Commonly used Orthomolecular Nutraceuticals in Veterinary Practice

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Introduction to Nutraceuticals

- The term nutraceuticals is used for compounds given orally that are legally considered neither food nor drug
- There are a wide variety of nutraceuticals, including essential nutrients that are given in supraphysiological doses, for example selenium and vitamin E
- extracted food compounds taken for medical purposes such as fish oils, botanicals and phytochemicals, and prebiotics

Definition of Nutraceuticals

- The **North American Veterinary Council** has defined a **nutraceutical** as: a non-drug substance which is produced in a purified or extracted form and is administered orally to a patient to provide agents required for normal body structure and function and administered with the intent of improving the health and wellbeing of animals
- Foods which provide health benefits are sometimes called **functional foods**, and these are included with nutraceuticals

Botanicals and Phytochemicals

- What are botanicals and phytochemicals?
- **Botanicals** are medicines of plant origin, including herbs such as ginkgo biloba
- **Phytochemicals** are the chemicals extracted from plants
- The active ingredients may include volatile oils such as those in catnip, garlic and citrus, and also non-volatile oils, resins, alkaloids and glycosides
- These may be labelled with a herb name rather than the drug name, such as guarana for caffeine

Introduction to Nutraceuticals

- How often are nutraceuticals used for cats and dogs?
- These novel products are very popular; it has been estimated that nearly 30% of pet owners have used or considered the use of novel ingredients for their pets
- However, up to 70% of people who use herbal remedies themselves do not report them to their doctors, and it's likely that pet owners also don't mention the use of nutraceuticals when asked about drug therapy for their pet
- The number of people using these products for themselves and their pets has probably grown as more people become familiar with these products

Are nutraceuticals safe?

- Because herbs and other novel ingredients are often perceived as natural, many people feel that they are safe and that they are a milder intervention than drugs; however, amanita mushrooms are also natural, and are highly deadly
- There are potential interactions with herbs and other medications that can result in adverse effects, such as a combination of ginger and aspirin resulting in prolonged bleeding times

Are nutraceuticals safe?

- Many of our current drugs are originally derived from plants, for example, digoxin was originally derived from the foxglove plant, so the potential effects and toxicity of these products should not be underestimated

How are nutraceuticals regulated?

- To become licensed, regular medical drugs must undergo rigorous safety and efficacy testing; however, nutraceuticals do not have the same requirements
- Labelling of licensed medications is highly regulated to ensure that the labelling reflects the contents of the package; nutraceuticals do not have these same regulations either
- A study has shown mislabelling in 84% of the nutraceutical products studied
- The amount of mislabelling ranged from there being no actual product in the package to 115% of the stated product in the package

How are nutraceuticals regulated?

- Cheaper products were more likely to be seriously deficient, suggesting that they should probably be avoided, although some of the more expensive products were also mislabelled.
- As they are not tested and licensed as drugs, these agents may not claim to treat or prevent disease, and they are usually marketed as ‘supporting health’
- The lack of regulations and guidelines should lead to caution in the use of these products
- Some products have been tested and used extensively, but veterinary professionals should ask questions about the testing of safety and efficacy of new products before using them

How are doses determined?

- Determining appropriate dosing for medications involves knowledge of the pharmacokinetics, or how the drug is absorbed, distributed within, and excreted from the body
- With compounds such as herbs, there may be hundreds of active ingredients, making this process challenging
- Determination of efficacy of the products requires measurable outcomes

How are doses determined?

- A few studies in nutraceuticals have been done to try to measure outcomes, and more scientific evidence is becoming available about some of the products
- However, most nutraceutical dosages are empirical, which means we dose with our best guess, as there are insufficient data on the efficacious dose

How are doses determined?

- In addition, the absorption, metabolism and excretion of products differ among species, so that the extrapolation from one species to another may be incorrect or unsafe
- For example, lipoic acid has been used as an antioxidant in dogs, but is very dangerous to use in cats

What nutraceuticals are used in veterinary medicine?

