



SURVEYING SUPPLEMENTS

Current Trends, Research, & Recommendations

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Veterinarians frequently encounter the use of dietary supplements in clinical practice. The exact prevalence of supplementation by pet owners is unclear, but economic indicators suggest the practice is widespread.

Estimated annual expenditures by American owners reached over \$1 billion in 2010, with 31% of dog owners and 22% of cat owners reporting use of such products.¹ A 2006 nutritional survey found that 9.9% of pet owners administered dietary supplements; most prevalent were multivitamins, joint supplements, and fatty acids.²

Limited data are available on particular products, but veterinarians should be aware of:

1. Owners' rationale for supplementation
2. Regulation of dietary supplements
3. Possibility of adverse effects
4. Theoretical or scientific basis of common ingredients encountered in products.

OWNER RATIONALE

While no definitive studies on the psychology of pet supplement use exist, clinical experience suggests that dietary additive use is based on several reasons:

1. Perceived deficiencies in commercial pet foods and/or distrust regarding food formulation
2. Preference for treatments marketed as "naturally" derived and safe, with few side effects
3. Belief that integration of dietary supplements and pharmaceutical drugs is more efficacious than the latter alone, and that these supplements may prevent drug side effects

4. Perceived reduction in disease morbidity or mortality, such as chondroprotectants to prevent/treat joint disease and dietary supplements to increase survival times in oncologic patients.³

ADVERSE EFFECTS

The safety profiles of most supplements are only anecdotally established. Adverse events from minerals and vitamins are well described and occasionally seen with high doses, while adverse events from herbal medications and extracted compounds generally occur due to one of the following:

1. Idiosyncratic or unpredictable interactions; for example, interactions have been reported between nutraceuticals, herbs, and drugs⁴
2. Off-label use, dose, or combination of these dietary additives⁵⁻⁸
3. Inappropriate processing or misidentification of products⁹
4. Contamination—intentional or inadvertent—and variability in ingredients and their concentration¹⁰⁻¹³

COMMON SUPPLEMENTS

Vitamins & Minerals

The recommended allowance of nutrients in most commercial pet foods is guided by current Association of American Feed Control Officials (AAFCO) standards and the National Research Council's (NRC) assessment of the scientific literature.¹⁴ **Table 1**, page 80, lists common vitamin and mineral supplements.

Commercial Foods. Commercial pet foods are replete with vitamins and minerals. Only in rare circumstances—gen-

erally due to underlying pathology—do pets fed commercial AAFCO-labeled foods require additional minerals and vitamins. Oversupplementation may be deleterious; administration of excessive dietary calcium during growth of large breed dogs may predispose to development of orthopedic disease.¹⁴

Home-Prepared Foods. Many home-prepared diets require vitamin and mineral supplementation. In general, human multivitamins are recommended because they are designed to complement the foods used in these diets. Multivitamins designed for pets are generally formulated to supplement commercial pet foods and to prevent toxicity by providing lower amounts of nutrients.

Fatty Acids

Fatty acids have received extensive attention in the human and veterinary literature. Most mammals synthesize saturated fats, but lack the ability to produce the omega-3 and omega-6 series of polyunsaturated fatty acids. Therefore, dietary sources of these essential fatty acids are required. A summary of relevant polyunsaturated fatty acids is provided in **Table 2**, page 80.

Feline Requirements. Delta-6 desaturase is an enzyme that adds an additional double bond to linoleic and alpha linolenic acids, starting a conversion process to longer, more unsaturated products. Cats, however, possess very low levels of this enzyme, which creates their conditional requirement for arachidonic acid in growth, lactation, and gestation.

