

Nutraceuticals to the Rescue!

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RxVitamins

Introduction

Veterinary nutraceuticals are an undervalued therapeutic for veterinary patients. Veterinarians need to know what they are and how to use them. (or at least be knowledgeable enough to answer their clients' questions, who had just consulted with Dr. Google before they came in to see you). Nutraceuticals are such a new category of therapeutic, that the FDA doesn't know what to call them. They aren't drugs, and they aren't food. By their definition they are compounds that help to "normalize health". This language defines these compounds as not drugs since the FDA instructs us that they don't treat medical conditions or they would be considered drugs, but instead, they serve to support the body to achieve homeostasis or what is commonly termed "health". Although nutraceuticals may be derived from food, they are not themselves designed to be nutrients. For instance, cod is a food, but the oil pressed from the cod's liver is a nutraceutical. Botanicals, which are compounds from plants and herbs, are also considered as a subset of the over-riding category of "nutraceuticals". When the plant material has been pharmaceutically standardized or concentrated over what is naturally occurring in the harvested plant is the situation in which we would call a botanical: a "nutraceutical". Whole plant materials would go under the general category of "herbals" or "botanicals".

A List of Commonly Used Nutraceuticals:

Examples of this category include, but are not limited to:

Cranberry extracts; Amino acids; Vitamin A, B, D, C, E, K; Glucosamine; Chondroitin sulfate; Flax seed oil, Krill oil, Flax seed, Chia seed, Milk Thistle extracts, Medical Mushrooms, Echinacea, Turmeric extracts, Boswellia extracts, Lecithin, cannabidiol, limonene, and the list could go on for pages.....

Nutraceuticals have a variety of ways they can affect biological systems. For instance, botanicals are complex compounds containing amino acids, proteins and peptides, vitamins, minerals, carbohydrates, polysaccharides, fats and oils, as well as a number of biologically active compounds like alkaloids, saponins, sterols, volatile oils and other "phytochemicals". There are nine classes of these biologically-active herbal phytochemicals that have been described in the pharmacognosy literature. Nutraceuticals derived from botanicals can have any or many of these compounds listed above.

Botanicals create their effects on biological systems by providing nutrients that can influence health, or from providing phytochemicals that have a direct or indirect biological effect on the animal at the system or cellular level. Often the effects of herbal compounds on biological systems are the result of the concerted interaction of multiple phytochemicals contained in the herb combined with the nutritive effect of the herb interacting with multiple molecular cellular targets in the animal as a whole. This complex interaction has been termed the "entourage effect". When multiple herbal formulations (whether the whole herbs are used or herbal extracts), the resultant response is even more complex, based on the multiple effects of the multiple constituents of the multiple ingredients in the formulation. Multiple herbals contain mixtures of 2 to 25 different herbs in the same formula, designed to produce a singular, cohesive effect in the patient.

Nutraceuticals Have Been Defined As:

"Compounds that are neither nutrients nor pharmaceuticals that play a "non-nutrient" role in normalizing health and overcoming disease." Nutraceuticals are derived from edible materials and are either concentrated, like fish oil, or pharmaceutically extracted, like glucosamine. There is a very fine line of distinction, if any, between pharmaceutically-extracted herbal compounds and pharmaceutically-extracted nutraceutical compounds.

Safety Considerations

"Natural" does not necessarily mean safe. For many herbs the difference between effective and toxic is a matter of dosage. Fortunately, except for a few extremely potent plants, the volume of material that needs to be ingested to achieve patient toxicity is usually greater than that which an animal would voluntarily accept. In

fact, in most cases, the toxicity is so low that even when administered against the animal's will, toxicity will not occur. There always are exceptions and exceptional patients; it is therefore important to continually be vigilant, and consider the potential of toxicity to a specific patient whenever prescribing an herbal formula. In most cases a potentially toxic herb is present only in small amounts as part of a larger formula. Many of the truly effective herbal remedies are made up of combinations of herbs, sometimes as many as 15 or 20 herbs. The actual amount of a single herb ingested is thus very small. The expert herbal formulator knows how to combine herbs for synergy of desired effects and reduction of adverse effects. Often one herb can "antidote" another herb's toxicity or tendency to create an adverse effect when used alone.