- Chondroprotective agents
- Omega-3 fatty acids
- Antioxidants
- Prebiotics and Probiotics
- Botanicals
  - Organ or system-specific
- Phytochemicals
  - Organ or system-specific
- Complex Botanical Formulae
  - Typical of TCVM

Safety Concerns in Non-humans?

- Generally, those nutraceutical agents that are safe for oral human use are safe at similar doses for our canine companions
- However, our feline friends have a relatively ineffective system of Phase II liver conjugation enzymes compared with dogs and humans
- This system is less effective at eliminating certain “toxic” molecules from the cat’s body
- For example, acetaminophen is toxic to cats
- And acetylsalicylic acid (aspirin) is safe in cats, but only 80 mg/adult cat every 72-96 hours!

Safety Concerns in Non-humans?

- Other substances may be unsafe for non-human consumption based upon "toxic" effects in the body, although there is no way to predict this *a priori*
- For example, onions are toxic to both cats (causes Heinz body anemia) and to horses (causing a type of liver damage)
- So, use caution if attempting to utilize "new" or previously untested nutraceuticals or botanicals with our furry friends

Chondroprotective Agents

- The chondroprotectants, such as glucosamine and chondroitin sulphate, are the precursors of cartilage and are used to support cartilage synthesis in companion animals with osteoarthritis
- These agents may also be used to prevent or slow the degradation of cartilage in animals at risk such as giant dog breeds, large equine athletes, and athletic performance animals in general

Anti-inflammatory and chondroprotective effects of nutraceuticals from Sasha's Blend in a cartilage explant model of inflammation

Mol Nutr Food Res. 2007 Aug;51(8):1020-30.
Pearson W, Orth MW, Karrow NA, Maclusky NJ, Lindinger MI.

Source

Department Biomedical Sciences, Ontario Veterinary College, University of Guelph, Guelph, ON, Canada N1G 2W1. wpearson@cantox.com

Abstract

- New Zealand green lipped mussel (NZGLM), abalone (AB), and shark cartilage (SC) are extensively used for treatment of and/or as preventatives for arthritis, despite a relative paucity of scientific evidence for efficacy
- This research integrated a simulated digestion protocol with ultrafiltration and cartilage explants to generate new information on the anti-inflammatory and chondroprotective properties of NZGLM, SC, and AB

Anti-inflammatory and chondroprotective effects of nutraceuticals from Sasha's Blend in a cartilage explant model of inflammation

- Each nutraceutical was artificially digested using simulated gastric and intestinal fluids, and the crude digest was ultrafiltered (50 kDa)
- Each filtrate was applied individually to cartilage explants before the explants were stimulated with IL-1 to induce an acute inflammatory response
- Media were collected daily for 48 h and analyzed for prostaglandin E(2) (PGE(2)), glycosaminoglycan (GAG), and nitric oxide (NO), and cartilage tissue was differentially stained to determine the relative proportion of live and dead cells

Anti-inflammatory and chondroprotective effects of nutraceuticals from Sasha's Blend in a cartilage explant model of inflammation

- SC and NZGLM significantly inhibited IL-1-induced PGE(2) synthesis and IL-1-induced GAG release, and AB was an effective inhibitor of IL-1-induced NO production
- The three test nutraceuticals affect at least three major pathways involved in the catabolic cycle of arthritis and may prove important treatments and/or preventatives for the pain and degradation associated with this condition
- The methodology and results describe a useful model for evaluating dietary nutraceuticals in vitro

Protective effect of the chondroprotective agent Cosequin DS on bovine articular cartilage exposed in vitro to nonsteroidal antiinflammatory agents

