Clinically Relevant Nutraceuticals Every Veterinarian Should Know

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Organization of Nutraceuticals by Category and Action(s)

Nutraceutical and botanical compounds can be categorized into 6 groupings. 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.

These categories are not mutually exclusive, but will help in organizing the large number 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.

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

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. The basic actions that these categories can have, and some of which will also be discussed further in the pages that follow are: 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 or cytostatic effect); and metabolic modifiers (alter detoxification processes, insulin responses, cellular and/or metabolic activity).

There is a wide variety of available nutraceuticals in today's marketplace. It is beyond the scope of this seminar to cover them all. The most useful nutraceuticals that are best adapted to veterinary practice will be covered in this first lecture, and Part Two will cover Vitamin D and carnitine.

Long-chain polyunsaturated omega-3 fatty acids (LCPUFA-n3) are in the fatty acids and oils category. These oils, such as derived from fish or algae and also from nuts and seeds like flax and walnuts, have the greatest amount of evidence in veterinary species for their inclusion into many clinical protocols. This is especially true for eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are commonly found in fish oil, krill oil, and algal oils.

Many people focus on fish oils when considering supplementing their patients with fatty acids. Yet each different type of fatty acid and oil has its own unique and important biological niche. Clinically, a veterinarian may choose only one or two of these fatty acids that are most pertinent medically. But, if supplementing with fatty acids for health and wellness, a blend of each of the different fatty acids will provide a broad spectrum approach to benefit your patient.

LCPUFA-n3

1. Alpha linolenic acid (ALA) C18:3w3; green leafy vegetables, broccoli, spinach, legumes, nuts, seeds

- Commonly found in flax (55%), hemp (25%), and pumpkin (15%) seed oils; also in nut oils like walnut (15%)
- Can convert to EPA and DHA by means of the delta 6 desaturase enzyme, an elongase enzyme, and finally, a delta 5 desaturase enzyme (20% conversion in humans, small animals not known)
- Thought to have beneficial biological properties of its own, in addition to serving as a precursor in the formation of EPA and DHA.
- Helps reduce inflammation in the body when present in the tissues at a proportion equal to < 1:6 (w3:w6)

2. Eicosapentaenoic acid (EPA) C20:5w3; fish oil
   - Biologically active fatty acid, either converted from ALA in humans (20%) or derived from diet. Natural source of EPA is fish and seafood. Adequate amounts of EPA will shunt the eicosanoid cascade from pro-inflammatory PG2 to less inflammatory PG3 eicosanoids.
   - Helps reduce inflammation in the body
3. Docosahexaenoic acid (DHA) C22:6w3; fish oil, algae
   - Biologically active fatty acid, elongated from EPA; good for the same conditions as EPA; has also been found to benefit cancer patients (30 mg/kg/day)[34]
   - DHA has a beneficial effect on the development of neonatal nervous systems and has been found to be beneficial to learning and training in children and in puppies.[35,36]

Other Biologically Significant Lipids

1. Medium chain triglycerides (MCT) are rapidly hydrolyzed in the GI tract; they are short enough (8–12 carbons per chain) to be absorbed directly into the portal blood; they bypass the lymph and enter the bloodstream within 20 minutes of ingestion. They are metabolized in the liver. Clinically used to correct catabolic states or with maldigestion issues. Inflammatory bowel disease, cancer cachexia, performance animals.
2. Phospholipids are the second largest lipid component of the body. Structurally, phospholipids have substituted for one of their fatty acids a phosphorus containing substance like phosphoric acid. They have a strong affinity for both aqueous and lipid soluble molecules, which makes them effective structural materials. Large amounts of phospholipids are found in the cell membrane, combined with proteins and fatty acids. They function to allow lipids to pass in and out of the cell as well as carry lipids (as lipoproteins) in the blood stream. The types of fatty acids found in phospholipids are dependent upon the fatty acid content of the diet.
   a. The best known phospholipid is phosphatidylcholine (PC), which contains phosphoric acid and choline. PC functions in the transport and utilization of fatty acids and cholesterol in lipoproteins.
   b. Lecithin is a phospholipid-rich compound that predominantly contains PC. Lecithin is found naturally occurring in liver, egg yolk, soybeans, peanuts, spinach, and wheat germ. Lecithin is commonly used to emulsify fats and oils to improve their digestibility. The dipolar nature of the phospholipids in lecithin facilitates this aqueous/lipid biphasic function.
   c. Phospholipids are found in high concentrations in nervous tissue. Sphingomyelin, a type of phospholipid, is found in nervous tissue as a component of the myelin sheath.
   d. Clinically, PC can be used for hepatoprotection, to help correct increased intestinal permeability, to help with behavior conditions, and to benefit skin and hair coat.

e. Although derived from soy, it is extracted from the fatty part of this legume and allergic reactions are usually quite rare. Soy allergies are usually to its protein fraction.

Fish Oil

Fish oil is one of the most researched dietary supplements in the marketplace today. There is no doubt that the health benefits of fish oil are many, and the downsides are few. With the increased use of fish oil, and with the continued and ongoing levels of marine pollutants such as mercury, there is increased concern regarding the purity of our fish oil supply. Currently, fish oil is the only source for EPA, but DHA is now being sourced from algae as well.

It has been suggested to substitute DHA from algae for DHA from fish due to global levels of contamination. The biological effect of DHA is the same regardless of its source. It is important to ask your supplier of fish oil to furnish a third-party certificate of analysis attesting to your fish oil's purity. The list of applications for fish oil grows daily.

Many suggest that ingesting fish is equivalent to taking fish oil supplements. For daily maintenance of health this may be OK, although there are some questions whether the heat involved in cooking fish doesn't disrupt those delicate double bonds found in fish oil fatty acids. For clinical conditions where the recommended dosing of EPA/DHA can be as high as 70 mg/kg per day or higher, it is necessary to use the more concentrated supplements that are available in the marketplace.

Clinical Applications for Fish Oil (EPA/DHA)

The fatty acids, EPA, and DHA found commonly in fish oils, but also available from other sources, have many clinical applications. In some cases, it has been found that the two fatty acids are interchangeable in their function, and in other cases, there are specific and different applications for each. EPA is commonly used to reduce inflammation, which it does through several different mechanisms of action. DHA is used in cancer patients, and has also been found when fed to neonates to facilitate neural development and to positively influence learning and, hence, training.

DHA and EPA have similar activities and actions, but DHA, as compared to EPA, is uniquely involved in the nervous system and mentation development in puppies and kittens. And although EPA is a very fatty acid to give to cancer patients, many studies point to DHA as playing an even bigger role in improving clinical outcomes in the cancer patient. These roles that DHA plays in the patient with neoplasia will be discussed in greater depth in the notes for the third lecture hour being given in this seminar.

EPA will be found to be most useful in the treatment of conditions such as atopic dermatitis and pruritis, epilepsy,[37] asthma,[38] osteo-arthritis,[39] rheumatoid arthritis,[40] renal inflammation and disease,[40] diabetes,[41] macular degeneration,[43] immune modulation,[44] exercise intolerance,[45] and hypertriglyceridemia,[46] to name a few of the applications and citations supporting these claims for EPA.

Two studies that support the effectiveness of EPA in the treatment of atopic dermatitis are described below. The dosage derived from the use of EPA combined with DHA as an intervention for atopic dermatitis by this author has been found to have benefit for many of these difficult-to-treat atopic patients.

In a double-blinded placebo-controlled washout study of 16 dogs with atopic dermatitis, one group was given EPA (180 mg) and DHA (120 mg) per 10 pounds of body weight (4.5 kg) daily for 6 weeks. The other group was given corn oil (570 mg linoleic acid and 50 mg gamma linolenic acid) per 10 pounds of body weight daily for 6 weeks. Following a 3-week washout period, the treatment groups were reversed.

Statistically significant reduction in pruritis scores, alopecia and self-trauma, and improved scores for coat character were found for the group receiving the high doses of fish oil.[47] This is a 40 mg/kg dose of EPA and a 27 mg/kg dose of DHA, or a combined dose of 67 mg/kg of EPA+DHA daily.

A 12-week randomized double-blind placebo-controlled multicenter clinical trial of 60 dogs with atopic dermatitis evaluated the steroid sparing effect of fish oil supplementation. These dogs were randomly assigned to receive a combination of borage seed oil (source of gamma linolenic acid [10.5–12.5 mg/kg]), fish oil (source of EPA/DHA [1–2 mg/kg EPA and 0.7–0.8 mg/kg DHA]) and linoleic acid (19–20 mg/kg) or a placebo consisting of medium chain triglycerides in addition to prednisolone. All dogs received the same basal diet.

A visual analog pruritis score was used by the dog's owners to record daily findings. The dosage of prednisolone was established based on this pruritis score according to written instructions. The use of prednisolone during the test period was lower in the treatment group, although it was not a statistically significant difference. It was found that by day 64 in this study, the difference between the treatment group and the control group became statistically significant and continued to increase as the study progressed.

At the end of the study, the pruritis score and the total clinical scores were lower for the treatment group. This study concluded that there is a steroid sparing effect of fatty acid supplementation in canine atopic dermatitis and that there is also a time lag before the effect is attained.[48] The clinical significance of this study is that it takes 2–3 months for the full effect of fatty acid supplementation, and clients need to be counseled to be patient and continue to supplement with fatty acids for at least 3 months.

Probiotics

The term probiotics was coined by Elie Metchnikoff, a Russian biologist who won the Nobel Prize in 1908. Metchnikoff proposed that the health, well-being, and longevity of the Balkan populations (humans) were attributable to their consumption of large quantities of fermented foods containing beneficial microorganisms.

Probiotics are defined as live microorganisms which when administered in adequate amounts confer a health benefit on the host. It is generally thought that probiotic strains are either found naturally occurring as the healthy microflora of the intestinal environment, or promote the growth of the native intestinal microflora. There are literally hundreds if not thousands of different species of beneficial bacteria in the bowel, and many of them are so fastidious that they cannot be cultured or identified.