It is important to be aware that there are animal species differences with respect to the potential toxicity of plants. Members of the feline species, as a result of their poor phase II hepatic detoxification enzyme systems, are especially sensitive to certain chemicals needing phase two detoxification, such as salicylates. With some patients, however, even the use of the very safe, food-like herbs (such as alfalfa or nettles) can be associated with undesirable side-effects. Diarrhea, appetite loss and lethargy are the most usual complaints following ingestion of herbal preparations. Occasionally vomiting or urticaria will also be observed. Usually these reactions are unique to that patient and may subside over time once oral tolerance develops.

The strategy, if an adverse event occurs that you are certain can be attributed to the herb or nutraceutical, is to first discontinue administering the material and see if the vomiting or diarrhea or lethargy or whatever you have observed goes away. If it doesn't go away, it might not be caused by the herb or nutraceutical and only occurred coincidentally to the herbal administration. If it does go away, give your patient a week off of that remedy and then start back up with 10-25% of the original starting dose, and observe for side-effects. If none re-occur, then continue at that dose for a week, before increasing to 25-50% of the dose and repeat until they are getting as close to the full dose as possible without adverse effects.

Herb-Drug-Nutraceutical Interactions

Nutraceuticals and botanicals may have the ability to reinforce the action of medication the patient may be on. This is not a bad thing; in fact, using herbal supplements may allow a reduction in pharmaceutical drug dosage without a reduction in clinical effectiveness. For instance, Licorice root and fatty acids from fish oil (EPA/DHA) can enhance the effect of cortisone, thus requiring a lower dose of glucocorticoid to produce the same effect. By enhancing their primary effect, we can potentially reduce the drug-induced side-effects by needing less drug dosage to produce the desired effect. Alternatively, herbs can be used to directly reduce drug side-effects. For example, using silymarin along with prednisone, phenobarbital, or carprofen can reduce these medications' potential toxicity to the liver.

By definition, herbs have effects. Side-effects are the effects not desired in the patient, and main effects are the effects desired for that patient. Minoxidil (Rogaine™), for example, was originally a poor-quality blood pressure medication. However, it was found that it also had the side-effect of growing hair where it had previously been thinned. This side-effect has become a very lucrative primary effect. Another pharmaceutical, Viagra™ (sildenafil), was originally developed as a pulmonary hypertension medication until its more marketable side effect was discovered, and then it became an erectile dysfunction drug. Sildenafil is recommended for use in dogs to treat their pulmonary hypertension.

Most commonly, an herb will interact with a drug (or vice versa) due to its interference with hepatic detoxification. For instance, it is known that ketoconazole reduces the rate of phase one liver detoxification systems. Thus, if you have a drug with a narrow margin of safety you may not want to use ketoconazole concurrently, due to its slowing of the breakdown of the toxic drug, thus prolonging its potential toxicity. Conversely, if you have a relatively harmless yet very expensive drug like cyclosporine, using ketoconazole concurrently can prolong the serum half-life of this drug, thus allowing for more cost-effective dosing. Transplant surgeons used to recommend to their patients on cyclosporine that they drink 8 oz of grapefruit juice with each dose of cyclosporine, because grapefruit juice contains a fucocoumarin that competitively competes with P450 binding sites, and thus slows down the metabolism of cyclosporine. Grapefruit juice is much less potentially liver toxic than ketoconazole (1) (2)

Pharmaceutically Standardized Extracts

Due to the physical chemistry constraints inherent in pharmaceutical technology, each plant has a specific amount of its active ingredient unique to its phytochemical properties that can be extracted and concentrated. For instance, milk thistle (*Silybum marianum*), standardizes to 70-80% flavonoid (silymarin) content. Boswellia (*Boswellia serrata*) standardizes to 95% Boswellic acids. Ginkgo (*Ginkgo biloba*) standardizes to contain 24% ginkgo flavone glycosides. Each herb has its own specific standardization value(s). Botanical compounds that have been standardized have the advantage of providing a consistent amount of active ingredients. Herbal potency can vary from harvest to harvest, from one grower to another, and from one method of processing and storage to another. Thus, by standardizing the amount of active ingredient in an herb, accurate dosing of the patient is improved, and predictable clinical outcomes are more likely.