Dosage. Doses of fish oil used to

TABLE 1. Common Vitamins & Minerals Administered by Owners

NUTRIENT	SUMMARY
Minerals	
Calcium	<ul style="list-style-type: none"> Calcium requirements for adult maintenance are low; additional supplementation does <i>not</i> provide much benefit. Avoid low, or high, calcium intake in growing animals. Carefully and deliberately supplement calcium only (1) in rare instances or (2) for animals on low-calcium, home-prepared diets.
Selenium	<ul style="list-style-type: none"> It is often administered to pets with cancer, but insufficient data exists supporting its use for cancer treatment or prevention in humans and animals.¹⁵
Zinc	<ul style="list-style-type: none"> Owners may supplement due to perceived benefits for immune function or dermatologic disease. Benefits are unlikely unless the animal (1) is fed a high-fiber diet low in zinc or (2) has a genetic predisposition for deficiency (northern breeds).
Vitamins	
B-Complex Vitamins	<ul style="list-style-type: none"> These vitamins are minimally toxic, and significant excesses are present in most commercial foods. Certain hereditary and pathological conditions result in vitamin B12 deficiency, but supplementation of B vitamins in normal animals is <i>not</i> likely beneficial.
Vitamin C	<ul style="list-style-type: none"> Vitamin C is synthesized from glucose in dogs and cats. High amounts of vitamin C can induce lipid peroxidation, which may be the basis for anecdotal reports of high-dose, IV vitamin C for cancer treatment. Vitamins C and E (50 mg/kg, each) decreased cisplatin-induced vomiting episodes in dogs.¹⁶ Supplementation has been shown to increase serum or plasma levels; in one study, it increased cartilage weight in experimental canine arthritis.¹⁴ Supplemented greyhounds ran slower when given vitamin C, and diarrhea has been reported.¹⁴ Most canine studies administered 1 g of supplemental vitamin C.
Vitamin D	<ul style="list-style-type: none"> Dogs and cats produce little vitamin D in the skin and, therefore, require dietary intake or supplementation (unlike humans).¹⁴ Commercial diets include vitamin D or contain organ meats rich in fat-soluble vitamins. Deficiencies of vitamin D in home-cooked and raw diets have been reported.¹⁷ A relationship between low vitamin D and neoplasia has been reported in dogs with mast cell tumors compared to controls,¹⁸ but a causal link has not yet been identified. Supplementation in animals consuming commercial pet foods is not recommended, and may cause toxicity (bone growth abnormalities, mineralization, hypercalcemia).
Vitamin E	<ul style="list-style-type: none"> Supplementation of polyunsaturated fatty acids generally increases vitamin E requirements.¹⁴ Vitamin E has been recommended for canine osteoarthritis (OA) (400 IU/day),¹⁹ hepatic disease,²⁰ atopic dermatitis, and other inflammatory conditions. Data is strongest for arthritis, but doses used have been variable (generally 10–20 IU/kg). High doses may impair blood clotting.¹⁴

TABLE 2. Relevant Polyunsaturated Fatty Acids

FATTY ACID	SUMMARY
Alpha Linolenic (n-3)	May be essential in dogs and cats but data is lacking
Docosahexaenoic (n-3)	May exert biologic effects, specifically in the retina and neural tissues
Eicosapentaenoic (n-3) & Arachidonic (n-6)	<ul style="list-style-type: none"> Arachidonic acid products generally promote inflammation and platelet aggregation. EPA produces less potent prostaglandins and leukotrienes. Proposed effects include: ²¹ <ul style="list-style-type: none"> Improved renal parameters in experimentally induced kidney disease Reduction of inflammation in OA; mild to modest decreases in lameness and NSAID requirements were noticed in clinical trials of therapeutic diets with EPA and DHA²² Decreased very-low-density lipoprotein in hyperlipidemia, pruritus and/or dermatitis, and cardiac cachexia and arrhythmias in heart disease Chemosensitization and improved oncologic survival Improved memory and learning in puppies.²³
Linoleic (n-6)	Essential fatty acid in dogs and cats

provide certain omega-3 fatty acids vary in relevant studies. Many conditions responded to doses approximating an intake of 1 to 1.5 mg of eicosapentaenoic acid and docosahexaenoic acid (EPA+DHA) per calorie, and most standard fish oil capsules contain 300 mg of EPA+DHA.

- A 15-kg dog consuming 1000 calories per day would require 1000 to 1500 mg of EPA+DHA daily, or about 3 to 5 fish oil capsules.
- A dose of 1 capsule per 4.5 kg (10 pounds) of body weight has been used by some practitioners as a general guideline.
- Some studies of specific conditions, such as OA and lymphoma, employed doses of > 3 mg of EPA+DHA per calorie, or 3 capsules per 4.5 kg of body weight.
- Some diets are high in fish oil, which should be considered prior to supplementation.

