Continuing Education for Pharmacists

Volume XXII, No. 1

Natural Products: Bovine Cartilage to Bupleurum

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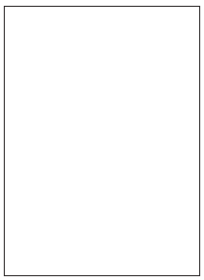
Goals. The goals of this lesson are to present information on the claims, mechanisms of action, typical dosages used and other items of interest on natural products and nutraceuticals alphabetically from bovine cartilage to bupleurum, and to provide background information for assisting others on their 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 other information of interest on natural products and nutraceuticals. Products reviewed in this article are listed in Table 1.



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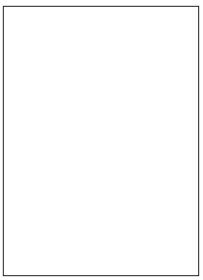

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The paramount difference between drugs and natural products was explained in the first article in this series. However, since natural products are a controversial topic for some people, the authors restate that the information presented is neither 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.

Bovine Cartilage, also known as antitumor angiogenesis factor (anti-TAF), bovine tracheal cartilage (BTC), catrix, psoriacin, and rumalon, is mainly comprised of collagen and proteoglycans. The latter contains a core protein referred to as mucopolysaccharide or glycosaminoglycans (GAG). The principle GAG in bovine cartilage is chondroitin sulfate.

There is some, but inconclusive, evidence that bovine cartilage may have antiarthritic and antitumor activities when taken orally. Its mechanism for antitumor activity has not been discovered, but it has been suggested that the chondroitin sulfate in bovine cartilage may have immunomodulary activity against arthritis. Chondroitin is commonly used in combination with glucosamine as a dietary supplement for treating arthritis. Other oral uses for bovine cartilage include treatment of allergic reactions caused by chemical toxins, cancer, herpes infections, psoriasis, scleroderma, and ulcerative colitis.

Topically applied bovine cartilage is claimed to have wound-healing activity by stimulating growth of granulation tissue within the wound. This action would establish a matrix that induces wound repair. Conclusive proof of this activity is lacking at this time.

Topically, it is used to treat psoriasis as well as acne, dry socket after tooth extraction, external hemorrhoids, poison ivy and poison oak dermatitis, and pruritus ani. Bovine cartilage is used rectally for treating internal hemorrhoids.

By subcutaneous injection, bovine cartilage is used for treatment of cancer of the cervix, lung, nose, ovaries, pancreas, prostate, rectum, and thyroid. Additionally, it

Table 1
Natural Products Covered in this Lesson

Bovine Cartilage
Bovine Colostrum
Branched-Chain Amino Acids
Brewer's Yeast
Bromelain
Broom
Buchu
Bupleurum

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 (*click on Food*)
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

is injected subcutaneously to treat osteoarthritis and rheumatoid arthritis, psoriasis, regional enteritis, systemic sclerosis, and ulcerative colitis.

Very few adverse effects have been reported with the use of bovine cartilage. Nausea and diarrhea with oral use end when therapy is discontinued. When injected subcutaneously, it may cause localized redness, itching, swelling and allergic reactions, but up to 40 grams per week and a total of 300 grams have been injected subcutaneously without evidence of toxicity.

A typical dosage of bovine cartilage that has been reported for oral use in treating ulcerative colitis is 3 grams four times a day. The oral dose for treatment of cancer is 3 grams every eight hours or 9 grams per day in two to three divided doses.

Topically, a 5 percent cream is recommended for pruritus ani, two or more times daily for three days; poison ivy/oak dermatitis, every two hours initially and less frequently as the itching subsides with resolution in one to two weeks; and, acne, application at least twice daily after thorough washing of the acne lesions.