There are a number of different proprietary pharmaceutical processes that pharmaceutical companies have developed to provide standardization of herbal compounds. When a botanical compound is standardized, it may be standardized to a single ingredient in the herb, or it may be standardized to several ingredients in the herb. In one method of standardization, a company will concentrate one or several "marker" compounds in order to produce a product with higher potency but similar effects to the original whole herb. When a single compound is used as a marker compound, the difference between a botanical and nutraceutical becomes rather indistinct. There is controversy amongst practitioners of botanical medicine regarding the relative effectiveness of the whole herb compound versus the pharmaceutically-extracted herbal compound when a single marker compound is extracted, versus when a group of marker compounds are extracted. Many traditional herbalists believe that the complex interactions of the many constituents of a plant produce a better impact on the patient than the use of a single- or multiple-extracted ingredients. Some of these traditionalists reject the use of any herbal compound that has undergone pharmaceutical processing. Some herbalists believe that the essence and effectiveness of the plant becomes disrupted by this processing. At the same time, though, because there are a number of factors that influence the potency of a whole herb, such as soil quality, weather conditions, genetic strain of plant, methods of harvesting, storage and preservation, many medical practitioners prefer to use herbal compounds that have been standardized in terms of potency of active ingredients. For a clinician, knowing that an herbal compound has a set potency allows for more effective and safe dosing.

Even with standardization there is controversy as far as which plant constituents should be concentrated and standardized. For instance, in the case of extracts of milk thistle (*Silybum marianum*), quite a bit of research has been done on two different extracts of this plant. Silymarin is considered to be the active constituent of the milk thistle plant. It is a flavonolignan complex that is made up of seven flavonolignans: silibinin A&B (AKA: silibin), isosilibinin A&B, silydiadin, silychristin, and taxifolin. Studies have been performed on both silymarin and silibinin and have found both to be effective in most cases. Some research, though, has found that some of the other flavonolignans found in silymarin (such as silydiadin and silychristin) also have effectiveness. For this reason, this author prefers to use the silymarin complex for his patients who need milk thistle, as it provides a broader spectrum of activity than just the silibinin alone.

Materia Medica Of Nutraceutical and Botanicals

Organization by Category and Action

Nutraceutical and botanical compounds can be categorized into 6 groupings or **categories**. Each category has a specific range of **actions** and applications, and member compounds within each category often can be substituted for each other based upon specific qualities that a given compound may have that would be better suited for a given application, or more available than the herb originally chosen for the task. These categories are not mutually exclusive but help in organizing these large numbers of compounds into a system that is easier to work with. For instance, the mineral selenium has a number of different actions, one of which is as an antioxidant, primarily due to its relationship as a co-factor with glutathione. But selenium also plays a role in thyroid metabolism and immune function.

Understanding more about each category and the compounds that belong to it will help to increase your knowledge and ability to effectively use nutraceuticals and botanicals in your daily practice of veterinary medicine.

The **categories** of these compounds are:

Probiotics; fats and oils; amino acids and proteins (including glandulars); vitamins; minerals; and phytochemicals (molecules derived from botanicals)

Understanding the **actions** of nutraceutical compounds can help with the clinical decision to use a compound or not. Nutraceuticals may have multiple actions depending on the context within which they are being used.