In a study of patients with ulcerative colitis, it was found that administering a purified fecal extract from healthy humans administered as a retention enema resolved symptoms and lesions of ulcerative colitis in all study subjects. Probiotic administration does not create these results. These results imply that there may be organisms too fastidious to culture, which were inoculated using the fecal extract that resulted in normalization of bowel function and structure.[49]

It is thought that the exact distribution of healthy microflora is a species-specific and probably an individual-specific "fingerprint" that is unique for each species and each individual within that species.

Probiotic growth is influenced by the nature of the diet. Dietary soluble fiber and oligosaccharides such as fructooligosaccharides, chicory, and inulin provide a substrate for the growth of beneficial microorganisms. These growth-promoting substances are called prebiotics, and the combination of prebiotics and probiotics is called synbiotics.[50] A further advantage of using a synbiotic is that the prebiotic component would promote the growth of indigenous organisms in the gut with probiotic properties. Synbiotics have been shown to have superior health benefits over either probiotics or prebiotics alone.[51]

Yogurt

Many people feel that by eating yogurt you are getting an adequate inoculum of probiotics. Most research studies are finding that it is not just the probiotic strains that are important, but the dose of the inoculum. The doses that are being reported can be as high as 60 billion viable organisms in clinical trials in humans. Extrapolated to animal size, these doses would lie in the range of 2–10 billion viable organisms per day. Yogurt just cannot supply that high

of an inoculate. Additionally, if the yogurt is commercially manufactured and stored for a sufficiently long period of time, the actual bacterial count in the yogurt container diminishes as the bacteria consume available nutritional resources for growth.

Yogurt, when freshly prepared, does have valuable enzymes and small inoculates of probiotics. In surveys of populations where yogurt is consumed as a staple of the diet, it has been observed (as with Dr. Metchnikoff's work) that these yogurt-consuming populations have longer lifespans and are healthier than comparable populations that do not regularly consume yogurt. Thus, yogurt can be a good "wellness" supplement for optimal health.

Probiotic Species

The bacteria that are considered to be probiotics include *Lactobacillus* spp., *Bifidobacterium* spp., *Bacillus subtilis*, and *Enterococcus faecium*. There are some studies that suggest that *E. faecium* is capable of transmitting methicillin-resistant *Staphylococcus aureus*, or MRSA, or antibiotic resistance, and there are other studies that suggest that *E. faecium* is capable of reverting to its pathogenic form. For that reason, *E. faecium* use as a probiotic may be associated with some risk.[52] *Lactobacillus sporogenes*, also known as *Bacillus coagulans*, is a gram-positive aerobic spore-forming motile rod that is marketed as a probiotic. There are a few studies that support this, although anecdotally, some users of this bacterium feel it has benefit.[53] Some yeast organisms *(Saccharomyces cerevisiae* and *Saccharomyces boulardii*) have been utilized effectively as probiotics.[54]

Probiotic Strains

Much of the research into probiotics is strain-specific. This means that each study is performed using a specific proprietary strain of probiotic. This may be because the research is funded by the company that is manufacturing and/or selling the probiotic. A positive study for a specific strain of probiotic, however, does not mean that strain is the only strain that has that property that is being studied. It is rare to find studies where different strains have been put head to head and compared within the same study parameters. As a result, many probiotic products are being marketed with multiple strains in them as a "shotgun" remedy. However, a recent *in vitro* study found that by combining strains which have all proven themselves to be beneficial the result is a less-beneficial combination.[55]

The *Lactobacillus acidophilus* strains are "acid-loving" and tend to inhabit the upper GI tract. In comparison, the *Lactobacillus bifidobacterium* strains inhabit the lower GI tract, mainly the colon. Bifidobacterium species are the primary probiotic found in neonates. Specific strains have specific biochemical properties, and as science and technology advances, strains are being developed to possess specific biochemical properties to produce specific effects.

Probiotics and the Digestive System

Controlled clinical trials have shown that probiotics can benefit patients with a variety of GI complaints. Problems such as antibiotic-associated diarrhea, infectious diarrhea, recurrent clostridial infections and some cases of inflammatory bowel disease will respond effectively to probiotic supplementation.[56-58]

Probiotics and the Immune System

The intestinal microflora provides a basic function in maintaining the body's immune system homeostasis. We do not as yet have a perfect understanding of exactly how probiotic bacteria "cross talk" with the immune system, but the evidence is mounting to indicate that the functioning of the immune system is modulated by bowel bacteria.[59]

Probiotics and Atopic Dermatitis

Studies of atopic pediatric patients have found that probiotics can serve as a primary intervention for that problem.[60] Additionally, it has been found that when antibiotics are given to young children or to rats, that without concurrent supplementation with probiotics, there is a statistically significant increased risk of developing atopy later in life. Most veterinarians agree that there is an epidemic of allergy cases. Perhaps some of this increase can be

attributed to the indiscriminate use of antibiotics without concurrent use of probiotics. If veterinarians were to dispense probiotics with each dispensing of antibiotics, it is possible that this allergy epidemic could become significantly reduced.

It is thought that probiotics contribute to the healthy development of the immune system. The gastrointestinal system, with its large surface area exposure to the external environment of pathogens, antigens, and toxins contains the majority of the immunocytes in the body 60–70%). This tissue is called the gut-associated lymphoid tissue (GALT). Probiotics modulate the immune system by communicating with the GALT, and by preventing the colonization of pathogenic bacteria in the immature and developing GALT.[61]

Probiotics and Stomach Acid

Many strains of probiotics are sensitive to the low-pH environment of the stomach and will be denatured during their transit through the stomach. In order to ensure viable organisms make it through to the intestinal tract, some manufacturers will micro-encapsulate their probiotics. Other manufacturers may pack the probiotic powder into capsules or tablets that do not dissolve in the acid environment of the stomach. Other probiotics, such as the DDS-1 strain of *L. acidophilus*, have been selected for their ability to resist stomach acid.[62]

Dosing of Probiotics

It is difficult to establish precise dosing of probiotic cultures. Doses are expressed as "viable organisms" or as "colony forming units" (CFU). The bacterial counts are expressed in the millions or billions of organisms. Most studies indicate that organisms need to be inoculated in numbers of billions of organisms. The older the individual, the higher the dose of probiotics necessary for effectiveness. In atopic dermatitis interventions, the younger the patient receiving the probiotic supplementation, the lower the dose needed to effect positive change. Probiotics are best given with food to blunt the effect of the gastric juices, and can be given only once daily. When probiotics are to be given with antibiotics to help create a steady state of healthy bowel microfloral levels, they should be given as far away from the antibiotic administration each day, and should be continued for a month following the cessation of bacteriotherapy.

Antioxidants

All animals require oxygen for life, yet as vital as oxygen is, when it participates in chemical reactions (via oxidation), it can produce intermediate metabolites that are damaging to living tissues. These intermediate 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 that 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 damage to DNA, proteins, and lipids; and **Exogenous** antioxidants are given in an effort to augment the activity of the endogenous antioxidants and serve to protect the same tissues.

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 in that when one class becomes oxidized, it can be recharged by reduction with a molecule from the other class.

Oxidative stress is created by 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.

Supplements with Antioxidant Properties

Plant-Based Antioxidants

Many plants contain compounds, like polyphenols, for example, have antioxidant properties. These antioxidants, being bound to plant constituents, tend to be present in smaller amounts, yet due to their being "bound" to these plant constituents of the plant can have as potent an effect as pharmaceutical antioxidants with none of the downsides of excessive oxidation. These plant-based antioxidants have not been found in studies to affect the outcome of chemotherapy agents. Plants from which antioxidant properties are found include silymarin from milk thistle; curcumins from turmeric; ECGC in green tea; and proanthocyanidins in cranberry, blueberry, and hawthorn berries.

Glutathione

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 that 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.

Whey Protein

This derivative of milk is rich in cysteine, a major component of glutathione. It has been shown through research studies to induce glutathione production when ingested. Whey protein is a highly assimilable and 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.[63] 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 cycling" 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.

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" that contained only alpha tocopherol. In the past 5 years, it has been recognized that, in fact, 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.

It has been found that 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. Most research studies have been performed using alpha tocopherol. Some of these studies, which were exploring the

antioxidant properties of vitamin E (alpha tocopherol), had negative results. It has been hypothesized that this may have been due to the use of the isolated alpha tocopherol versus the complexed tocopherols.

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)

Coenzyme Q10 is a benzoquinone, which is a lipid-soluble vitamin-like substance found naturally occurring in the mitochondrion of most mammalian cells. It is not found in red blood cells or 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 address a number of disease conditions that CoQ10 deficiency is involved in. CoQ10 is prescribed to treat disorders of the mitochondria.

References

References are available upon request.