For dry socket, powdered bovine cartilage is mixed into a paste with normal saline and packed into the socket after extraction of the tooth. In treating psoriasis, a 5 percent ointment is applied to the affected area two or three times a day after washing. The ointment is mixed with 0.1 percent coal tar for application to dry, elevated lesions, followed by the ointment with or without coal tar, to red and smooth skin after initial sloughing of psoriatic skin has been accomplished.

Rectally, a 2 percent bovine cartilage suppository is inserted at least three times a day. Adjunctively, 100mg of docusate sodium is taken orally as a stool softener.

For subcutaneous use, bovine cartilage is diluted 1:10 with a 1 percent lidocaine solution to reduce discomfort. It is used in a 50mg/mL concentration. Typically, 1.25 to 2.5 grams of bovine cartilage (25 to 50mL of the mixture) are injected slowly under the skin of the abdomen, anterior thigh, anterior thorax or flanks for a total of 5 grams per treatment. This is given weekly or biweekly for a total dosage of 25 grams for most conditions. Larger amounts are injected for arthritis, up to 40 grams; psoriasis, up to 75 grams; and cancer, 100 to 300 grams.

Local reactions to the injection can reportedly be prevented by taking 25mg of diphenhydramine orally along with the first four treatments.

Bovine Colostrum, also known as bovine immunoglobulin and cow milk colostrum, is the pre-milk fluid produced by a cow's mammary glands during the first two to four days after the birth of her calf. It is rich in nutrients, antibodies and growth factors for the newborn. It contains proteins (three to four times greater than regular cow's milk), carbohydrates, fats, vitamins and minerals, as well as the immunoglobulins IgA and IgG in concentrations reported to be about 100 times greater than commercial dairy milk.

Hyperimmune bovine colostrum (HBC) is derived from cows immunized against specific pathogens. Currently HBC IgG concentrate is an orphan drug available for treatment of HIV patients with diarrhea caused by *Cryptosporidium parvum* infection. It is also used to treat diarrhea associated with bone marrow transplants and rotavirus diarrhea in children.

Claims have been made that bovine colostrum is a performance enhancer and anti-aging/healing supplement. It is used for stimulating the immune system, decreasing healing time, repairing damage to the nervous system, burning fat, building lean muscle, increasing stamina, elevating mood, and slowing or reversing the aging process.

Although there is adequate proof of effectiveness for HBC to gain orphan drug status for the *C. parvum*-induced diarrhea in HIV patients, there is insufficient evidence on its effectiveness for the other claims at this time.

There does not appear to be any significant adverse effects caused by bovine colostrum. Persons allergic to cow's milk would be allergic to it as well.

The typical dose for bovine colostrum is 10 grams of its powdered form, four times a day for 21 days for HIV-related *C. parvum*-induced diarrhea.

Branched-Chain Amino Acids (BCAA) also known as isoleucine, leucine and valine, are products containing the above three listed amino acids that comprise approximately one-third of muscle protein.

They are important for building and maintaining muscle mass, which leads to their greatest use by proponents. BCAA have been called "stress amino acids" by body builders and athletes undergoing intense exercise because muscles have a greater need for them in times of physical stress.

They are also used in the treatment of liver damage caused by alcoholism, to restore muscle mass in patients recovering from surgery or trauma, for amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease), and for hepatic encephalopathy (brain disorder caused by excessive toxic nitrogenous substances in the blood leading to coma and death).

The beneficial effects of BCAA before intense exercise are thought to be due to increased serum ammonia levels which decrease muscle breakdown. While not normally an essential source of energy, BCAA are important fuel supplies for skeletal muscle during metabolic stress. Therefore, they may assist in protein synthesis during extreme exercise, suppress protein breakdown and become substrates for glucose production.

Proponents of the use of BCAA for treating hepatic encephalopathy state that some of the symptoms seen in these patients are due to an accumulation of false neurotransmitters in the brain. This results, in part, from alterations in plasma levels of BCAA. Their opinion is that supplemental BCAA can reverse this and the encephalopathy-related damage. For healthy individuals not undergoing intense exercise, there is a lack of evidence that additional intake of BCAA is of any significant benefit.