Nutraceutical Actions:

Antioxidant (scavenges free radicals); anti-inflammatory (reduces inflammation); adaptogen (supports healthy response to stress); nutritive (nutritional support); immune-modulating (helps to regulate healthy immune system response); anti-infective (direct cytotoxic effect); metabolic modifiers (alter detoxification processes, insulin responses, cellular and/or metabolic activity)

Nutraceutical Materia Medica Organized by Action:

Compounds are listed based on their most well-documented action.

This organization will help the practitioner match up the best compound with their patient's presentation.

NOTE: Due to space and time limitations for this class and this paper, only a few nutraceuticals will be covered in greater depth.

Adaptogens:

Ginseng
Ashwaganda
Astragalus

Anti-infective:

Berberine HCL and the berberine containing herbs
Isatis
Andrographis

Anti-inflammatory:

Cannabidiol
EPA/DHA
Boswellia

Anti-Neoplastic:

Beta glucans
PSP Coriolus
Cannabis

Antioxidants:

All animals require oxygen for life. Yet as vital as oxygen is, when it participates in chemical reactions (via oxidation) it can produce metabolites that are damaging to living tissues by virtue of the exposed ionic charges they contain that damage tissues. These metabolites are called free radicals or reactive oxidative species (ROS).

An antioxidant, by definition, is a molecule that can retard or prevent the oxidation of other molecules.

Antioxidants can be divided into two categories. *Endogenous* antioxidants are produced in the body and are part of complex systems of antioxidant metabolites and enzymes designed to scavenge free radicals so as to prevent tissue damage. *Exogenous* antioxidants are given as supplements to augment the activity of the endogenous antioxidants when their activity isn't sufficient to quench oxidative damage.

Antioxidants are further divided into two divisions dependent upon whether they are hydrophilic or lipophilic.

Water soluble antioxidants react with oxidants in the cell cytoplasm and the blood plasma. Lipid soluble antioxidants protect cell membranes from lipid peroxidation. There is a synergism between these two classes of antioxidants; when one class becomes oxidized it can be recharged by reduction with a molecule from the other class.

Oxidative stress occurs when there are more free radicals than antioxidants available to manage them. This oxidative damage is considered to underlie the development and/or pathology of a wide range of diseases such as pancreatitis, Parkinson's and Alzheimer's diseases, diabetes, rheumatoid arthritis, cardiovascular disease, cataracts, macular degeneration, stroke, and cancer, as well as many others.

Glutathione, the "Mother of all Antioxidants"

This peptide molecule contains the amino acid cysteine and is found in most forms of living beings that have an aerobic metabolism. It is synthesized in the body from its precursor amino acids which are cysteine, glycine and glutamate. Its antioxidant properties are the result of a thiol group found in cysteine which is a reducing agent, and which can be reversibly oxidized and reduced.

Glutathione is one of the most important cellular antioxidants. It is maintained intracellularly in its reduced state by the enzyme glutathione reductase and is responsible for reducing other metabolites and enzyme systems, as well as reacting directly with oxidative compounds. Glutathione, when taken orally is primarily degraded via digestive enzymes, but can be administered intravenously. There also are several nutraceuticals which induce glutathione production when taken orally. Many herbal compounds will also induce glutathione. Silymarin has been found to induce glutathione. N acetylcysteine, a cousin of cysteine, is also a glutathione inducer.

N acetylcysteine (NAC)

NAC is the acetylated form of cysteine, as discussed previously in this paper. Rich in sulfhydryl groups, NAC functions as a very powerful donor of these thiol groups. The beneficial effect of NAC is as a thiol source to stimulate glutathione synthesis and activity, to promote the detoxification of certain hepatic toxins as well as to neutralize reactive oxidative species. (3) There are numerous veterinary applications for NAC, including its parenteral use for acute pancreatitis and for acetaminophen toxicity. (4)

NAC also has been shown to help in the treatment of toxicity from heavy metals and organic solvents.