Amino Acids

Table 3 outlines common amino acids and their derivatives used for dietary supplementation.

“Joint” Supplements

A variety of supplements are marketed for the management of OA. Recent meta-analyses of supplements for this purpose found limited evidence except for omega-3 fatty acids.³⁴ Common joint supplements are reviewed in **Table 4**, page 82.

A double-blinded, positive-controlled trial of a supplement product (475 mg glucosamine HCl, 350 mg chondroitin sulfate, 50 mg N-acetyl-D-glucosamine, 50 mg ascorbic acid, and 30 mg zinc sulfate per ≈ 20 kg of body weight) improved subjective OA scores at 70 days compared to 42 days with carprofen (4 mg/kg for 7 days, 2 mg/kg for maintenance).³⁵ Improvements were not significantly different between groups at day 70. A shorter study comparing a different glucosamine and chondroitin product to meloxicam and to carprofen, but for only 60 days, found improvements only in the NSAID groups as measured by ground reaction forces and subjective scores.³⁶

“Joint” diets are unlikely to produce improvement through supplementation with glucosamine and chondroitin as many of these diets have concentrations equivalent to maintenance pet foods and often have lower concentrations than those administered in supplement form. Omega-3 fatty acids are

TABLE 3. Common Amino Acid Products

AMINO ACID	SUMMARY
Aromatic Amino Acids	<ul style="list-style-type: none"> • Phenylalanine and tyrosine contribute to production of dopamine, other catecholamines, thyroid hormones, and melanin; effects on behavior are unknown • Tryptophan is precursor to serotonin and melatonin; elevations have been suggested to produce mild behavioral changes in dogs, but no increases in serotonin were observed when compared to other study groups²⁴ • 5-hydroxytryptophan should be avoided due to reports of serotonin syndrome like effects at doses > 20 mg/kg²⁵
Branched Chain Amino Acids	<ul style="list-style-type: none"> • Includes leucine, isoleucine, and valine; leucine has been shown to stimulate skeletal muscle protein synthesis in a number of species • A role in reducing severity of hepatic encephalopathy has been suggested, but debate persists and little work has been done in small animals²⁶ • Dosing branched chain amino acids is difficult without knowledge of dietary amino acid composition
Glutamine	<ul style="list-style-type: none"> • Nonessential amino acid that is the principle source of metabolic fuel and intermediates for enterocytes • Parenteral supplementation in critical human patients improves outcome²⁷ • Supplementation in small animals without supportive feeding is unlikely to be successful, but additive supplementation beyond that in food could be helpful
L-carnitine	<ul style="list-style-type: none"> • Not technically an amino acid, but critical for transporting long-chain fatty acids in the mitochondria, contributing to cellular energy production • Deficiency induces dilated cardiomyopathy (DCM), and empiric supplementation is recommended for this condition • Suggested for feline hepatic lipidosis, but does not appear to prevent the condition, instead producing some changes in fatty acid oxidation²⁸ • Others postulate that it promotes weight loss during caloric restriction
L-theanine	<ul style="list-style-type: none"> • May alter brain chemistry through effects on dopamine and serotonin • Small study in dogs showed mild effects at variable doses (approximately 3–5 mg/kg Q 12 H)²⁹ • Naturally found in tea
Lysine	<ul style="list-style-type: none"> • Frequently administered to cats with upper respiratory tract infections (URIs) • A dose of 400 mg/day/cat reduced viral shedding after housing changes³⁰ • Another study which provided a slightly higher dietary intake demonstrated increased severity of URIs, which did not support supplementation for feline URIs³¹
S-adenosyl-methionine (SAM-e)	<ul style="list-style-type: none"> • Contributes to production of glutathione • Most frequently supplemented in cases of hepatic disease • Conditions characterized by oxidative stress may benefit • Chronic liver disease may impair normal production of the substance from methionine³² • Data in dogs and cats is limited²⁰
Taurine	<ul style="list-style-type: none"> • Essential in cats, due to their increased conversion of cysteine to pyruvate for energy as opposed to production of taurine (as in dogs) • Deficiency causes DCM in dogs and cats, and can induce feline central retinal degeneration¹⁴ • Precise cardiac function of taurine is unclear, but some authors suggest, even with normal taurine levels, supplementation in DCM • No reports of toxicity³³

also elevated in many foods and found in joint supplements.