Speaker Information

(click the speaker's name to view other papers and abstracts submitted by this speaker)

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Thai Culinary Herbs and How They Can Help Companion Animals

Safety - Following applies to fresh or dried form of plant

Ginger: Rhizomes, Gingerols
- Biological Activities: Anticancer, Antiinflammatory, Antioxidation
- Suppresses prostaglandin synthesis: inhibition of COX-1 and COX-2, also inhibits 5-lipoxygenase
- More recent: Extract from Ginger/Galangal - inhibits induction of genes for inflammatory response: genes encoding cytokines, chemokines, inducible COX-2
  - so → Ginger modulates biochemical pathways in chronic inflammation.
- Human: OA - reduction of pain and disability
- Dogs: Antiemetic - chemotherapy induced nausea and vomiting
- Potential uses:
  - Nausea control in cancer care
  - Osteoarthritis
  - improve circulation - geriatric/non-ambulatory
- Doses: D: dry 15-200mg/kg divided
  - C: 0.1-0.5g divided
  - infusion

Galangal
- Similar to Ginger
- Human: Traditional → anti leishmanial, carminative, antipyretic, antiinflammatory, antifungal, antiulcer, antiflatulent, antiallergic, hepatoprotective, analgesic, antibacterial, antiamoebic, antioxidant
- Veterinary Potential:
  - IBD, colitis, nausea, vomiting, spasms/cramps, fever support, topical (sprains/strains)
- Doses: D: dry 15-20mg/kg divided
  - C: dry 100 divided
  - infusion

Tumeric
- Human: Anti inflammatory, antioxidant, anti microbial, antiplatelet effects, cholgretic (bile ↑), carminative effects (flatulence)
  - Traditional: ulcers, wounds, diabetes, eye disease, anemia, bronchitis, liver disease
  - Polyphenol curcumin - interests: anticancer, intestinal permeability disorders, chronic kidney
  - Cytokine storms: severe viral infections, acute pancreatitis, severe burns/trauma (blocks multiple cytokine release)
- Veterinary Potential:
  - Surgical wound healing - improvement of periodontal treatment.
  - Topical to ulcerative lesions, small tumors, dermatitis, adjunct to cancer tx/prevention, OA, adjunct viral infection - parvo (admin. rectally), uveitis, hepatitis, post-dental surgery
- Dose: Curcumin 50-250mg/kg divided
  - C: 50-100mg/kg divided
  - Dry: 50-600mg/kg divided (give with fat to improve absorption)
  - Needs to have absorption assistance - majority ingested - excreted unchanged in feces
    - Black pepper, cooked with oils too
    - improves absorption and slows GI transit time. 1.5x
    - BCM-95 - 6.9x
    - Meriva - 19.2x
    - Curcuwin 45.9x

Lemon Grass
- Human: Antiamoebic, antibacterial, antidiarrheal, antifungal, antiinflamatory property
  - Stalk: antidiarrheal and reduces fecal output
  - Tea: dried leaves. antiinflammatory
    - oral or topically
- Veterinary
  - Adjunct tx diarrhea, GI inflammation,
  - Topical: fungal and bacterial skin
    - insect repellent properties

Sweet Basil
- Human: Poor digestion, nausea, abdominal cramps, gastroenteritis, insomnia, depression, dysentery, chronic diarrhea
  - Neurological disorders: anxiety, headaches, migraines, nerve pain, carminative, antispasmodic
- Dog: tick repellent
  - Adjunct to GI conditions: mild diarrhea, poor digestion,

Popular Thai Culinary Herbs and How They Can Help Companion Animals

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Background

In Thailand the use of Thai traditional medicine is promoted and accepted as an important medical section in public health.[1] Many herbs and spices used in Thai cuisine are identified as having traditional medical uses. These include but are not limited to chili (Phrik), cumin (Yira), garlic (Kra thiam), ginger (Khing), galangal (Kha), several different types of basil, kaffir (Me Krut), lemon grass (Ta khrai), lime (Ma nao), pepper (Phrik thai) and turmeric (Kha min). Many of the traditional medicinal properties are supported with pharmacological and clinical studies (albeit not in cats and dogs) and this reservoir of plentiful, inexpensive plants provide potential new opportunities for some common health problems in people and animals.

Safety

Note that the following applies to use of the fresh or dried form of the plant. Patch testing for topical application is recommended for sensitive individuals; however, all of these have been used by the author without adverse events observed.

Ginger (*Zingiber officinalis*)

Ginger rhizome contains pungent phenolic substances known as gingerols. They exhibit a variety of biological activities including anticancer, anti-inflammatory and anti-oxidation.[2] Ginger suppresses prostaglandin synthesis through inhibition of cyclooxygenase-1 and COX-2 and also inhibits 5-lipoxygenase.[3] More recently an extract common to both ginger and galangal has been shown to inhibit the induction of several genes involved in the inflammatory response including genes for encoding cytokines, chemokines and inducible cyclooxygenase-2 thus ginger modulates biochemical pathways activated in chronic inflammation.[4]

A recent meta-analysis of the efficacy and safety of ginger in 593 human osteoarthritis (OA) patients showed a significant reduction in pain and disability following ginger intake and concluded ginger had modest efficacy and reasonable safety for treatment of OA.[5] Ginger has been studied using dogs as models and demonstrated anti-emetic effects against chemotherapy induced nausea and vomiting[6], an earlier study showed anti-emetic efficacy of ginger against cisplatin induced emesis in dogs[7]. Ginger also possesses *in vivo* antimicrobial effects.[8]

Potential veterinary uses: adjunct to nausea control in cancer care and chemotherapy; osteoarthritis, improving circulation in geriatric or non-ambulant patients. Dose: dried 15–200 mg/kg divided dose daily (cats 0.1–0.5 g divided); infusion 5 g per 250 ml administered ¼–½ cup per 10 kg divided daily.[9]

Galangal (*Alpinia galangal*)

Galangal has similar properties to ginger. It has been used traditionally in human traditional medicine for its anti-leishmanial, carminative, antipyretic, anti-inflammatory, antifungal, antiulcer, anti-flatulent, anti-allergic, nerve tonic, stimulant activities and for its anticancer,

hepatoprotective, analgesic, antibacterial, anti-amoebic and antioxidant activity. It has been used to treat a broad range of conditions including bronchitis, heart disease, chronic enteritis, renal calculus, diabetes mellitus, rheumatism and kidney disorders.[10]

Potential veterinary uses: gastrointestinal disorders such as IBD, colitis, nausea, vomiting, spasms and cramps, for fever support, topical poultice for sprains and spasms. Dose: dried 15–20 mg/kg divided dose daily (cats 100 divided); infusion 5 g per 250 ml administered ¼–½ cup per 10 kg divided daily.

Turmeric (*Curcuma longa*)

Turmeric has shown numerous potential therapeutic activities, including anti-inflammatory, antioxidant, antimicrobial and antiplatelet effects, as well as choleretic and carminative actions and gastro-protective effects through its anti-inflammatory action.[11] Turmeric has a traditional use for ulcers and wounds and has been used for diabetes, eye diseases, ulcers, anemia, bronchitis, and liver disease.[12] The yellow coloured polyphenol curcumin, derived from turmeric, is receiving an immense amount of interest as a source of anticancer activity. It also may prove to be a key herb for the treatment of intestinal permeability disorders and also chronic kidney disease.[13] It has been recently suggested as a treatment for cytokine storms in humans associated with severe viral infections as well as acute pancreatitis, severe burns and traumas because it blocks multiple cytokine release.[14]

Turmeric (powdered) mixed with ghee (to 70 degrees C) has a potential therapeutic effect on surgical wound healing in dogs, particularly improvement of periodontal treatment consequences after surgery.[15]

Potential veterinary uses: topical application to ulcerated lesions, small tumours, dermatitis (note it stains fabrics), adjunct to cancer treatment and prevention, osteoarthritis, adjunct to several viral infections such as parvovirus (administered rectally), uveitis, hepatitis, post-dental surgery. Dose: curcumin 50–250 mg/kg divided dose daily (cats 50–100 mg divided); dried 50–600 mg/kg divided (give with fat to improve absorption); decoction 5–30 g per 250 ml administered ¼–½ cup per 10 kg divided daily.

Lemon Grass (*Cymbopogon citratus*)

Lemon grass possesses various pharmacological activities such as anti-amoebic, antibacterial, antidiarrheal, antifungal and anti-inflammatory properties. Various other effects like antimalarial, anti-mutagenicity, anti-mycobacterial, antioxidant, hypoglycemic and neurobehavioral have also been studied. Decoction of the lemongrass stalk has antidiarrheal activity and reduces fecal output in a dose dependent manner[16]; a tea (hot water extract) of the dried leaves has anti-inflammatory activity given orally[17] and when applied topically. It has antiseptic qualities against skin infections (bacterial and fungal).

Potential veterinary uses: adjunct to treatment of diarrhea, gastrointestinal inflammation. Topical use for fungal and bacterial skin infections. It may have some insect repellent properties too. Dose: infusion 2.5 g dried stem per 250 ml administered ¼–½ cup per 10 kg divided daily. Cats love lemon grass.

Sweet Basil (*Ocimum basilicum*)

Basil (note Thai basil is *basilicum* var. *thyrsiflora*)l has been used as a traditional medicine for the treatment of various conditions such as poor digestion, nausea, abdominal cramps, gastro-enteritis, insomnia, depression, dysentery, chronic diarrhea and exhaustion.[18] It is also demonstrated the following activities: cardiotonic, anti-diarrhea, hypolipidemic, hypoglycemic, anti-inflammatory and anti-oxidant.[19] It has been used for a variety of neurological disorders such as anxiety, headaches and migraines, nerve pains and as carminative and antispasmodic.[20] Basil represents a potent source of anticancer materials.[21] An extract of the leaves of basil have shown strong efficacy against *Rhipicephalus microplus* in various cattle[22] and might therefore have some potential as tick repellent in dogs.

Ocimum basilicum leaf extract 100 mg/ml solvent/kg BW given orally to mice was shown to improve neuromuscular coordination, exploratory behaviour, object recognition ability and short term memory and was safe.[23] Studies show basil could be useful in the prevention of stroke.[24]

Potential veterinary uses: Adjunct to treatment gastrointestinal conditions such as mild diarrhea, poor digestion, with suspected stroke or neurological damage. Topical use may have insect repellent properties too. Dose: infusion 2.5 g fresh leaves per 250 ml administered ¼–½ cup per 10 kg divided daily.

Speaker Information

(click the speaker's name to view other papers and abstracts submitted by this speaker)

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The SkeptVet
A Vet Takes a Skeptical & Science-Based Look at Veterinary Medicine

From SBM: The Top Ten Pet Supplements–Do They Work?

Posted on May 19, 2011 by skeptvet

From Science-Based Medicine: The Top Ten Pet Supplements–Do They Work?

An Embarrassment of Riches?

Much has been written here about the dietary supplement industry, a multibillion dollar industry with powerful political connections, and about the woeful inadequacy of regulation which allows widespread marketing of supplements without a solid basis in science or scientific evidence.