Intravenous NAC has been used for the treatment of Heinz body hemolysis or for major liver toxicosis. The dosage is 140 mg/kg IV as a bolus followed every 8-12 hours with 70 mg/kg IV or orally. NAC has also been recommended for animals with aggressive hepatic failure caused by hepatotoxicosis (e.g. diazepam in cats, carprofen or trimethoprim sulfa in dogs) and in cats with severe hepatic lipidosis associated with Heinz body anemia or hemolysis or who are in liver failure. (3)

S-adenosylmethionine (SAME)

S-adenosylmethionine, an amino acid derived from the combination of methionine with ATP, has been found to have benefit to the liver as well as an influence on behavior and arthritis. SAME is manufactured in the body, however a deficiency of methionine, vitamin B12 or folic acid can result in decreased SAME synthesis.

Diminished levels of SAME are found in the elderly (humans), and in patients with liver disease, arthritis or depression. SAME is involved in over 100 biochemical reactions in the body, working hand-in-hand with B12 and folate as methylation agents. SAME is one of the most potent methyl donors. Methylation reactions are critical to the manufacture of many different molecules within the body and is an important aspect of the detoxification process. SAME also is involved in the manufacture of all sulfur-containing compounds in the body, which includes the antioxidant glutathione as well as components of cartilage. Other reactions that SAME is involved in include the biosynthesis of phospholipids, carnitine and creatine, the formation of neurotransmitters and certain neurotransmitters and a variety of other endogenous metabolites such as the steroid hormones. (3)

Veterinary applications for SAME include the treatment of liver disease, behavioral problems, and for arthritis.

There is a published paper on the use of SAME for cognitive dysfunction syndrome in dogs. (5)

SAME is a "delicate" molecule, being very sensitive to the damaging effects of air and moisture. For this reason, the tablets need to be coated and packaged in blister packs. If the blister pack is damaged or if the tablet looks damaged, do not use it. The recommended dose for SAME products is 18-20 mg/kg/day for dogs and 200 mg/day for cats. (6)

Whey protein

This derivative of milk is rich in cysteine, a major component of glutathione. It induces glutathione production when ingested. Whey protein is highly assimilable and a high quality animal protein. If not sensitive to it, one

can use it in large amounts for long periods of time with no problems. Because of its ability to induce glutathione, studies using whey protein have been able to measure improvements in immune function. (7) Whey protein is also considered to be a “comfort protein”, which makes it well-suited for feeding cancer patients.

Melatonin.

Melatonin can cross cell membranes and the blood brain barrier, but unlike other antioxidants, it does not undergo “redox recycling” as does glutathione. In redox recycling an antioxidant can be repeatedly reduced and oxidized. Melatonin cannot continue to function as an antioxidant once it has become oxidized. Melatonin has uses for companion animals including antioxidant, reversible estrus suppression agent in cats, treatment of alopecia and follicular dysplasia in dogs, sleep and behavior disorders in cats and dogs, adjusting seasonally controlled fertility in sheep, goats and horses, and adjunctive treatment for adrenal disease in ferrets. (21) Other cited applications include management of stress and anxiety and stimulation of platelet production in IMTP. Dosages in dogs are very application dependent, ranging from 0.1 mg/kg TID for anxiety and stress to 9 mg per dog for night pacing and anxiety. (22)

Vitamin E

Vitamin E is a collective term used to represent a complex of molecules that are fat soluble and possess antioxidant properties. These 8 related molecules are known as tocopherols and tocotrienols. For years it had been thought that alpha tocopherol was the active molecule in vitamin E, and supplements have been sold that were called “Vitamin E” which contained only alpha tocopherol. More recently studies have found that the entire complex of vitamin E better represents the functional nature of this food-bound antioxidant. The naturally occurring vitamin E complex that includes the mixed tocopherols and the full blend of tocotrienols is found in wheat germ oil. Wheat sensitive individuals may not be able to tolerate wheat germ oil in large amounts. For optimal antioxidant function you need to have all of the tocopherol molecules present, including the beta and gamma fractions. When you use only alpha tocopherol it actually depletes the body of the other tocopherols. In some cases this may defeat the function of vitamin E as an antioxidant.