- Vet Ther. 2002 Summer;3(2):128-35.
- Lippiello L, Han MS, Henderson T.
- **Source**
- Nutramax Laboratories, Inc., Edgewood, MD 21040, USA.
- **Abstract**
- Studies were conducted to test the hypothesis that exposure of articular cartilage to a combination of the "chondroprotective" agents glucosamine hydrochloride, low-molecular-weight chondroitin sulfate, and manganese ascorbate (Cosequin DS [CDS], Nutramax Laboratories, Inc.) prevents the potentially adverse effects of NSAIDs on cartilage
- Articular cartilage proteoglycan synthesis and degradation were used to monitor in vitro cartilage activity following timed exposure to levels of NSAIDs routinely applied in veterinary medicine

Protective effect of the chondroprotective agent Cosequin DS on bovine articular cartilage exposed in vitro to nonsteroidal antiinflammatory agents

- Etodolac exposure for 144 hours induced significant inhibition of cartilage matrix synthesis and increased the rate of matrix breakdown
- Addition of CDS reversed both activities. Cartilage metabolism was not affected by exposure to indomethacin and remained responsive to CDS with an increase in synthetic activity
- Aspirin significantly stimulated chondrocyte synthetic activity in the presence and absence of CDS
- Carprofen at therapeutic levels had a mild (15%) stimulatory effect on cartilage metabolism and reduced matrix breakdown

Protective effect of the chondroprotective agent Cosequin DS on bovine articular cartilage exposed in vitro to nonsteroidal antiinflammatory agents

- Addition of CDS significantly accelerated (30%) matrix synthesis
- At higher levels carprofen was toxic, reducing cell activity by 80%
- The data suggest that CDS may be a useful adjunct therapy for preservation of articular cartilage by reversing the adverse metabolic effects of etodolac and providing accelerated cartilage synthetic activity in the presence of therapeutic levels of carprofen

Omega-3 Fatty Acids

- Modern research on Omega-3 fatty acids has revealed that their supplementation in a human or non-human diet may have many diverse and positive benefits
- Fatty acids have been found to have ratios in domestic animal tissues that is dominated by Omega 6's and Omega 9's relative to their wild relatives
- Omega 3 fatty acid supplementation helps to normalize these ratios to the non-domestic type

Omega-3 Fatty Acids

- Omega 3 fatty acids have an ever-increasing role to play in many of the body's metabolic pathways
- Forms of Omega 3 fatty acids vary and have variable biological availability in non-humans
- For carnivores, it seems that plant-based Omega 3 fatty acids need to be fed at much higher doses than animal-based products

Responses of dogs to dietary omega-3 fatty acids

- J Am Vet Med Assoc. 2007 Dec 1;231(11):1657-61.
- Bauer JE.
- **Source**
- Department of Small Animal Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX 77843-4474, USA.
- **Abstract**
- Long-chain omega-3 fatty acids from fish oil and other marine sources appear to be capable of modifying inflammatory and immune responses in dogs
- Information is provided on the capacity of dogs to metabolize omega-3 fatty acids and the effects of omega-3 fatty acids on skin and coat, inflammatory responses, and neurologic development in puppies

Effect of a diet enriched with green-lipped mussel on pain behavior and functioning in dogs with clinical osteoarthritis

Can J Vet Res. 2013 Jan;77(1):66-74. Rialland P, Bichot S, Lussier B, Moreau M, Beaudry F, del Castillo JR, Gauvin D, Troncy E.

Source

Research Group in Animal Pharmacology of Quebec (GREPAQ), Department of Veterinary Biomedicine, Faculty of Veterinary Medicine, Université de Montréal, PO Box 5000, St-Hyacinthe, Quebec J2S 7C6, Canada.