The veterinary supplement market is a pittance compared to the human market, but still a billion-dollar pittance that is growing rapidly. Unfortunately, the resources available for good quality research in veterinary healthcare are also a pittance, and it is not at all unusually for our pets to suffer, or even be euthanized, as a result of treatable diseases for want of money to pay for needed care. So $1 billion a year spent on nutritional supplements may not be such a good deal if these products don't effectively prevent or treat disease.

The variety of supplements available is staggering. Many proprietary concoctions of vitamins, minerals, herbs, and other ingredients are marketed for health maintenance, "boosting the immune system," retarding aging, or treating specific diseases. A comprehensive review of this multitude of moving targets is impossible. But the lion's share of the pet supplement market goes to a few specific compounds, so I will focus on these. Most of these ingredients are also among the most popular supplements for humans, with a few exceptions, so there will be substantial overlap with previous discussions of the plausibility and evidence for many of these substances.

1. Glucosamine

The biggest name in the veterinary supplement world by a large margin is glucosamine. It is sold alone or in combination with chondroitin, MSM, green-lipped mussle extract, and a zillion other ingredients. It is sold over-the-counter and through veterinarians and as an additive in commercial pet foods, and it is ubiquitous. It is also widely believed by pet owners and veterinarians to be an effective treatment for osteoarthritis.

Glucosamine for arthritis in humans has been discussed at length here before. There is some reasonable plausibility to the underlying theory, but decades of clinical trials have failed to find any consistent benefit, and the balance of the evidence strongly suggests it is no better than a placebo in treating arthritis in humans. Given the subjective nature of pain and the multitude of ways biologically inert interventions can influence people's perceptions of their own discomfort, this placebo effect might be of marginal value in humans, but the same kind of psychology does not apply to dogs and cats, though it certainly does apply to their owners.

There is very little clinical research on glucosamine as a treatment for arthritis in dogs and cats. In preparing a recent brief literature review, I found only two clinical trials in dogs. One found no benefit for glucosamine and the other, which had a weaker design, showed little benefit. Both showed far greater and more predictable benefit

to non-steroidal anti-inflammatory (NSAID) therapy, which is a consistent feature of clinical research on glucosamine.

Because cats are poorly tolerant of NSAIDs, there is particularly great interest in glucosamine and other nutraceutical therapies for osteoarthritis in this species. Nevertheless, I have found no published clinical trials studying this supplement in arthritis cats. The closest is a study of a diet containing glucosamine, chondroitin, and a number of other supplements purported to have benefits in managing arthritis. I have addressed this study in detail elsewhere, but in brief there were not consistent differences between the experimental diet and the control diet even on subjective measures of comfort and no differences at all on objective measures of activity. And, of course, the role of glucosamine, if any, in any effect that might have been seen would not be demonstrable in a study of a diet with many other ingredients.

Glucosamine is also marketed for treatment of feline interstitial cystitis, an uncomfortable and potentially very serious chronic inflammatory disease of the urinary bladder. However, the only clinical trial to investigate this use did not find any evidence of benefit.

2. Fish Oil

After glucosamine, one of the most popular supplements for pets is fish oil. In humans, the most common use of this supplement is for lowering blood lipid levels and prevention of cardiovascular disease. There is some controversy about exactly how much of which components is useful for which specific conditions, and whether eating fish is better than taking fish oil supplements, but in general there is good evidence for some benefit in cardiovascular disease prevention.

Cats and dogs don't have the problems humans do with atherosclerosis and cardiovascular disease, so this is not a reason for use of fish oils. Instead, this supplement is most commonly used in the treatment of skin allergies. A 2010 narrative review of the evidence for various approaches to treating canine skin allergies concluded that there was some evidence that fish oil supplements can improve coat quality and reduce the dosage of steroid medications needed to control itching, but that these effects are small and not great enough to substitute for other therapies. There is also not evidence to support the use of any particular source, dosage, or formulation of fish oil over any other.

The other common use of fish oils in pets is for treatment of arthritis. There is weak evidence in humans for the use of fish oil supplements as an adjunctive treatment in patients with rheumatoid arthritis, but in general this is not a well-supported intervention for degenerative osteoarthritis in people. There have been several studies of fish oil as a therapy for osteoarthritis in dogs, which I have reviewed in detail (here and here). These are pretty well-designed studies, all by the same group of investigators, and as is common for studies of dietary supplements, they report mostly negative results but then focus on the few statistically significant findings, generally with subjective measures, to conclude the studies are proof of a benefit. The idea that fish oil supplements might have some small benefit for arthritis in dogs and cats is not out of the question, but so far the evidence is not encouraging.

3. Probiotics

Mark Crislip has eloquently addressed the theory and science of probiotics for humans, and the bottom line for pets appears to be much the same. We understand very little about the important and complex ecology of the gastrointestinal tract, about what bugs are there and what they do for or to us. So while the idea of influencing this flora to restore or maintain health makes some sense, adding a few *Lactobacillus* to the mix and expecting it to

have a major effect seems a bit like tossing a few grass seeds into the Amazon rain forest and expecting a golf course to grow there (thanks Mark!).

Clinical studies in humans support some benefits for some conditions, particularly antibiotic-associated diarrhea, but many of the claims made for probiotic products, especially for health maintenance or "boosting the immune system" are unsupported. There is less research on probiotics for dogs and cats, but there are some encouraging studies which show a likely benefit of some products for acute idiopathic diarrhea in dogs (e.g. here and here, analyzed in detail here). There are also serious problems with the quality control of largely unregulated veterinary probiotics. A recent study found the majority of products tested had inaccurate labels, with many not containing the amount or species of organisms claimed on the label. There are also many products marketed with ridiculous and completely unsupported claims.

So overall, the idea of probiotics as a therapy for gastrointestinal disease seems promising, and there are some early suggestions that some products may be useful for some conditions. But this optimism must be tempered by the very limited, preliminary understanding we have of gut ecology and how to manipulate it, the minimal reliable clinical trial evidence to support probiotic use, and the concerns about poor quality control and exaggerated, unscientific claims for probiotic products.

4. Multivitamins

Multivitamins are widely touted as a preventative health measure or as "insurance" for a nutritionally imperfect diet. As Harriet Hall has discussed previously, taking a multivitamin is more a form of self-administered psychotherapy than a preventative health practice. A 2006 review of the available evidence, as well as more recent studies, do not support claims of health benefits in humans from vitamin supplementation in the absence of confirmed deficiencies. And there are circumstances in which vitamin supplementation can be harmful (for example raising cancer risk, interfering with cancer therapy, or even increasing mortality).

As usual, there is virtually no research on the subject in dogs and cats. Commercial pet diets are nutritionally balanced in a way that the rather haphazard eating habits of most humans is not, so there is even less reason to think a multivitamin would be necessary in dogs and cats eating such a diet. In fact, such supplementation could very well lead to excessive, even toxic levels of fat soluble vitamins or some minerals. Homemade and raw food pet diets, however, are more likely to be nutritionally inadequate, so multivitamin supplementation might be more appropriate when feeding such diets. However, the bottom line is there is no good quality epidemiological or experimental research to suggest that dietary deficiencies are common or that non-targeted vitamin supplementation of apparently healthy pets eating a balanced diet has any value. And there is some evidence that supplementation under certain circumstances can be harmful (for example, calcium in growing large-breed dogs).

The lack of evidence may preclude a definitive statement that such supplements are unnecessary or harmful, but it also makes the confident, sweeping claims of supplement marketers entirely unjustified.

5. Lysine

Lysine is an amino acid which is hypothesized to be useful in the prevention and treatment of Feline Herpesvirus (FHV-1) infections. This virus is extremely common, and many cats will be exposed and become infected as kittens. Clinical symptoms include sneezing, nasal congestion, and conjunctivitis, and they range from mild and self-limiting to very severe. Most cats will get over the initial infection, but many remain chronically infected. With suppression of immune function from stress, medication, or disease, the virus can re-emerge and cause symptoms

again. A small subset of cats may develop chronic, ongoing symptoms associated with this infection. Vaccination reduces the severity of symptoms but does not prevent infection.

Lysine is proposed to interfere with the replication of FHV-1 by blocking the uptake of another amino acid, arginine. There are theoretical concerns that lysine supplementation could make cats arginine deficient, but experimental studies suggest this is unlikely in practice. So it appears to be safe, but does it work?

Well, maybe. For once, numerous studies have been done, but there is no clear, consistent pattern of results. Some show that oral supplementation is ineffective and might even make infection worse (Drazenovich, 2009; Rees, 2008; Maggs, 2007). Others do seem to demonstrate some benefit (Maggs, 2003; Stiles, 2002). So while lysine supplementation appears to be safe and there is a plausible rationale for its use, no definitive conclusion about its efficacy is justified.

6. Milk Thistle

Milk thistle is an herbal product that is widely recommended and used. Like glucosamine, it is a supplement which has leapt over the gap between alternative and conventional medicine. The active ingredient is a cluster of compounds called silymarin, There has been extensive *in vitro* research on silymarin, and it has a wide range of potentially useful effects. It appears to interfere with pro-inflammatory chemicals, functions as an anti-oxidant, and may interfere with the metabolism of some chemicals into toxic compounds in the liver. It also has some activity which could be potentially harmful, including interfering with the metabolism of a number of drugs and stimulating the effects of hormones like estrogen.

The primary uses of silymarin in humans are to protect or treat liver damage from toxins and infectious diseases, to improve the condition of diabetics, and to protect the kidneys from toxins. In dogs and cats the primary use of for non-specific "support" of the liver regardless of the specific disease.

In humans, clinical trial evidence is mixed. A couple of studies have suggested it reduces insulin resistance in diabetic and may lower blood lipid levels. A Cochrane review of 13 studies including 915 people "could not demonstrate significant effects of milk thistle on mortality or complications of liver disease in patients with alcoholic and/or hepatitis B or C liver disease." High quality trials were negative, and low quality trials suggested a benefit.