Vitamin C

Vitamin C, like Vitamin E represents a tissue complex including ascorbates and bioflavonoids which is more biologically active than the isolated ascorbic acid. Ascorbic acid in the cells is maintained in its reduced form by glutathione. Ascorbic acid scavenges the water soluble free radicals and is responsible for “recharging” the vitamin E complex once it becomes oxidized.

CoEnzyme Q10 (Ubiquinone)

CoQ10 is a benzoquinone, which is a lipid soluble vitamin-like substance found naturally occurring in the mitochondria of most mammalian cells. It is not found in red blood cells and the cells of the lens of the eye where there are no mitochondria. Its primary function in the body is to produce 95% of the body’s energy in the form of ATP. The body tissues with the highest requirements for energy, such as myocardial cells and hepatocytes, have the highest concentrations of CoQ10.

CoEnzyme Q10 was first discovered in 1957. In mammalian cells CoQ10 is found in the membranes of the endoplasmic reticulum, peroxisomes, lysosomes, vesicles and the inner membrane of the mitochondrion where it is an important part of the electron transport chain. CoQ10’s function is to pass reducing electrons on down the cytochrome oxidase chain in the eventual formation of ATP.

CoQ10 is naturally occurring in certain foods. It is found in higher amounts in mackerel and herring. Pork heart is high in CoQ10 as is heart tissue in general; soybean, canola, sesame and peanut oils also contain higher amounts of CoQ10 than other oils. When these foods are cooked their CoQ10 content is reduced by 14-32%.

CoQ10 is an antioxidant by virtue of its ability to reduce oxidized materials by its transfer of electrons. As the body ages, its ability to synthesize CoQ10 diminishes. Dietary supplementation with CoQ10 can help to counteract the progressive aging deficiency of CoQ10 and thus provide both wellness benefits as well as addressing a number of disease conditions that CoQ10 deficiency is involved in. CoQ10 is prescribed to treat disorders of the mitochondria.

Conditions addressed by CoQ10 for which there is credible research include migraine headaches. (8) Neurodegenerative diseases such as Parkinson's, Alzheimer's and Lateral Amyotrophic Sclerosis have been shown to respond favorably to the antioxidant properties of CoQ10. (9) CoQ10 has been found to be helpful to patients with congestive heart failure and dilated cardiomyopathy (10). CoQ10 can help to modulate hypertension. One study found that CoQ10 can help hypertensive patients lower their blood pressure by up to 10 mm Hg without adverse side-effects. (11) CoQ10 has also been found to help counteract the cardiotoxicity associated with doxorubicin chemotherapy. (12)

Longevity studies have found that supplementation with a diet rich in polyunsaturated fatty acids and CoEnzymeQ10 produced a significantly longer lifespan in rats. (13)

Statins, which are cholesterol-lowering drugs, reduce serum levels of Q10 by up to 40% due to the fact that CoQ10 shares a common metabolic synthesis pathway with cholesterol. Similar drug interactions for CoQ10 can also occur with some beta blockers. Supplementation with exogenous CoQ10 is recommended for individuals who are on these medications. CoQ10 has been found to inhibit tumor-promoting factors that are fatty acid hydroperoxides derived from dietary unsaturated fatty acids in the gene expression of colorectal tumor cells in vitro. (14)

PLANT BASED ANTIOXIDANTS

Plant-based antioxidants are considered safer than pharmaceutical antioxidants because they are complexed with other compounds naturally occurring in the plant which work synergistically with its antioxidant compounds to have a gentler and more effective result. 70 mg of plant-based vitamin C is equal to 700 mg of pharmaceutical ascorbic acid. Their use concurrent with chemotherapy does not interfere with its cytotoxicity. Only a few of many plant-based antioxidants will be discussed. Other plant-based antioxidants not discussed here, but are still very important, include milk thistle, turmeric, Rhodiola and Boswellia.

