SUPPLEMENTS: FOR PETS AND PEOPLE!
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The benefits of nutritional supplements, for both people and pets, are increasingly more accepted and understood. It’s another issue, however, to know how to choose amongst the myriad of options (within any given category of supplement) and find the supplement products that offer quality and value.

When assessing a particular nutritional supplement, it is important to be knowledgeable about label information, ingredients, manufacturing information, and whether research or safety and toxicity studies have been conducted. This part of the presentation is intended to help veterinary professionals critically evaluate available supplements in order to educate clients and help them select the best product for their pet.

Is the label easy to understand?

Look closely at the label on a nutritional supplement product to see whether it contains the information necessary to use and store the product appropriately.

The instructions for giving the product should make sense, i.e., either so many tablets per a recommended number of times during the day per patient weight range or so many mg per kg. If the ingredients are in milligrams the recommended amount should also be in milligrams; if the product is a liquid, then the recommended amount should be stated in measures of volume.

The target species for the product should be on the label. If the product is best given on an empty stomach, or preferably with food, those specific instructions should be noted. Storage conditions necessary to preserve stability and activity of ingredients should be easy to find. This might include, for example, recommended environmental temperature ranges and, if applicable, whether exposure to light or humidity must be limited.

Lot numbers are important. In the event of an adverse incident, lot numbers facilitate tracking the original source of the ingredients. An expiration date on a label (as opposed to its absence) gives some credence that the ingredients have been evaluated for duration of activity and/or stability.

• The administration amount and frequency, in addition to target species, proper storage conditions, a lot number, and an expiration date, should be clearly stated on the label.

Are the active ingredients identified on the label?

Some nutritional supplement labels do not list ingredients. It is important that the ingredients that are identified on a product’s label are consistent with those listed in product brochures and marketing materials for that particular supplement. An inconsistency between the product brochure or marketing piece and the product label is problematic and raises concerns as to why an ingredient is mentioned in a brochure but is not listed on the label.

Products may sometimes contain the source material for an active ingredient as opposed to the purified extracted ingredient, or the labeling may not be clear as to
which is present. Differences in absorption and ultimately efficacy may occur between an ingredient present in its purified extracted form and the ingredient present in its unrefined form combined with other ingredients in the source material. An example is the notation of “milk thistle” on a label but not the specification as to whether the milk thistle in the product reflects processing to the ingredient silymarin (and how much silymarin), or preferably, extraction and presence of the most active component of silymarin, i.e., silybin.

- The active ingredients should be identified and quantified on the product’s label.

**Are the ingredients that are listed on the label actually in the supplement?**

“Short changing” (i.e., what is on the label is *not* actually in the bottle) occurs frequently with nutritional supplements. Researchers from the University of Maryland School of Pharmacy analyzed over-the-counter products for people that “claimed” to contain chondroitin sulfate; 84% of the products did not meet label claim. Some of the products had *zero* active ingredient and some that cost $4.00 a day had less than 10% of the label claim (illustrating that paying a lot of money for a supplement does not guarantee label accuracy). The results on over-the-counter products for people are relevant for veterinary clients, as some clients may wish to purchase or may already be purchasing human products for their pets.

Short changing is also likely to occur with products for pets as evidenced in an April 2007 Consumerlab.com report noting 2 of 5 veterinary products tested in the glucosamine-chondroitin sulfate-MSM category that did not meet label claim. Equine products are not immune to the issue of label “in”accuracy. A published evaluation of equine joint health supplements revealed that 9 out of 23 products did not contain labeled amounts of glucosamine with 4 of these products containing less than 30% of the amount claimed on the label.

Even if the ingredients are present in the product, issues of quality and activity should be considered, in the same sense that not all cars are of the same quality and not all cars are equally reliable. For example, an analysis of various chondroitin sulfate raw materials revealed that they were not equally effective in inhibiting the expression of inflammatory mediators.

- The ingredients on the label should not only be guaranteed to be in the bottle but should be verifiable with a finished product analysis using a reproducible method.