Very little research exists in dogs and cats. A small study of 20 cats given acetaminophen, a known liver toxin, found that those given a single oral dose of silymarin did not show the elevation of liver enzyme levels seen in those not given the compound. A similar study in dogs found some differences in elevations of kidney values between those that got silymarin and those that didn't following exposure to a kidney toxin, though there was not a completely consistent pattern.

A study done in 1978 showed that dogs given a toxic mushroom compound orally and then given silymarin intravenously did not show the increase in liver enzymes that was seen in control dogs. Another in 1984 found that 30% of the control dogs died whereas none of the dogs given IV silymarin along with the mushroom toxin died, and the livers from the treated dogs did not appear damaged by the toxin. What relevance this has for the value of oral supplementation isn't clear.

As far as risks, there appear to be few. Nausea, diarrhea, and other gastrointestinal effects are sometimes seen in humans and animals, and allergic reactions have been reported in humans.

So overall, the *in vitro* and laboratory animal evidence indicates it is plausible that milk thistle extract might have beneficial effects, though harmful effects in some situations could be possible as well. In humans, the clinical trials show weak evidence for benefit in some conditions and no evidence of benefit in others. Very little experimental, and apparently no high quality or controlled clinical research exists in dogs and cats. So once again, harm seems unlikely and a benefit is possible for some dose and some form of silymarin in some conditions, but we lack the information to use the compound rationally or to know for certain if it is even useful in most cases.

7. S-adenosyl methionine (SAM-e)

SAM-e is a chemical which occurs throughout the body and has a fascinating array of *in vivo* functions and *in vitro* effects. In humans, it is marketed for use in depression and arthritis, and a variety of other conditions. The clinical trial evidence is mixed and not generally high quality (for example, Cochrane Reviews for arthritis and alcoholic liver disease, Mayo Clinic summary for various conditions).

In pets it is primarily promoted as protecting the liver from damage due to disease of toxins, often in combination with Milk Thistle, though its use for arthritis and other conditions is also sometimes recommended. While the theoretical arguments for these uses, especially in the case of liver disease, are plausible, there is virtually no clinical research that the compound actually benefits patients when given as an oral supplement. There is one study which found no significant benefit in preventing liver changes associated with steroid use, one case report claiming some possible benefit in a dog with acetaminophen toxicosis, and one clinical study that suggest some possible value in treating age-related cognitive dysfunction in dogs. And despite how widely used this supplement is, and how sweeping the claims made for it often are, that's about it.

8. Digestive Enzymes

The claims made for digestive enzyme supplements are often sweeping and dramatic, and they can make you wonder how anyone ever digests their food without them. The usual arguments are that these enzymes exist in raw foods but are destroyed in the production of commercial pet foods, so if you are so foolish as to feed a nutritionally balanced commercial diet, you'd better give your pet these supplements, or else! These exaggerated, unsupported, sometimes outright mythical claims for raw food diets in humans and dogs have been discussed here before. They are based on fundamental misconceptions about digestive physiology and nutrition, and they hold no water.

Healthy humans and dogs have all the enzymes they need to effectively digest foods. The organs that produce such enzymes do not become stressed or fatigued by doing what is, after all, their normal function. Commercial diets and their constituent ingredients are extensively tested for digestibility, and there is no evidence that any deficiency of enzymes in these foods creates nutritional deficiencies or any specific health problem.

In addition to use in healthy individuals, enzymes are also recommended for cancer treatment, anti-inflammatory effects, and treatment of many other disease conditions. Though the occasional study is published to support these recommendations, often in "integrative medicine" journals, there is no consistent, high-quality clinical evidence in humans that digestive enzymes are effective therapy for any condition other than true pancreatic enzyme deficiency. And there is evidence that this approach may be ineffective or even harmful.

There is, surprise surprise, no clinical research at all on the subject in cats and dogs. Apart from pancreatic insufficiency, in which enzyme supplementation is often effective, the claims made for the use of enzyme supplements are based solely on anecdote, theory, or extrapolation from *in vitro* research.

9. Coenzyme Q10

Like most dietary supplements, coenzyme Q10, also known as ubiquinone, is recommended for a wide range of apparently unrelated conditions. It is recommended in humans for cardiovascular disease, Alzheimer's disease, migraines, diabetes, and many others, as well as a general tonic and, of course, the inevitable "boosting" of the immune system. In dogs and cats it has primarily been recommended for treatment or prevention of heart disease and age-related cognitive dysfunction.

There is controversy about many of the recommended uses in humans, with mixed and generally low-quality clinical trial evidence for most uses. And, as you will no doubt have anticipated by now, there is virtually no reliable research on its use in pets. One small experimental study failed to find evidence of decreased Coenzyme Q10 levels in dogs with congestive heart failure. There appear to be no clinical trials for any specific indication, and the recommendations for this supplement are again based entirely on theory, anecdote, and pre-clinical research or clinical research conducted in humans.

10. Azodyl

Azodyl is a proprietary mixture of probiotic organisms and prebiotics (substances intended to promote the growth of supposedly beneficial gastrointestinal bacteria) that is marketed for the treatment of kidney failure in dogs and cats. The theoretical argument advanced to support its use is "enteric dialysis," the idea that populating the gastrointestinal tract with bacteria that breakdown some of the nitrogenous wastes the kidneys normally remove from the body can lower the levels of these substances and improve clinical symptoms of renal failure. While this idea is not inherently unreasonable, it does suffer from the weakness of other probiotic therapies in that it requires relatively small additional to the gastrointestinal flora to have significant systemic physiologic effects, which may or may not actually be possible. In any case, it is not a concept that has been validated in practice.

A single pilot clinical trial of the product in humans, sponsored by the manufacturer, has been published. This identified statistically significant changes in one out of three laboratory measures and in a subjective assessment of clinical symptoms. An unblinded, uncontrolled case series in 7 cats reported small changes in laboratory values in 6 of the subjects. And similar small studies *in vitro and in rats* and miniature pigs, again all supported by the manufacturer, have reported some positive changes in some measures of kidney disease.

Overall, the theory is possible but of uncertain plausibility in the real world, and the clinical evidence is limited and highly vulnerable to bias in terms of methods and funding source.

Bottom Line

So to answer the original question, do these popular supplements work? Well, glucosamine almost certainly does not, and the case for multivitamins and digestive enzymes are extremely weak. Fish oil likely does have small benefit for allergies, and no definitive conclusion can be made concerning arthritis, though the early veterinary trials haven't been promising. Probiotics are a promising avenue for research, and there is reasonable evidence for some benefit in acute idiopathic diarrhea, but overall they are really not ready for prime time. Lysine, SAM-e, Milk Thistle, and Coenzyme Q10 all have reasonable theoretical foundations based on preclinical research, and none have adequate clinical evidence to draw any firm conclusions.

So should veterinarians and pet owners use these products? The decision whether or not to employ a particular medical intervention is always a matter of balancing the urgency of acting with the risks and benefits of the therapy, and always in the context of the limitations on the available information. In cases where the therapy is

very unlikely to provide a benefit, such as glucosamine, there is really no rational argument for its use even if it is harmless, and the resources wasted on such treatments could better be spent on more plausible therapies or research to find better treatments.

In cases where there is a plausible theoretical rationale but inadequate clinical evidence to make a firm conclusion, I am personally reluctant to recommend using such supplements because in the face of such uncertainty we are as likely to do harm as good. For example, Milk Thistle and the combination SAM-e and Milk Thistle products seem to induce loss of appetite in cats and dogs fairly frequently in my experience, and they are usually given to patients who are pretty sick and already taking many other medications. So in the absence of stronger evidence of benefit it seems imprudent to use them routinely. However, in urgent cases where there is no validated therapy and the clinical circumstances are dire, I can't fault anyone for grasping at straws, and I have certainly done so myself.

And, of course, if there is a sound theoretical rational and some reasonable clinical evidence, as in the case of fish oils for allergies and probiotics for acute uncomplicated diarrhea, use of such supplements seems perfectly reasonable. We must be careful not to let the perfect become the enemy of the good, and in veterinary medicine where the quantity and quality of the research evidence will always be less than optimal, we are justified in trying out things that are reasonable but unproven if the clinical circumstances warrant it.

Of course, the marketing used to promote these supplements goes well beyond anything justified by real scientific evidence and is almost universally untrustworthy. Likewise, the testimonials and anecdotes about their effects, whether from patients, pet owners, veterinarians, or Nobel Laureates, are all just stories with almost no probative value. And since most good ideas in medicine ultimately fail to become real, effective clinical therapies, it is likely that many even of the more plausible of these products will turn out not to be useful or to have unknown risks. Without adequate supporting evidence and without effective quality control, regulation, and post-market surveillance, we can never be sure we are helping and not harming our patients by using them.

However, it is also possible that some of these products will survive the rigors of real scientific investigation, if they are ever subjected to them, and will turn out to be truly useful therapies. And in the meantime, it may be reasonable to use some of them if the existing evidence and clinical need of the particular case are sufficient to justify doing so.

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16 Responses to *From SBM: The Top Ten Pet Supplements–Do They Work?*

Pingback: *The facts on supplements | Gilgablog*

boxer *says:*
May 23, 2011 at 4:00 am

Another herb that some dog breeders swear by is raspberry leaf. It is supposedly a uterine tonic that makes delivery easier, improves milk supply and prevents pseudo-pregnancies. I sounds too good to be true ...

Virginia@fish oil *says:*
March 15, 2012 at 9:00 pm

Our cat began having lots of dandruff looking specks in his fur and it was recommended we give him fish oil supplement. It worked wonderfully in just a short time. His fur is soft and smooth and smells sweet. Should have know since fish oil is so good for many things in humans, apparently it is good for cats too.

skeptvet *says:*
March 16, 2012 at 10:33 am

Well, there is some evidence that fish oil is useful in reducing the intensity of allergy symptoms. That said, anecdotes like this are, unfortuntaely, totally unreliable. Every failed medical treatment ever devised had stories like this to support it. And the fact that fish oil has some usefulness in humans is suggestive, but the details matter. It may have some protective benefits in terms of cardiovascular disease, for example, but that would have no bearing on whether or not it helps flaky skin in cats. In order to find the treatments that truly work, we need to rely on more rigorous testing and objective evidence.

