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Lauren Chattigré, DVM, DVetHom, CVA, CVCP
Cascade Summit Animal Hospital, 22320 Salamo Road, West Linn, OR 97068
Phone: 503-655-1722. Fax: 607-0136

Nutraceuticals

The term *nutraceutical* is a combination of *nutrition* and *pharmaceutical*. Initially coined in the 1980s referring to compounds that were neither nutrients nor pharmaceuticals, it has no single official definition. One of the more narrow definitions includes any non-toxic food component that has scientifically proven health benefits, including disease treatment or prevention. Looser definitions include any purified or extracted substance given orally to improve general health and well-being. Commonly used nutraceuticals include vitamins, minerals, amino acids and their derivatives (e.g. SAMe, glutamine), herbs, concentrated greens (e.g. barley, algae), colostrum, glycosaminoglycans, probiotics, glandulars, and fatty acids. Many such ingredients have proven themselves in multiple studies (e.g. the benefits of omega-3 fatty acids in cases of heart disease). In veterinary care, the term nutraceutical is often reserved for supplements used to assist in treating specific disease processes, while products used for general well-being are simply referred to as nutritional supplements or functional foods. Nutraceuticals are used commonly by most veterinarians these days, but it's not always possible to influence where clients obtain those products. Many clients would rather buy generic glucosamine, rather than purchase Cosequin or SynoviG3. And many veterinarians don't know enough about nutraceutical manufacturing to confidently educate clients about the cautions of over-the-counter products.

Regulation of the nutraceutical industry primarily involves self-management with FDA oversight. The FDA, which considers nutraceuticals for human consumption under the general heading of nutritional supplements, has established regulations for Current Good Manufacturing Practices (CGMPs) to ensure quality production and accurate labeling, but does not inspect facilities unless they are alerted to a potential problem. Their CGMPs Final Rule for Dietary Supplements became effective in June 2007; there is a three year phase-in for small businesses. The rule requires manufacturers to evaluate the identity, purity, strength, and composition of all ingredients contained in any given product and to accurately label all active and inactive ingredients. The rule contains provisions related to the design, construction, maintenance, and staffing of manufacturing facilities, quality control procedures, product testing, handling of consumer complaints, and record-keeping. While this is a step in the right direction, it is far from the CGMPs observed for drugs. There is also no requirement for labeling of potential side effects. With the FDA's limited resources, it focuses first on public health emergencies and products that have caused harm, second on products that may be unsafe or fraudulent, and lastly on products pulled from store shelves and other routine investigations. It is their responsibility to go after illegal (unsafe or fraudulent) products that are already out there, not to provide approval or oversight to products heading out to market. The only time a manufacturer must demonstrate safety to the FDA is when introducing a new dietary ingredient (NDI) to market, which includes any new ingredient not in use prior to October 1994; however, there is no authoritative list of preapproved ingredients.

It is important to note that nothing in the FDA’s Final Rule applies to veterinary nutraceuticals. Nutritional supplements for animals do not have their own legal status like those for humans. They are considered under the umbrella of animal feeds and feed additives, requiring only that they be generally regarded as safe (GRAS). As proof of safety can be a difficult process, demonstration of low risk based on adverse event reporting data is considered acceptable. Many ingredients used in veterinary nutraceuticals have not received official GRAS status, however, and are considered technically illegal by the FDA. Veterinarians may therefore wish to note informed consent

from clients in their medical charts, but should not be overly concerned about legal status as the problem is industry-wide. Despite more extensive regulations for human nutraceuticals, clients should be reminded that use of reliable veterinary products is still preferred since they are designed and dosed with the unique needs of animals in mind. Small animals are not small humans, and each species has its own response to particular ingredients.

Since the FDA does not require proof of nutraceutical safety or efficacy prior to market (as is required for drugs), nor are manufacturers legally required to report adverse events associated with their products, it's no surprise that numerous problems go undetected. (The FDA does not even maintain a registry of nutraceutical manufacturers.) Several independent studies have discovered serious problems with many nutraceuticals. On the human side, one study found deviations from label claims for chondroitin sulfates in nine of eleven products tested. Another study on prenatal vitamin tablets found that two thirds did not dissolve (resulting in poor bioavailability). Yet another study on 136 brands of calcium supplements found 67% with unacceptably high lead levels. On the animal side, a study evaluating six glucosamine and/or chondroitin products found that no chondroitin sulfate existed in two pet supplements despite the label assurance of a guaranteed analysis. It has also been found that the chronic use of creatine by human athletes may result in toxic levels of its aldehyde metabolites, but no such warning is required on product labels.

