used in dentistry as an analgesic and local anesthetic. Clove oil is also applied topically as a counter-irritant.

The active component of clove is eugenol, which is a local anesthetic. On contact with sensory receptors for pain perception, eugenol inhibits prostaglandin production and alleviates pain. It also has been

reported to provide platelet inhibition activity, and antibacterial, antifungal, antihistaminic and antispasmodic activities.

The typical dose of clove oil for treatment of toothache is one to five drops around the affected tooth.

**COENZYME Q10**, also known as CoQ10, CQ-10 and ubiquinone, is a vitamin-like substance synthesized in nearly all living organisms from bacteria to plants to animals. This has led to it being called ubiquinone, for its ubiquitous existence “everywhere.” Ten different coenzyme Q compounds have been identified, but only the Q10 form is synthesized in humans.

Coenzyme Q10 (CoQ10) is involved in electron transport and energy production in mitochondria of all aerobic cells. In humans, it is an essential coenzyme in many metabolic pathways, particularly in the production of adenosine triphosphate (ATP) in oxidative respiration.

CoQ10 is among the most studied nutraceuticals. While it is known to be an essential component for life, it has not yet been proven to be as absolutely necessary in nutrition as “vitamins.” While CoQ10 was in the pipeline for development as a drug in this country decades ago, it was not pursued by the pharmaceutical industry for the prescription drug market. Nonetheless, there are many advocates for the supplemental and therapeutic use of CoQ10.

There is evidence that CoQ10 improves the quality of life and decreases hospitalization rates, pulmonary edema, cardiac asthma and other signs and symptoms of congestive heart failure (CHF), such as shortness of breath, enlarged liver and insomnia. It is approved for treatment of CHF in Japan (since 1974) and several European countries. The widespread use in Japan has been attributed to the American pharmaceutical firm that had been working on CoQ10, assigning development and

marketing rights to a Japanese company back in the late 1950s.

Systemically, CoQ10 is used in the treatment of angina, CHF, chronic fatigue, diabetes, diarrhea, Huntington’s disease, hypertension, male infertility, muscular dystrophy and Parkinson’s disease. It is also used for preventing cardiotoxicity caused by doxorubicin chemotherapy, increasing exercise tolerance, stimulating the immune system in patients with HIV infection and treating breast cancer. CoQ10 is used topically to treat periodontal disease.

Claims are made that CoQ10 is an antioxidant that prevents the oxidation of LDL-cholesterol, which is useful in preventing and treating atherosclerosis. Further claims are made that HMG CoA reductase inhibitors (“statin” cholesterol-lowering agents) deplete endogenously-produced CoQ10 and, therefore, exogenous supplementation is needed in patients for whom they are prescribed.

The purported therapeutic benefits of CoQ10 are attributed to its role in the generation of ATP (“cellular fuel”) and its antioxidant effects. It reportedly helps preserve myocardial sodium-potassium ATPase and stabilizes myocardial calcium-dependent ion channels. CoQ10 is described as being a free-radical scavenger and membrane stabilizer.

CoQ10 appears to be safe when used in recommended doses. However, there are reports that it can cause gastritis, loss of appetite, nausea and diarrhea at high doses in some individuals. Doses in excess of 300 mg daily can elevate serum aminotransferase levels, but the clinical significance of this has not been determined.

Two classes of drugs have been reported to consistently reduce serum levels of CoQ10: the antidiabetic sulfonylureas and, as stated earlier, the HMG CoA reductase inhibitors. Again, the clinical significance of this has not been fully elucidated. Typical doses for CoQ10 are listed in Table 3.

Angina	50 mg three times a day
CHF	50 mg twice a day
Diabetes	150 mg daily
Huntington’s Disease	600 to 1200 mg daily
Hypertension	225 mg daily
Muscular Dystrophy	100 mg daily
Parkinson’s Disease	1200 mg daily

For adjunctive use with HMG CoA reductase inhibitors, 120 mg daily is recommended, and for preventing cardiotoxicity caused by doxorubicin, 50 mg daily is suggested.