Virginia@fish oil *says:*
April 6, 2012 at 6:08 pm

Skeptvet sounds very closed minded. We have seen the evidence in our pet and other opinions are unimportant since we have success. "The proof is in the pudding as the old saying goes."

skeptvet *says:*
April 8, 2012 at 9:36 am

"We have seen the evidence in our pet and other opinions are unimportant "

How you can say this and then call someone else closed-minded without noticing the hypocrisy is amazing.

Pingback: *European Food Safety Authority Rejects Prostora, a Probiotic Product for Dogs | The SkeptVet Blog*

Jolie Cosette *says:*
March 27, 2014 at 1:15 am

So what do we feed our cats? Or, conversely, what do we NOT feed them? Of course, this depends on health, age, activity, allergies and other factors of which I'm probably not aware. From the taurine-deficient Science Diet of the 70s to the thiamine-deficient unnamed canned foods recently discussed by Winn, I don't rely on ANY food as being complete and balanced. Thus, I rotate wet foods, add some supplements (B vitamins, krill oil and azodyl) and distilled water to their wet food. (Water pH where I live is 7.8; sodium, magnesium, calcium and other elements I'm trying to avoid are added to filtered water for taste.)

As a (retired) psychologist, both clinical and applied, I know the importance of double blind studies. I know the importance of statistically significant samplings. I read at the university, on line and in Davis, Ohio and Cornell publications, among others. When I began my odyssey into cat nutrition in 2003, I knew nothing. I still know nothing, except for lab values.

My vets are too busy to analyze patterns and trends in labs. That's my job. After repeated sloppy T4 processing, I now draw my cats' labs every six weeks or so and a microbiologist processes them. The cats see their vets three or four times a year

(dentist, ophthalmologist, feline specialists) and I bring in hard copies of the labs plus graphs. "Keep doing what you're doing," I'm told. But I don't know WHAT I'm doing. I don't know what I SHOULD be doing.

What should we feed our cats? What supplements, if any, should we use? What should we avoid?

Thank you.

skeptvet *says:*
March 27, 2014 at 7:39 am

I would start by considering this book– Dog Food Logic: Making Smart Choices for your Dog in an Age of Too Many Choices Though it pertains to dogs, it is not so much a book about what to feed as about how to make rational, evidence-based decisions about feeding, so the "logic" applies equally well to choosing what to feed your cats.

Though I don't intend to offend you, I also think you should consider your goals and motivations in intensively managing your cats clinical labwork and diet. Of course, we all want our pets to be healthy and happy. But I find there is an element of magical thinking in the effort to find the perfect combination of diet and supplements and other preventative care practices. There is a sense that we can ward off all the frightening things that might happen to our pets if only we find just the right food, just the right supplement, avoid the "toxins" in their environment, etc. It is easy to slip from rational, evidence-based preventative medicine into magic rituals to treat our own fear.

In most cases, this probably does little harm. But more extreme our choices and actions become, the more disconnected from good scientific evidence, the more likely we are to be doing harm in an attempt to exert control and ward off evil. I see nothing wrong with rotating foods, for example, but I think there is the potential for harm in many untested supplements, especially for cats. And there is absolutely no evidence that doing bloodwork every 6 weeks, and in human medicine there is clear evidence that excessive and undirected use of diagnostic testing leads to overdiagnosis and harms patients.

So the short answer to your question is that no one knows the optimal strategy for preventative nutrition and healthcare for each and every cat. Logically, there should be no such thing since individuals and circumstances vary so much and chance plays a huge role in disease. The best we can do is make reasonable choices based on the best current evidence and not let our anxieties drive us to extremes. The existing data most strongly support feeding a balanced commercial cat food, possibly towards the high end in terms of protein content and moisture, and restricting calories to maintain an optimal body condition. There is no evidence to indiate one brand or type of food is clearly superior to any other, or to support most of the fads that come and go (grain free, raw, low ash, etc). While individualized preventative care is improtant (tailoring vaccinations to risk level for individual cats, for example), we have little data about precisely what risk factors support what management changes, so again the perfect world in which we know precisely what to do to prevent disease in a particular cat simply doesn't exist. I suspect by saying "Keep doing what you're doing," your vets are really saying "If it ain't broke, don't fix it" and suggesting that it may not be possible to have as much contrl as you seem to want over the long-term outcome of your cats' health.

Good luck!

Jolie Cosette *says:*
March 29, 2014 at 12:37 am

You're absolutely right that I'm a control freak. And yet I know there are so many things out of my control. I observe; I research; I tinker. I control what I can, which is very little.

I have only two cats now, a 16-year-old and a 19-year-old, having recently euthanized my 24-year-old and the 19-year-old's sister. I know they are geriatric. I know they are mortal. Given their ages, I think six months, even three months, is too long to go between urinalyses and chem panels. No, I'm not engaging in magical thinking; it's something far worse.

I'm waiting for CRF.

And when it occurs, what then? Well, I'm prepared. But do I want to travel down that road again, knowing where it ends? Fluids, ok. But then there's medicine to control nausea. Medicine to control hypertension and hyperthyroidism. The mad alchemy of phosphorus binders and potassium supplements and calcitriol.

I don't think that's a life I want for my rocket cats who fly from catwalk to catwalk, touching the ground only to eat, use the litterboxes and investigate the greenhouse. Yes, they have the flattened skulls of elderly cats, one has had cataract surgery, but their musculature and energy is amazing.

So, I am waiting for the inevitable, but we are living while we are waiting, and, of course, searching for the holy grail that I know does not exist.

WScott *says:*
July 18, 2014 at 2:15 pm

Thanks for writing this. I'm a little embarrassed to admit I tried fully half of these when our dog fell sick last year. Some of them did *seem* to cause some improvement, but of course that could all be observer bias. Part of me wishes I'd found this article a year ago, but honestly I don't know if it would've made a difference. "Grasping at straws" as you say. I can at least say that we regarded all these supplements as as (potential) compliments to real medicine, not replacements for it.

One question I don't see covered here (or much of anywhere other than the supplement manufacturers) is the practice of giving dogs Vitamin C to make their urine less of a grass-killer. Any sound basis for that, or just more snake oil? Thanks,

skeptvet *says:*
July 19, 2014 at 5:59 am

I haven't seen any literature regarding this specific question, though I have not conducted an extensive search, so it might exist. It is not implausible that Vit C could change urine pH, which might effect lawn staining. In humans, Vit C can increase oxalate concentrations in urine, which could be a problem for dogs with a history of oxalate bladder stones, but in general I would imagine the potential side effects are minimal at reasonable doses. Mega-doses, however, could create health risks.

If I get a chance, I'll check for any specific information on this one. Thanks!

Michael Moyer *says:*
April 16, 2015 at 12:37 pm

http://www.northscaping.com/IZArticles/IS-0111

The brown "burn" from urine is from nitrogen (thank you, Penn State agricultural B.S. degree), not from pH. Notice the ring of brighter, taller green grass around the burns–that's where the nitrogen concentration becomes fertilizer again, when it's not in the toxic high dose delivered by the dog's urine.

Pingback: *Canine Nutrigenomics by Dr. Jean Dodds: Science as Windowdressing | The SkeptVet*

Linda Horn *says:*
March 28, 2017 at 6:01 pm

I didn't see chitosan (brand name Epakitin) mentioned anywhere in this article, or in a search of this website. I've dealt with two cats with CRF, this far. For my first CRF cat, my former vet recommended Hill's Science Diet K/D canned food. The poor cat's urine output decreased somewhat, but he wasted away, and he didn't last long. With my second CRF cat, I had a different vet, who at first recommended the usual prescription kidney diet cat foods. When I told him I wasn't going to feed my cat any of those prescription cat foods, he recommended Epakitin. As I understand it, Epakitin is actually chitosan, which is a weak phosphorus binder. It sounds like Epakitin MIGHT work, in theory. My cat's urine output did seem to drop, initially. Is there any evidence as to whether chitosan is effective for treating CRF in cats?

skeptvet *says:*
March 29, 2017 at 5:05 pm

Epakatin (chitosan) does reduce phosphorus level sin cats with renal disease. However, this is only one of the goals of diet change, so Epakatin is not a treatment for renal disease or something we would expect to alter the general well-being of a cat with kidney disease. It is useful for the specific function of lowering phosphorus levels, and cats seem to take it better than some of the other phosphate binders, but there is no reason to think that, by itself, it will have the same effects on symptoms and longevity as seen with renal diets.

Spicy Health: Ginger Root and Turmeric Root for Veterinary Applications

Wild West Veterinary Conference 2017

Robert J. Silver, DVM, MS, CVA
RxVitamins

Tumeric

From: Wynn & Fougere: Veterinary Herbal Medicine; Mosby, 2007.

***Curcuma longa* L.**

Family: Zingiberaceae.

Other names: Indian saffron, yellow ginger.

Part used: Dried rhizome, tuber.

Distribution: Cambodia, China, India, Indonesia, Madagascar, Malaysia, Philippines, Vietnam. Cultivated throughout the tropics including Africa.

Selected constituents: Volatile oil (6%) composed of monoterpenes and sesquiterpenes, including zingiberone, curcumene, and α-and β-turmerone. The bright yellow color is due to the curcuminoids, 50–60% are a mixture of curcumin, monodesmethoxycurcumin, and bisdesmethoxycurcumin.

Introduction

Turmeric (*Curcuma longa* L.), a member of the Zingiberacea plant family which includes ginger and cardamom, is a spice and food coloring found primarily in India, but also grown in China, Thailand, and Indonesia. For centuries it has been used for its culinary and medicinal properties in these countries. Turmeric is the base found in most Indian curries, it has a bright yellow color, and is used to enhance the flavor of foods. As is true of most culinary spices, their purpose is not just flavoring but also, as a food preservative due to their antioxidant properties. This is how they helped to keep food fresh, in a world before refrigeration.