**How is the product manufactured?**

Manufacturers should track the product throughout the manufacturing process and use proven (= reproducible) methods for analysis of raw materials *as well as* the final product. An analysis of raw materials alone does not take into account how the product is manufactured and changes that occur during the transition from raw materials to finished product.

Consistency of ingredient content from lot to lot and bottle to bottle should be assured. Without quality controls and consistent standards of manufacturing, end products vary greatly in purity, content, and quality. Proper shipment and storage of
finished products (including humidity and temperature controls) should occur to avoid degradation and exposure to contamination.

The reputation of the manufacturer is a factor when it comes to assessing veracity and quality, i.e. does the manufacturer stand behind its products (ready with replacement or refund if warranted), respond promptly when issues arise, support the veterinary community (with independent veterinary research, sponsorship of continuing education meetings, in-clinic seminars, involvement in non-profits, to name a few), and is there a high comfort level amongst veterinary professionals regarding the purity and safety of a particular manufacturer’s products?

• Quality control programs, from raw materials to finished product, should be in place.

Are there any safety or toxicity studies?

A wide variety of nutritional supplements are considered “natural” but just because something is “natural” does not mean that it is always safe. Mushrooms are “natural” but it’s well known that not all kinds of mushrooms are safe! The presence of harmful levels of contaminants (microorganisms such as bacteria or molds, environmental toxins such as insecticides and pesticides as well as heavy metals such as lead or mercury) in a nutritional supplement can present safety concerns. The purity of a product can be related to adverse reactions or unpleasant consequences.

A nutritional supplement must be evaluated (through safety studies) in terms of its potential for (and frequency of) adverse effects, its effect on laboratory analysis and clinical tests, and its potential to interact with other prescribed treatment regimens. Safety issues should be addressed in the target species, due to species variations in metabolism and tolerance.

• Insist that a product, or at a minimum its ingredients, be evaluated as to safety and the potential for adverse reactions in the target species.

Is there any scientific evidence to support claims?

All claims should be truthful, not misleading, and substantiated by competent and reliable scientific evidence. Many outrageous claims are still made, though, such as “cures arthritis”. It is common for multiple testimonials (often by famous people or individuals mirroring and/or appealing to the target audience) and anecdotal “evidence” to be used to promote products, rather than adherence to scientific data and research. It is important to note that no matter how many testimonials (or how persuasive the people are delivering the testimonials) the plural of testimonial is not data! Scientific research trumps opinion and if something sounds too good to be true, it probably is.

Research should be objective, assuring data and conclusions that can be repeated and substantiated, data that veterinary professionals must proactively seek (in technical journals, medical websites, reference books and from manufacturers of veterinary supplements). Look for studies showing mechanisms of actions as well as seek out additional solid research which might include double-blind, placebo-controlled studies demonstrating efficacy (double-blind means that neither the investigator nor the recipient knows whether the active ingredient or the placebo has been administered to
the recipient, thus the results are not biased with preconceived notions as to whether or not the ingredient under investigation will have effects).

Contact the manufacturer and request copies of research done on a nutritional supplement product that is under consideration for use in practice. If a manufacturer claims to have research, it should be made available. If a manufacturer sends research, the research should have been done on that particular manufacturer’s product or ingredients and not on another company’s product. Look for brand-specific research because there can be no “generic” comparison amongst products that have no benchmark specifications. Each product must stand alone on its own merits.

Nutritional supplements under consideration for use in veterinary patients should ideally have research in the target animal species. Veterinary professionals should support and patronize the companies that sponsor and underwrite independent veterinary research.

Information received should be evaluated for content, scientific basis and quality. Unsubstantiated claims will continue to be made and products without documented benefits will continue to be used unless veterinary professionals insist that nutritional supplements undergo scientific substantiation.

Consider the following recommendation from the Arthritis Foundation, which applies equally to both human and veterinary nutritional supplements:

- “When a supplement has been studied with good results, find out which brand was used in the study, and buy that.”

Is technical support available from the manufacturer?

The manufacturer or supplier of a veterinary nutritional supplement should employ technical staff, which may include veterinarians or veterinary technicians, to answer questions or address concerns. When recommending a product to clients, it is important to make sure that the manufacturer’s contact information is listed on the label.