Green tea (*Camellia sinensis*)

Green tea is one of the most widely consumed beverages in the world. It is inexpensive and safe to consume under most circumstances. Green tea contains a number of active compounds, the two most important being polyphenols and the amino acid theanine. The major polyphenols in green tea are flavonoids such as proanthocyanidins, catechin, epicatechin, epicatechin gallate, and epigallocatechin-3-gallate (EGCG). Green tea is one of the most researched herbal supplements in the world.

Green tea polyphenols produce their effect through their direct antioxidant activity, as well as stimulating the body's endogenous antioxidant, glutathione. EGCG is the most potent of all the green tea polyphenols, and it exerts an anti-inflammatory effect through its inhibition of the pro-inflammatory cascade by inhibiting interleukin 8, a pro-inflammatory cytokine, as well as inhibiting the effects of inflammatory mediators such as NF kappa B. EGCG competitively binds gp120 receptor sites, thus inhibiting HIV viral replication. The many benefits of ingesting green tea come not just from its EGCG content, but also from the amino acid theanine which has an effect on mood, cognition and the immune system. (15) EGCG and theanine both pass through the blood-brain barrier.

EGCG and Folate

EGCG has been found to be a potent inhibitor of dihydrofolate reductase in vitro, and although green tea has been consumed by millions if not billions of humans for thousands of years with no problems, scientists are worried that by inhibiting folate one may create problems during pregnancy. There are no actual studies in vivo of pregnant animals or case reports of pregnant women having trouble from this. (16)

EGCG Clinical Applications

EGCG's inhibition of folate explains to some extent EGCG's benefit to cancer patients, as well as its antibacterial effects. Other explanations of EGCG's benefit to cancer patients include its effect on tumor necrosis factor alpha as well as other mechanisms of action. EGCG has been shown to inhibit angiogenesis in part through its inhibition of VEGF (Vascular Endothelial Growth Factor).

Some applications for green tea that have good supportive scientific evidence include: bladder cancer, breast cancer, colorectal cancer, inflammatory bowel disease (17), colitis (18), lung cancer, atherosclerosis, pancreatic cancer, prostate cancer, skin cancer, stomach cancer, skin health, joint health, diabetes, oxalate bladder stones (19), and liver disease. One study found that rats that had been nephrectomized resulting in left ventricular hypertrophy, when administered a 0.25% green tea extract, had significantly less incidence of this left ventricular hypertrophy than those rats who were not administered the extract. (20)

Cranberry Extract (*Vaccinium macrocarpon*)

Cranberry juice is a safe and inexpensive food that has been in common use for thousands of years. This humble little berry possesses a multitude of biomedical benefits based on its antioxidant properties and other biochemical constituents that it contains.

Polyphenols in Foods

Foods that contain antioxidants are often brightly colored. This includes fruits, berries and vegetables. These colored pigments are a type of polyphenol different than those found in green tea, but like the polyphenols from green tea, have potent antioxidant properties. Polyphenols can be flavonoids (bioflavonoids are flavonoids with biological activity) which typically are more yellow in color. Cranberries, which derive their name from that fact that cranes like to eat them, have been part of the diet of humans since they were first discovered, millennia ago. Research has found that the polyphenols known as proanthocyanidins and anthocyanidins have many biomedical applications.

Proanthocyanidins are colorless, but when converted to anthocyanidins become pigmented red. The conversion of proanthocyanidins to anthocyanidins is responsible for the bright colors of fall leaves. Oligomeric proanthocyanidins (OPC) are naturally occurring flavonoids. Antioxidant potency has been standardized in the ORAC Value Scale. ORAC stands for "Oxygen Radical Absorbance Capacity". It is expressed in ORAC units per unit of material. Although commonly used, be careful when looking at ORAC values to be sure you are comparing the same amount of material that is in the same state. (e.g. dry, fresh, steamed, etc.) Cranberries score higher on the antioxidant scale at 8983 ORAC units per cup of fresh fruit than raspberries who have an ORAC score of 7701 ORAC units per cup of fresh cultivated berries.

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