Curcuminoids are found in the rhizome of the *Curcuma longa* plant. A rhizome is a "creeping rootstalk, growing underground in horizontal stems, like its cousin, ginger. The rhizome of this plant, in addition to the curcuminoids found in it also contains sesquiterpenes (turmerone, atlantone, zingiberone, turmeronol, germacrone and bisabolene), carbohydrates, proteins, resins and caffeic acid. The active molecules in the plant are considered to be the brightly yellow-colored polyphenolic curcuminoids. Curcuminoids make up 2–5% of the rhizome.

Naturally occurring curcuminoids are: Curcumin (diferuloylmethane), demethoxycurcumin, and bisdemethoxycurcumin. The distribution of these curcuminoids in commercially available turmeric is: 75–85% curcumin, 10–15% demethoxycurcumin and 5–10% bisdemethoxycurcumin.[8,9,10]

Biological Activity

Historically, turmeric has been used in both the Ayurvedic and Traditional Chinese Medicine systems of Ethnobotany for the treatment of skin disorders, pulmonary and gastrointestinal ailments, pain, wounds and liver disorders.[1]

Over 3000 preclinical and clinical studies have found that there are many medical applications for this common Indian spice. It has been found to have a benefit in the treatment of cancer, immune deficiencies, cardiovascular health, Alzheimer's' disease, diabetes, arthritis, and Crohn's disease, as well as cancer, psoriasis and others.

Curcumin works by modulating multiple molecular targets, cell signaling proteins, cell cycle proteins, cytokines and chemokines, enzymes, receptors and cell surface adhesion molecules. Curcumin works "up-stream" to down-regulate inflammation, modulates the pro-inflammatory enzymes (cyclooxygenase and lipoxygenase), the inflammatory transcription factors nuclear factor kappa B (NFκB) and signal transducer and activator of transcription 3 (STAT3) and their genomic expressions.

Curcumin has been found to be a neuroprotectant as a result of its polyphenolic antioxidant properties. These antioxidant properties also protect DNA from single strand breaks induced by singlet oxygen. Curcumin suppresses the mutagenicity of several common mutagens including cigarette smoke and benzopyrene. Curcumin also has potent anti-inflammatory effects by inhibiting neutrophil function, inhibiting platelet aggregation, inhibiting lymphocyte activity, promoting fibrinolysis, and stabilizing lysosomal membranes.[1,10]

Curcumin has cancer-preventative activity (chemoprevention) which results from the ability of curcumin to: 1) inhibit Phase 1 cytochrome P450 activation of pro-carcinogens; 2) enhance Phase 2 detoxification activity, including glutathione transferase; and inhibits multiple signal transduction pathways that trigger cancer proliferation, angiogenesis and tissue invasion. The inhibition of NFκB activation by curcumin down-regulates multiple inflammatory genes which in turn result in decreased proliferation, signaling, anti-angiogenic effects and decreased cell invasiveness. Turmeric has been found to sensitize only cancer cells to the cytotoxic effects of chemotherapy agents.[11]

Other properties for curcumin include altering serum lipids such as cholesterol, LDL, and HDL cholesterol as well as LDL peroxidation. Curcumin has been shown to increase HDL cholesterol (the "good" cholesterol) in humans. Curcumin interferes with intestinal cholesterol uptake, increases the conversion of cholesterol into bile acids by increasing the activity of hepatic cholesterol-7-alpha-hydroxylase, which is the rate limiting step in bile acid synthesis. Curcumin, for the reasons just stated also increases bile acid secretion, increasing bile output by almost 100%.[13]

And if all of these properties weren't enough, curcumin has been found to have hepato-protective and cholerectic properties. It prevents lipid peroxidation *in vivo* due to its potent anti-oxidant properties. Historically, turmeric has been used to improve digestive function, in part due to its ability to stimulate the digestion of fats and carbohydrates.[1,10]

Absorption

In spite of having all of these beneficial health properties, turmeric, and it active ingredients, the curcuminoids, are very poorly absorbed from the digestive tract. It is a lipophilic molecule, and in ethnobotanical use turmeric is commonly cooked with oils and other spices like black pepper all of which improve its absorption and slow down GI transit time.

There have been a number of attempts to chemically modify the curcuminoid molecules to improve their intestinal absorption, but before pharmaceutical technology was applied to this plant extract, there was "Yellow Paste" This is a home cooking way to improve the absorption of the curcuminoids in this healthy spice.

Recipe for Turmeric Paste (aka Yellow Paste or Turmeric Bomb)

4 oz. organic turmeric
1/4 cup water
Mix together and heat slowly on low heat until thickens.

Add ¼ teaspoon ground black pepper
Add 2 tablespoons virgin coconut oil

Slow heat 5–10 minutes. Let cool. Put into glass. Store in fridge.

Curcumin is very unstable at the pH of the GI tract, decomposing in less than 10 minutes, and has a very low oral absorption. Doses as high as 12 grams daily only resulted in plasma levels of less than 50 ng/ml in one study.[12]

Currently there are several patented curcumin modifications in the marketplace that are using pharmaceutical technology to increase the absorption of curcuminoids. Curcuminoids have poor solubility, low absorption from the gut, rapid metabolism, and rapid systemic elimination. The major amount of curcumin ingested orally is excreted unchanged in the feces.

Molecular Strategies to Increase Absorption

Co-administration of curcuminoids (aka: simple curcumin complex) with black pepper extract (piperine) has been shown to increase absorption 1.5 times over simple curcumin complex. The combination of curcuminoids and volatile oils of the turmeric rhizome resulted in a 6.9 fold increase in the absorption of curcumin (BCM-95™) over turmeric in animal models.[8] The lipophilic matrix of curcumin with phosphatidylcholine and microcrystalline cellulose (Meriva™) has been shown to increase the oral absorption of curcumin in the human by 19.2 times over the simple curcumin complex.

One of the most highly absorbable formats for oral curcumin absorption studied utilizes a water-soluble complex in which the curcuminoids are dispersed with the antioxidants tocopherol and ascorbyl palmitate and combined with the water soluble carrier molecule polyvinyl pyrrolidone. This complex, called Curcuwin™, in a pharmacokinetic study using human subjects, comparing its oral absorption with that of the simple curcumin complex, BCM-95™ and Meriva™, was found to be 45.9 times better absorbed.

When compared to the relative absorption of BCM-95 to simple curcumin complex, Curcuwin™ was 34.9 times more orally absorbable, and 5.8 times more absorbable relatively than Meriva™. This study used each subject as its own control, by having a washout period between administration of each different test material. It's very rare to find "head to head" studies that compare different proprietary products in the same experimental subject, using them as their own control such as with this study.[8]

In addition to the advantages of the improved absorption of the Curcuwin™ complex over the other two patented products evaluated, peak serum levels of curcuminoids from Curcuwin™ persisted for at least 12 hours in this pharmacokinetic study in humans. These peak serum levels of curcuminoids may actually persist longer, but the study duration was only 12 hours. The authors note that future studies will carry the curve out to 24 hours. The duration of therapeutic serum levels of curcuminoids with Curcuwin™ far exceeds the duration of therapeutic serum levels in the other absorption technologies described in this paper. It is still suggested to administer Curcuwin™ twice daily, but it may be that once daily administration could also have its benefits.

Another finding of this study was that the distribution of each of the three individual curcuminoids in the serum varied from product to product. It is known that the antioxidant potency of curcuminoids decreases according to the number of methoxy groups present on the curcuminoid molecule.

Decreasing Antioxidant Potency

Curcumin>Demethoxycurcumin>Bismethoxycurcumin.

Each curcuminoid has similar but different properties. For instance, the anti-ulcer and anti-inflammatory aspects of the curcuminoid curcumin has been found to be stronger than that of demethoxycurcumin. However, with respect to the growth-modifying activity of curcuminoids the methoxy groups do not play a role.[14]

It is interesting to note here that the phospholipid-curcumin complex increases the amount of demethoxycurcumin in the serum greater than the amount of curcumin. Demethoxycurcumin is not as anti-inflammatory as curcumin. In the simple curcumin complex there is 4 times the amount of curcumin than demethoxycurcumin. The phosphatidylcholine-curcumin complex (Meriva™) has demethoxycurcumin as the major plasma curcuminoid in the serum. This comparison study found this to be true for the this complex, but it was not found to be true for either the BCM-95™ or Curcuwin™ formulations.[8]

Research in our Veterinary Species

As many studies as have been conducted studying curcuminoids, there are very few that are in our target veterinary species of dogs, cats, and horses, and most of those are basic research versus interventional studies. There is an abundance of studies in laboratory animals, and there are studies from India, Iran and other countries where turmeric is widely consumed and widely used for medical purposes. Many of those studies use whole powdered turmeric which is very poorly absorbed, even in large dosages. Studies of the more bioavailable forms of curcumin in veterinary species exist only for the phosphatidylcholine bound format, and those were sponsored by the Italian company that owns the patent on this effective product.

One study in dogs measured the gene expression of peripheral white blood cells in dogs with osteoarthritis (OA). Two groups of dogs were studied, one group with OA and the other without this problem. They were administered either an NSAID (Previcox™) or Meriva™. The curcumin formula was administered at 4 mg/kg BID and the NSAID at 5 mg/kg/day. The response of genes involved in the inflammatory response was measured for the two groups after 20 days on the different treatments.

The study found that curcumin regulated the same molecular target of inflammation as has been found to be true in humans. Molecular targets of curcumin that were not similar to the targets of the NSAID were those related to the inhibition of macrophage proliferation and strongly down-regulated TNF-α and activated fibrinolysis. The authors feel that for these reasons curcumin can provide complementary support in the treatment of OA.[6]

This study was modeled on a parallel study in mares.[4] In this study 7 mares aged 4–9 years were given 4 mg/kg of Meriva™ once daily for 15 days. Whole blood was analyzed for the effects of curcuminoids upon expression of COX-2, TNF-α, IL1β, IL1RN, and IL6 in the mares and the foals studied.