Herbal Supplements

Single and combination herbal products are widely available in human and veterinary markets. Herbs are often subtly sold as drug alternatives, and some may have biologic effects. A brief list of frequently encountered herbs is provided in **Table 5**.

Prebiotics & Probiotics

Gastrointestinal bacteria are increasingly thought to influence health and disease, and numerous veterinary products with ingredients (**Table 6**, page 83) that capitalize on this area of research are now available.

IN SUMMARY

Veterinarians should be prepared to ask about dietary supplements and provide

guidance. Unfortunately, the evidence quality is low and dosing protocols are uncertain for many common dietary supplements.

Veterinarians should ask manufacturers of any recommended products for quality control and efficacy information. Further work is needed for many of the products commonly employed by veterinary professionals and owners. ■

TABLE 4. Common Supplements Used for Osteoarthritis

SUPPLEMENT	SUMMARY
Glucosamine & Chondroitin	<ul style="list-style-type: none"> • Glucosamine is a precursor to glycosaminoglycans, such as chondroitin and hyaluronic acid—critical components in cartilage. • Oral absorption of these products has been demonstrated in dogs; however, clinical effects have been mixed. • If given, owners should be prepared to administer for at least 2 months before making a determination about clinical utility.
Green-Lipped Mussel	<ul style="list-style-type: none"> • It contains omega-3 fatty acids, minerals, and other compounds. • One study found that some owners perceive huge improvements in OA even when dogs are given placebo,³⁷ which questions the validity of anecdotal success.
Methylsulfonylmethane (MSM)	<ul style="list-style-type: none"> • Dietary sulfur compound with unclear mechanisms, but interestingly, dimethyl sulfoxide (DMSO) is metabolized in part to MSM. • Limited evidence of efficacy is available.

TABLE 5. Common Herbal Supplements

HERBAL SUPPLEMENT	SUMMARY
Artemisinin	<ul style="list-style-type: none"> • Reported role in treatment of protozoal diseases and cancer • <i>In vitro</i> study found inhibition of canine osteosarcoma cell lines³⁸ • Clinical efficacy not established, but oral doses are commonly employed
Chinese Herbal Formulas	<ul style="list-style-type: none"> • Yunnan Baiyao, one of the most common formulas in the veterinary market, is a proprietary mixture that increases primary hemostasis through promotion of platelet adhesion and aggregation • Dosage recommendations for acute or chronic hemorrhage are available in Table 7 (page 84) • <i>In vitro</i> study demonstrated some inhibitory effects on canine hemangiosarcoma cell lines; small case series for other herbs are available in the literature³⁹ • Gui Pi Tang has been suggested as a primary thrombopoietic agent⁴⁰ • Concerns about standardization of Chinese herbs are widely disseminated; only one study has examined these issues in veterinary formulae³
Curcumin	<ul style="list-style-type: none"> • May function as an inhibitor of NF-kB • Included as a natural anti-inflammatory in several veterinary OA supplements • <i>In vitro</i> research shows inhibition of all stages of abnormal cell cycle in tumors⁴¹ • In dogs, poorly absorbed from gastrointestinal tract⁴² and may, therefore, be best for gastrointestinal conditions
Milk Thistle	<ul style="list-style-type: none"> • Contains silymarin, a mixture of compounds with possible antioxidant effects, including silybin, which is present in some veterinary products • Milk thistle and derivatives are frequently prescribed for liver disease in dogs and cats • Study of co-administration of silybin and SAM-e (Table 3) with lomustine (CCNU) demonstrated reduced hepatocellular and cholestatic enzyme elevation compared to CCNU alone⁴³ • Study doses were variable but were likely 1 to 2 mg/kg of silybin and 15 to 20 mg/kg of SAM-e
Mushroom Products	<ul style="list-style-type: none"> • Reishi, shiitake, maitake, and coriolus mushrooms have been extensively studied in humans to evaluate medicinal properties⁴⁴ • Many contain immunomodulatory polysaccharides; owners of animals with cancer frequently inquire about their benefits • In a small pilot study, <i>Coriolus versicolor</i> (Yun Zhi) has shown promise in canine hemangiosarcoma through use of a proprietary extracted form (100 mg/kg/day)⁴⁵ • Doses for mushroom products are not well-established