Be open-minded, but ask lots of questions and proceed with knowledge!

All supplement products should be evaluated for label content and accuracy, the existence of research and safety studies, and the reputation of the manufacturer.

The nutritional supplement products that meet or exceed high standards of quality, value and efficacy will be those that can be wholeheartedly recommended to clients and those that clients will, with your guidance, now be empowered to choose (and use) with confidence!

Highlighting Timely Nutritional Supplements

**Joint Supplements:**

The use of joint supplements (in particular glucosamine, chondroitin sulfate, ASU and long chain Omega-3 fatty acids, EPA and DHA) for dogs and cats to protect joints and to relieve the symptoms of arthritis is now common and well accepted, given the depth and number of independent studies that have built up over many years and that are also
ongoing. Pets may benefit even more if they receive joint supplements early in life, rather than waiting until symptoms of osteoarthritis are already evident. Supplements nourish and protect joint cartilage, maintaining and supporting asymptomatic, healthy joints as well as helping pets with arthritis experience less pain.

**Glucosamine and Chondroitin sulfate**

Glucosamine and chondroitin sulfate have progressed over approximately the last twenty years from initial hesitance to alternative therapy to mainstream medicine for improving joint comfort in dogs and cats and retaining/restoring the balance between destruction and production of cartilage.

Glucosamine benefits the health of joints by “up” regulating cartilage metabolism, stimulating the production of cartilage. Glucosamine is also a long established nutrient for cartilage and the connective tissue associated with the joint.

Chondroitin sulfate not only increases fluidity of the cartilage but also inhibits destructive enzymes (such as aggrecanase, collagenase, and metalloproteinases) and cytokines (inflammatory mediators) that cause considerable damage when elevated and aggravated due to any number of inciting joint issues. Glucosamine and chondroitin sulfate also support and protect the cartilage ahead of an injury (chondroprotection) and facilitate the return to best possible function after an injury.

**Avocado Soybean Unsaponifiables (ASU)**

ASU is an ingredient concentrated directly from avocados and soybeans shown in studies to improve joint function and comfort levels. In vitro studies (studies done in the lab with cartilage cell cultures) have shown that ASU inhibits production of various compounds, called mediators, that are involved in the process of cartilage breakdown (specifically the mediators cyclooxygenase-2 (COX-2), tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), prostaglandin E₂ (PGE₂), and inducible nitric oxide synthase (iNOS)) and that it is at least three times more potent at doing so than chondroitin sulfate.

A specific combination of an exclusive low molecular weight chondroitin sulfate, glucosamine hydrochloride, and avocado soybean unsaponifiables (ASU) has been shown in published research to stimulate cartilage cells to increase production of cartilage matrix components, as well as suppress inflammatory mediators and inhibit degradative enzymes in the joint.

**Long Chain Omega-3 Fatty Acids, EPA and DHA**

The benefits of long chain Omega-3 fatty acids (EPA and DHA) have been well substantiated for organs and systems throughout the body, including the brain, heart,
kidneys, skin and joints. EPA and DHA result in the production of natural anti-inflammatory mediators (known as eicosanoids), which reduce inflammation in joints as well as reduce the clinical symptoms of swelling, heat and pain that characterize inflammation in joints.

**Liver Supplements:**

**S-Adenosylmethionine and Silybin**

S-Adenosylmethionine is an endogenous molecule synthesized by cells throughout the body and is formed from the amino acid methionine and ATP. It is an integral part of three major biochemical pathways: transmethylation, transsulfuration and aminopropylation. As part of these pathways, S-Adenosylmethionine is essential to all cells but is of particular importance to hepatocytes because of their central role in metabolism.

A deficiency of S-Adenosylmethionine in the body, therefore, may initiate or contribute to abnormalities of cellular structure and function in the liver as well as many other body tissues. Conversely, exogenous administration of S-Adenosylmethionine has been shown to result in improvements in hepatocellular function in both in-vivo and in-vitro studies, without cytotoxicity or significant side effects. 1-4

Precursors of S-Adenosylmethionine do not have similar effects. Administration of methionine to animals with compromised liver function may not increase hepatic S-Adenosylmethionine levels and may be toxic.5 The best way to increase S-Adenosylmethionine levels in the body is by direct supplementation with S-Adenosylmethionine.