They found that curcumin inhibited the expression of all of these pro-inflammatory cytokines which play a role in the pathogenesis of osteoarthritis, with only IL1β, IL1RN having statistically significant values. In foals, curcumin significantly inhibited the expression of COX-2, TNF-α, IL1RN and significantly increased the expression of IL6. The authors conclude that curcumin has potential as a natural anti-inflammatory agent for treating osteoarticular disorders by suppressing pro-inflammatory cytokines and catabolic enzymes.

A 2009 Italian study compared the modulation of neutrophil function and apoptosis by standardized extracts of *Echinacea angustifolia*, *Butea frondosa* (an herb of the Ayurvedic tradition) and *Curcuma longa* (another herb from Ayurveda) in sheep neutrophils. This study was sponsored by the company that manufactures Meriva™.

This *in vitro* study determined that the curcumin-phosphatidylcholine complex stimulated spontaneous apoptosis of neutrophils and inhibited gene expression at T22 compared to the *Echinacea* and *Butea* extracts, suggesting to the researchers that Curcuminoids have more of an anti-inflammatory activity as compared to the immunomodulatory effect of *Echinacea* and *Butea* extracts on neutrophil function.[5]

Another study in dogs with osteoarthritis used force plate measurements of limb placement, which is the best way to measure response to a pain relieving agent, such as curcumin, and used a randomized placebo-controlled parallel group study of a proprietary turmeric product to

determine if it had any better effect on their pain as measured by a force plate than a placebo. This turmeric product consisted of curcuminoid extracts of two different Curcuma species combined with essential oils extracted from turmeric. It was administered at a dose of 4 mg/kg per day of curcuminoids.

No attempt was made to measure serum curcuminoid levels in this study. The study did not find a statistical difference in force-plate values in the group treated with this enhanced turmeric formula as compared to those treated with the placebo. However, the investigator's assessment of the dog's overall responses showed a statistically significant treatment effect in favor of the proprietary curcuminoid product. The owner's overall evaluation of the dog's responses approached statistical significance. This is most likely due to the poor bioavailability of the curcuminoids in this particular proprietary product. This is why the bioavailability of curcuminoids is very important to see clinical effects.[3]

There is a recent study in beagles using a proprietary liposomal curcuminoid product that was designed for intravenous use, which doesn't apply to those products that are designed to be administered orally. This pharmacokinetic study used a 2-hour intravenous infusion of this liposomal curcuminoid product and found that the plasma half-lives of tetrahydrocurcumin (THC) and curcumin both ranged from 0.4–0.7 hours, and was the consequence of both liver and renal clearance.

One take-away from this study is the short plasma half-life of curcumin and THC when administered intravenously in a 2 hour liposomal infusion. For best clinical results plasma levels of curcuminoids need to be maintained at a therapeutic level for 24 hours, such as is found with the oral administration of Curcuwin™.[7]

Potential Veterinary Applications for Curcuminoids

- **Inflammatory conditions**
  - Osteoarthritis
  - Atopy
  - Inflammatory bowel disease
  - Autoimmune disease
- **Neoplastic diseases**
  - Both prevents and treats cancer
  - Inhibits metastasis
  - "Chemo-sensitizer" - improves effect of chemotherapy agents
  - Activates apoptosis
  - Inhibits proliferation and survival of almost all types of neoplastic cells
    - Cellular uptake of curcumin is higher in neoplastic cells than healthy cells
  - Prevents tumor-induced T-cell apoptosis
- **Metabolic diseases**
  - Improves symptoms associated with Type 2 diabetes
  - Improves glycemic control in mouse models of type 2 diabetes
  - Prevents alcohol induced liver disease in laboratory rats
- **Neurologic disease**
  - Epilepsy
  - Senility
  - Head trauma

Empirically Determined Dosage of Curcuminoids in Veterinary Species

- Curcuminoids bound to phosphatidylcholine (Meriva™ = 4 mg/kg QD)
  - Innes 2003 (dogs)
  - Farinacci 2009 (mares)
  - Colitti 2012 (dogs)
- Curcumin[2]
  - 50–250 mg TID dogs
  - 1200–2400 mg daily for horses
- Curcuwin™ (20% curcuminoids like Meriva™)
  - No studies in target species yet
  - Presumptive dose = 4 mg/kg daily
  - Dosage may be less due to superior absorption of Curcuwin™ over Meriva™

Toxicology, Herb-Drug Interactions and Adverse Effects

- Turmeric is classified as very safe.
  - The acute LD50 for turmeric in rats was 5 grams per kg.
- The only contraindications to its use are obstruction of the biliary tract and hypersensitivity to turmeric.
  - Allergic reactions have occurred and contact sensitivity.
- Caution is advised with anti-platelet or anti-coagulation medication.
  - Rare cases it may affect bleeding times but this is unlikely.
- No known herb or drug interactions or common adverse effects other than an unusual skin odor at higher dosages.

GINGER

From: Wynn & Fougere: Veterinary Herbal Medicine; Mosby, 2007.[1]

Zingiber officinale.

Family: Zingiberaceae.

Other names: African ginger, common ginger, ginger root, Jamaica ginger, **etc**.

Part used: Rhizome.

Distribution: Native to southeast Asia and cultivated in tropical regions worldwide. India is the world's largest producer.

Selected constituents: 1–4% essential oil, zingiberone, zingiberole, sesquiterpene hydrocarbons such as zingiberone, arcurcumene, sesquiphellandrene, bisabolene, monoterpene aldehydes and alcohols, gingerols which convert to shagoals upon heating.

Introduction

Many spices and some foods have healthy properties, such as reducing the growth of pathogenic organisms that grow on food that spoil food when not refrigerated. In the world before refrigeration, culinary spices played a crucial role in reducing food-borne diseases and preserving food for many days or more.

Of all the spices, none stand out like ginger root, with its sweet and pungent odor, and the sharp and bubbling sensation it creates when in contact with the tongue. Yet few spices have as many applications for medical problems as ginger root does. It's safe, it's tasty to drink or eat, and it can help a multitude of problems, as seemingly diverse as vomiting from inflammatory bowel disease to helping with arthritis.

Historically, ginger has been found effective to reduce the symptoms of gastrointestinal disease. It is termed a **carminative** in herbal medicine terminology, which means it relieves gas and bloating, and can relax smooth muscle spasms of the intestinal loops, which can be very uncomfortable.

Studies have shown that ginger's anti-emetic effect is comparable to Dramamine for motion sickness. It reduced dizziness, nausea, vomiting, and cold sweating in the patients in this study.[2]

Some of the compounds in ginger are anti-inflammatory and anti-oxidant in their properties. Gingerols are some of these potent constituents of ginger. Ginger is one of the most studied herbs in our knowledge base. Other similarly well-studied herbs include garlic and ginseng and others such as green tea, gingko, St John's Wort, licorice root, *Echinacea*, etc.

Of the thousands of studies conducted on ginger in the information database, very few are in our veterinary species, especially for clinical conditions, unless they are being used as research animals. But, if you can extrapolate the data from human, from *in vitro* and *in vivo* work, there are an impressive array of applications for ginger and its many active compounds.

Clinical Applications Based on the Evidence

- The compounds, **6-gingerol and 6-shogaol** have been shown to have to have a number of pharmacological properties, including anti-pyretic, analgesic, antitussive, and hypotensive effects.[3]
- **Nausea** from pregnancy, motion sickness, chemotherapy, even **hyperemesis gravidum**.
- Ginger's **anti-inflammatory effects** can be used to address painful **osteoarthritis** or **rheumatoid arthritis symptoms**.
  - One study found 75% of patients with arthritis found relief using ginger extracts.[4]
  - This review also found that significant side-effects were absent with ginger.
- **Chemopreventative** for cancer.
  - Two groups of knockout mice to lack an immune system were either fed gingerols or were the control. Both groups had colon cancer cells implanted in their flank subcutaneous tissues. The gingerols group was observed to have significantly fewer tumors arise, and those that did were smaller on average than the control group tumors.[5]
- **Antiemetic in Dogs.**
  - Dogs were given cisplatin to induce nausea, and then were given ginger extracts. Ginger administration significantly reduced the number of vomiting episodes at doses as low as 25 mg/kg per os. The highest dose tested for vomiting was 200 mg/kg which produced the lowest number of vomiting episodes.[6]
  - Dogs diagnosed naturally occurring *Dirofilaria immitis* heartworm infections were treated with ginger extracts given subcutaneously at 100 mg/kg reduced micofilarial concentrations by 83% in 55 days.[7]

Evidence-Based Dosages

- Dried powder human dose: 250–1500 mg 4 times daily, usually put into capsules.
- **WYNN**[2]
- **Human**
  - **Dried herb**
    - **Motion sickness adults and children >6 years**: 0.5 g 2–4 times daily.
    - **Dyspepsia**: 2–4 g/day powdered plant material or extracts.

- **Infusions and decoctions:** 5 g/cup of hot water (1 tsp/cup).
- **Tincture**: available as 60–90% ethanol preparation; dose is lower for high alcohol concentrations. 1:2 or 1:3: 0.25–0.75 ml TID.

- **Small animal**
  - **Dried herb**: 15–200 mg/kg divided daily (optimally TID).
  - **Infusion**: 5 gram per cup water, administered at a rate of ¼–1/2 cup per 10 kg divided daily, optimally TID.
  - **Tincture**: 1:2–1:3: 0.25–0.5 ml per 10 kg divided daily (optimally TID) and diluted or combined with other herbs.
  - **For nausea associated with travel**, give at least **30 minutes before travel**: 25–50 mg powder per kg divided daily dose or 0.5 ml per 10 kg 2–3 times daily.

Toxicology, Herb-Drug Interactions and Adverse Effects

- Ginger is classified as very safe.
- Rare cases it may affect bleeding times but this is unlikely.
- No known herb or drug interactions or common adverse effects.

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Ginger

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Speaker Information

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