TABLE 6. Common Gastrointestinal Supplement Ingredients

INGREDIENT	SUMMARY
Dietary Fiber	<ul style="list-style-type: none"> Soluble fibers are thought to influence fecal flora and numbers; examples include pectins, beet pulp, and gums. While they have been extensively studied in small animal nutrition, their application in many non-gastrointestinal disease states and optimal doses remain unclear.
Prebiotics	<ul style="list-style-type: none"> Indigestible dietary ingredients, such as fructooligosaccharide (derived from inulin), that selectively stimulate growth of certain intestinal bacteria Frequently discussed in human nutrition
Probiotics	<ul style="list-style-type: none"> Live strains of microorganisms that provide health benefits to the host Likely species-specific; therefore, the use of human probiotics in animals is questionable Most commonly shown to prevent or reduce acute diarrhea^{46,47} Some products are advertised for administration to pets with renal failure Reductions in blood urea nitrogen may be possible if there is increased colonization of bacteria that convert urea to ammonia; however, clinical benefit has not yet been shown Quality control in animal probiotics appears poor⁴⁸

A ROLE FOR ANTIOXIDANTS?

Oxidative stress and decreased antioxidant concentrations are frequently documented in hospitalized patients, but the influence of antioxidant interventions is less clear.^{49,50}

- Vitamins C and E assist in antioxidant support, but Vitamin E has more evidence supporting its use.¹⁴
 - Alpha lipoic acid possesses an antioxidant effect, primarily through reduction of other antioxidants, and is a cofactor in several critical metabolic enzymes within cells.⁵¹
- Co-administration of alpha lipoic acid (11 mg/kg) with acetyl-L-carnitine (27.5 mg/kg) improved cognitive function in older beagles.⁵² In addition, some oncologists report reduced hepatocellular enzyme induction when given concurrently with chemotherapeutics. However, administration in cats should be avoided until additional information is available.

TABLE 7. Anecdotal & Experimental Doses: Common Veterinary Nutraceuticals

CATEGORY	SUPPLEMENT	DOSE PER DAY*
Antioxidants	Vitamin C (ascorbic acid)	50 mg/kg
	Vitamin E (alpha-tocopherol)	10–20 IU/kg
	Alpha lipoic acid	11 mg/kg (dogs only)
Polyunsaturated Fatty Acids	Eicosapentaenoic + docosahexaenoic acids	1–3 mg/calorie
Amino Acids	L-carnitine	50–200 mg/kg
	S-adenosylmethionine	15–20 mg/kg
	Taurine	50 mg/kg
	Glutamine	50–200 mg/kg
	Lysine	400 mg/cat
	L-theanine	3–5 mg/kg Q 12 H
Joint Supplements	Glucosamine	≥ 25 mg/kg
	Chondroitin	≥ 15–20 mg/kg
	MSM	> 10 mg/kg
	Green-lipped mussel	30 mg/kg
Herbal Supplements	Artemisinin	> 4 mg/kg
	Curcumin	5–50 mg/kg
	Silybin or Milk thistle extract	1–2 mg/kg (silybin) or 5–10 mg/kg (extract)
	Yunnan Baiyao	12.5–25 mg/kg Q 6–8 H as needed
	Yun Zhi (<i>C versicolor</i> extract)	100 mg/kg

*Except where noted otherwise

AAFCO = Association of American Feed Control Officials; DCM = dilated cardiomyopathy; DHA = docosahexaenoic acid; EPA = eicosapentaenoic acid; MSM = methylsulfonylmethane; NSAID = nonsteroidal anti-inflammatory drug; OA = osteoarthritis; SAM-e = S-adenosylmethionine; URI = upper respiratory tract infection

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