Trials with a specific veterinary S-Adenosylmethionine product showed that it increased hepatic glutathione levels in cats and dogs. 1,6 Glutathione is a potent antioxidant that protects hepatic cells from toxins and death. A study found that low liver glutathione concentrations are common in dogs and cats with decreased hepatobiliary function.7

S-Adenosylmethionine is recommended to support normal function of the liver, to improve hepatic glutathione levels to help maintain and protect liver function and in cases where liver compromise is suspected. S-Adenosylmethionine may also be used in other areas of tissue oxidant injury and RBC fragility caused by certain toxins or drugs (including acetaminophen) related to reduced glutathione concentrations or compromised metabolic pathways.

Stability issues with S-Adenosylmethionine include getting past the stomach for absorption in the small intestine as well as sensitivity to humidity and air; S-Adenosylmethionine products that have addressed these stability issues are both enteric-coated and blister-packed. Advancements in stability include the ability to coat groups of SAMe molecules and distribute the active component throughout a chewable tablet.
S-Adenosylmethionine products for human use are available in pharmacies and health food stores; however, the quality of these products is not assured due to a lack of standardization in the human dietary supplement industry.  

There are no known interactions between S-Adenosylmethionine and any drug or other dietary supplement. The recommended administration amount for oral use in dogs and cats is 20 mg/kg/day. Pharmacokinetic studies have demonstrated that administration of S-Adenosylmethionine on an empty stomach improves absorption.

Silybin/silymarin has many different mechanisms of action. In-vitro and in-vivo studies have shown that it protects against oxidative stress, promotes hepatocyte protein synthesis (a mechanism for liver cell regeneration), inhibits leukotriene production (which can be beneficial as production of leukotrienes is a component of the inflammatory response), stimulates biliary flow and production of hepatoprotective bile salts (e.g., beta-muricholate and ursodeoxycholate), and increases levels of glutathione (a potent anti-oxidant).

In a study, silybin was shown to be protective in acute Amanita phalloides mushroom poisoning in dogs, (one-third of the untreated dogs died, while all dogs in the silybin-group lived). Silybin-group dogs also had lower bilirubin, AST, ALT, and ALP levels and improved prothrombin times compared to control dogs. In another report, the liver enzymes improved in five out of six dogs with 30 days of silymarin administration.

Silybin and silymarin have low bioavailability. Silybin, when complexed with soybean phosphatidylcholine, results in superior absorption and bioavailability compared to silymarin or silybin administration alone (see graph). Studies in rats showed that administration of the silybin/phosphatidylcholine complex was capable of reaching effective intracellular levels in liver microsomes not achieved with silybin administration alone.

There are no known drug interactions or contraindications to the use of silymarin/silybin in animals. While mild side effects, such as gastrointestinal upset, itching and headache, have been rarely reported in primates, no side effects have been noted in dogs. The specific silybin-phosphatidylcholine complex in one veterinary product* has been evaluated in both acute and chronic use safety studies: an acute toxicity study in dogs using levels greater than 80x the amount in the aforementioned veterinary product* revealed no adverse physiologic effects, and a chronic toxicity study in monkeys who received greater than 80x the amount in this product* for 26 weeks showed no compound-related adverse effects.

**Supplements are “For Life”!**

Advocacy for the benefits of nutritional supplements (those with proven safety, absorption, stability, label accuracy and research to back up claims) as well as education of the owner of how to choose products that offer quality and value are a part
of maintaining health and prevention of disease. Veterinary professionals can also advise a pet owner about the specific use of nutritional supplements for identified issues such as joint issues, liver conditions and overall wellness.

The benefits of nutritional supplements are becoming better understood and accepted; clients are asking about them in increasing frequency. As part of an overall regimen supporting health, the incorporation of quality nutritional supplements as adjunctive therapy can assist with the best outcome for the patient as well as the happiness of both the owner and pet.

References available upon request