The dose range of BCAA-containing nutritional supplements is extensive, ranging from 200mg of each BCAA up to 5 grams of each. Concomitant biotin and vitamin B-12 are often recommended since they are required for BCAA metabolism.

Brewer's Yeast, also known as medicinal yeast, is derived from the fungus *Saccharomyces cerevisiae*. Its common name comes from the fact that *S. cerevisiae* causes the fermentation process used in brewing beer. Interestingly, other strains of *S. cerevisiae* are used in the fermentation of dough for baking bread. Those strains are called "baker's yeast."

Brewer's yeast was originally obtained as a by-product from brewing beer made from an abstract of grains and hops. It is rich in niacin, pantothenic acid, pyridoxine, riboflavin, thiamine, folic acid, vitamin B-12 and biotin. It also contains trace minerals including chromium and selenium.

Brewer's yeast has been such a popular dietary supplement that much of what is now produced commercially is grown specifically for the marketplace rather than as a by-product of the brewery industry. The supplement is made from dried, dead, crushed *S. cerevisiae* yeast cells.

Brewer's yeast is used to treat diarrhea, loss of appetite, chronic acne, and as a dietary source of vitamin B complex and protein. While not proven at this time, there is evidence that brewer's yeast may have activity in ending diarrhea caused by overgrowth of *Clostridium difficile* and enterotoxic *Escherichia coli* in the intestine. It reportedly reduces water and electrolyte influx into the intestine stimulated by toxins from these organism.

There are reports that brewer's yeast can increase the activity of intestinal disaccharidases, saccharidases, lactase and maltase to alleviate nonbacterial-induced diarrhea.

A typical dose for brewer's yeast is 6 grams daily.

Bromelain (*Ananas comosus*), also known as bromelainum, bromelin, and plant protease concentrate, is a general term denoting a group of proteolytic enzymes derived from the stem and fruit of pineapple plants. The type of enzymes contained in bromelain include cysteine proteases, acid phosphotases, peroxidase as well as amylase and cellulase. These enzymes have been used for years in the food industry as meat tenderizers and in cosmetics to improve skin texture. Pineapple has been used for centuries in tropical folk medicine as a digestive aid, cleansing agent for the skin and to promote wound healing.

Up until the FDA's Drug Efficacy Study Implementation (DESI) review in the 1970s, bromelain, papain and other proteolytic enzymes were commercially available prescription drugs commonly used for trauma-induced inflammation. These agents did not meet the safety and effectiveness studies required for continued marketing as "drugs" (i.e., proof of effectiveness for treating, curing or mitigating a disease or symptom), and they were removed from the market as prescription drugs. Since bromelain is a naturally derived substance, it returned to the market in the U.S. as a dietary supplement.

Bromelain continues to be used orally for acute post-operative and traumatic inflammation, arthritis, mild ulcerative colitis, minimizing angina attacks, muscle relaxation, potentiating antibiotics; as an anticoagulant, digestive aid, an adjunct to chemotherapeutic drugs for reducing and remitting tumors; and, to stimulate the immune system. Topically, bromelain is used for burn and wound debridement. While not approved for therapeutic use in the U.S., the German Commission E (similar to the FDA in this country) approved the use of bromelain for reducing surgical swelling and inflammation of nasal sinuses.

The mechanism of action for bromelain as a digestive aid is based on its ability to hydrolyze protein into smaller peptides and amino acids. Other activities are less well-defined, but claimed to involve proteolytic degradation of circulating immune complexes and inhibi-

of T-cells, interferon and tumor necrosis factor for its immunomodulary action; and disruption of adhesion molecules on tumor cells for its antitumor effects. None of these have been proven at this time.