In recent years, non-governmental groups have been formed to combat these problems. The NASC (National Animal Supplement Council) was formed in 2001 - several years before the FDA's Final Rule - by concerned U.S. suppliers of animal products to create guidelines and standards for nutraceutical production. Members who receive the NASC seal of approval have successfully completed a facility audit, and must adhere to high quality standards and written quality procedures, maintain an adverse event reporting system, follow proper label guidelines, and include any cautionary statements recommended by the FDA's Center for Veterinary Medicine and the NASC Scientific Advisory Committee. Compliance is verified through a Member Accountability Contract along with independent audits. The NASC works in close cooperation with the FDA and AAFCO, and provides the FDA with risk management data for all its members' product ingredients. Members are also instructed to register their products and facilities with the FDA. The NASC's website, www.nasc.cc, lists member information.

A well-known independent group which tests both human and animal nutraceuticals for label accuracy and toxic contaminants is Consumer Laboratory, which offers its seal of validation for products that pass their analysis. Subscription to their website, www.consumerlabs.com, provides access to information on products they've tested including reasons for pass/failure. Consumer Laboratory's techniques and tactics have come under scrutiny, however, and the reliability of their reports has been questioned by industry experts. An important issue is the variability of testing methods used by different laboratories, each of which can produce different results. Only recently was a standardized test agreed upon for chondroitin. Some ingredients like flavorings can also affect results, and others may not be testable for lack of a specific analyte. While ingredient testing is important, the ultimate sign of good manufacturing is the presence of a complete quality control system.

Doctors and consumers should look for several things in selecting a nutraceutical, especially those not approved by a reliable independent organization. The label should include a descriptive product name stating that it is a supplement, a lot number and expiration date, the manufacturer's information, a full listing of ingredients in order of magnitude by weight, and a listing of non-active ingredients. Labels that state "special blend" and refuse to list individual ingredients are suspect, as there is no way to research potential effects on patients with specific cautionary conditions or to determine what may have caused a particular side effect. Nutraceuticals should not make specific drug claims (e.g. "for the prevention and treatment of arthritis") unless appropriately tested and approved as a drug, but rather simply state what body functions/structures

are supported (e.g. "supports normal joint function"). By law, human nutraceutical product labels and marketing materials can make three types of claims: health claims, structure/function claims, and nutrient content claims. This can include describing the link between an ingredient and a particular health-related condition. Different requirements apply to each type of claim. Any structure/function claim (describing an intended effect of the nutraceutical on body structure or function) must be accompanied by the following disclaimer: "This statement has not been evaluated by the FDA. This product is not intended to diagnose, treat, cure, or prevent any disease." There is no such law for claims made by veterinary nutraceuticals, again because they lack their own FDA category. Claims are, however, expected to be substantiated and truthful. Consumers should be suspicious of products making very extensive or extreme claims.

To help ensure the quality of nutraceutical formulations, consumers can ask if the manufacturer follows USP (United States Pharmacopeia) specifications. This non-governmental organization has set standards for most nutritional supplements regarding potency (what is on the label is in the product), disintegration (the product will dissolve in a time normal for digestion), and uniformity (each tablet or capsule is the same throughout the bottle and lot). Consumers can also ask if the company follows CGMP standards for drug grade rather than just food grade products. And if the product is sold in Canada or Australia where governmental regulation and investigation are routine, proof of inspection can be requested.

Beyond ensuring quality production and labeling, there is the more elusive question of efficacy. While a company approved by an organization like the NASC is more likely to have adequately researched the appropriateness of their formulations, there's no guarantee. Companies that employ the services of a certified nutritionist, herbalist, or other trained professional to select synergistic ingredients in the right proportions are more likely to create effective formulations. Consumers should ask for information regarding who designs the formulations, and if the product is widely used by health care professionals. Products that have been used with good results repeatedly in a veterinary setting are more reliable than those without a clinical track record. Finally, if any studies have been conducted the manufacturer should be able to provide information on how the study was conducted (in vitro or in vivo, species tested, control groups, peer-reviewed) and if minimum effective and maximum safe dosages were established. In the end, clients must gauge how the nutraceutical has affected their pet and should be encouraged to keep a diary to record subtle changes throughout an adequate trial period.