The typical dose of bromelain is 80-500mg three times a day, one-half hour before meals for seven to 10 days. Topically, a 35 percent lipid-based cream is applied to the burn/wound site, two to three times a day.

Broom (*Cytisus scoparius*), also known as bannal, broom tops, hog week, Irish tops, and Scotch broom, is native to southern and central Europe. It also grows in America along the East coast and Pacific Northwest as well as Africa, Chile and Japan. Often grown as an outdoor ornamental to hold loose soil in place on shore and river banks, the portion of broom used in herbal medicine is the short fragments of its twigs.

In times past, a fluid extract of broom was used as a cathartic (strong laxative), diuretic and emetic. In Europe, broom has been used for centuries as a tea to improve circulation in edema, lower blood pressure and for cardiac arrhythmias. It has also been used to induce labor and reduce hemorrhaging after birth.

An alkaloid derived from broom (sparteine) does have oxytocic and antiarrhythmic activity, similar to quinidine. Until the early 1900s, sparteine was used for these effects. The German Commission E has a monograph for broom listing it as an effective agent for functional disorders of the heart and circulation. In this country, FDA considers broom to be an unsafe herb and its use has diminished.

Buchu (*Barosma betulina, B. crenulata, B. serratifolia*), also known as booku, bucka, buka, and diosma, is indigenous to the Cape region of South Africa. The Hottentots (the natives living in the Cape region before European colonization) used buchu leaves to treat a variety of ailments including gout, bladder disorders, enlarged prostate and rheumatism.

Buchu was first exported from Capetown to London in the late 1700s, and by 1821 was listed in the *British Pharmacopoeia* as a treatment for "cystitis, nephritis, urethritis and catarrh of the bladder." The German Commission E currently contains a monograph on buchu listing its uses for treating inflammation of the kidney, urinary tract infections and as a diuretic, but explains that its activity in these claimed uses has not been exhibited.

In the era of patent medicine in this country, buchu was hailed for use in the management of diseases ranging from diabetes to anxiety. It was included in early editions of the *National Formulary* for use as a diuretic and antiseptic. The use of buchu as a recognized therapeutic agent was abandoned in the U.S. in the mid-1900s with the discovery of thiazide diuretics and effective urinary tract anti-infectives. However, it is still used in Western world herbal medicine for urinary tract ailments, including inflammation of the bladder and prostate gland.

Bupleurum (*Bupleurum chinense, B. falcatum, B.fruticosum, B. rotundifolium, B. scorzonerifolium*), also known as bei chai hu, chi hu, Chinese thoroughwax, hare's ear root, Sho-saiko-to, and sickle-leaf hare's ear, is a perennial herb native to China, but cultivated elsewhere around the world. It is a traditional Chinese herbal medicine with recorded use dating back over 2000 years.

Bupleurum is a member of a group of herbs the Chinese use to provide harmony in the body and energy. It has been used as a liver, spleen and stomach tonic and is claimed to alleviate fever and flu symptoms, promote perspiration, and relieve premenstrual syndrome and dysmenorrhea.

Other claimed benefits from the use of bupleurum include relief of angina, anorexia, arthritis, asthma, bronchitis, cancer, common cold symptoms, constipation, cough, depression, diarrhea, epilepsy, inflammation, indigestion, lung congestion, malaria, muscle cramps, prolapsed uterus and ulcers. It has been used as an antifungal, antioxidant, antiseptic, antiviral, cholesterol lowering agent, immune system stimulator and sedative.

Bupleurum contains saponins (glycosides of plant origin that have surfactant activity) called saikosides or saikosaponins which are claimed to be liver protectants with beneficial activity in both acute and chronic liver disease. Saikosaponins also reportedly improve immune function by causing proliferation of B-lymphocytes and stimulating them to produce immunoglobulins and increasing macrophage activity.

A typical dose for bupleurum root is 1.5 to 6 grams daily. For the fluid extract (at a 1:2 ratio), 1.5 to 3mL daily is recommended.