Abstract

This study aimed to establish the effect of a diet enriched with green-lipped mussel (GLM) on pain and functional outcomes in osteoarthritic dogs

Twenty-three client-owned dogs with osteoarthritis (OA) were fed a balanced control diet for 30 d and then a GLM-enriched balanced diet for the next 60 d

We assessed peak vertical force (PVF), which is considered to be the gold standard method, at Day (D)0 (start), D30 (end of control diet), and D90 (end of GLM-enriched diet)

The owners completed a client-specific outcome measure (CSOM), which is a pain questionnaire, once a week

Effect of a diet enriched with green-lipped mussel on pain behavior and functioning in dogs with clinical osteoarthritis

- Motor activity (MA) was continuously recorded in 7 dogs for 12 wk
- Concentrations of plasma omega-3 fatty acids were quantified as indicative of diet change
- Statistical analyses were linear-mixed models and multinomial logistic regression for repeated measures
- The GLM diet (from D30 to D90) resulted in an increase in concentrations of plasma omega-3 fatty acids ($P < 0.016$) and improvement of PVF ($P = 0.003$)

Effect of a diet enriched with green-lipped mussel on pain behavior and functioning in dogs with clinical osteoarthritis

- From D0 to D30, PVF did not significantly change ($P = 0.06$), which suggests that the GLM diet had a beneficial effect on gait function
- Moreover, PVF ($P = 0.0004$), CSOM ($P = 0.006$), and MA ($P = 0.02$) improved significantly from D0 to D90
- In general, the balanced control diet could have contributed to reduced OA symptoms, an effect that was subsequently amplified by the GLM diet

Biological effects of short-term salmon oil administration, using distinct salmon oil sources in healthy dogs

- J Small Anim Pract. 2012 Dec;53(12):699-704. doi: 10.1111/j.1748-5827.2012.12000.x.
- Hesta M, Verbrugghe A, Gulbrandsen KE, Christophe A, Zentek J, Hellweg P, Janssens GP.
- **Source**
- Laboratory of Animal Nutrition, Ghent University, Merelbeke, Belgium.
- **OBJECTIVES:**
- To assess the short-term effects of feeding distinct salmon oil sources in healthy dogs

Biological effects of short-term salmon oil administration, using distinct salmon oil sources in healthy dogs

- **METHODS:**
- A diet containing chicken fat as major fat source was fed to 17 dogs for 14 days
- For the next 14 days, dogs received one of two diets, both with 1% of chicken fat exchanged for 1% salmon oil; Norwegian or Scottish salmon oil, harvested using a distinct procedure
- Finally, all dogs were fed chicken fat again for 14 days
- **RESULTS:**
- Salmon oil increased serum phospholipid total n-3 polyunsaturated fatty acids, eicosapentaenoic and docosahexaenoic acid and decreased total n-6 polyunsaturated fatty acids and n-6:n-3

Biological effects of short-term salmon oil administration, using distinct salmon oil sources in healthy dogs

- The phospholipid fatty acid profile returned to initial values within 2 weeks of discontinuing salmon oil administration
- Blood coagulation, acute phase response and plasma immunoglobulin concentrations were not affected by salmon oil and no differences were detected for the measured indices between the two salmon oils
- **CLINICAL SIGNIFICANCE:**
- Low-dose salmon oil administration alters serum phospholipid fatty acid profile within 2 weeks, but without affecting selected immunologic and coagulation indices
- Salmon oil sources from different sources and harvested using a distinct procedure did not induce different effects, most probably because of their similar fatty acid profiles

Potential adverse effects of omega-3 Fatty acids in dogs and cats

J Vet Intern Med. 2013 Mar-Apr;27(2):217-26. doi: 10.1111/jvim.12033. Epub 2013 Jan 16. Lenox CE, Bauer JE.

Source

Gulf Coast Veterinary Specialists, Houston, TX 77027, USA. drlenox@gcvs.com

Abstract

Fish oil omega-3 fatty acids, mainly eicosapentaenoic acid and docosahexaenoic acid, are used in the management of several diseases in companion animal medicine, many of which are inflammatory in nature

Potential adverse effects of omega-3 Fatty acids in dogs and cats

- This review describes metabolic differences among omega-3 fatty acids and outlines potential adverse effects that may occur with their supplementation in dogs and cats with a special focus on omega-3 fatty acids from fish oil
- Important potential adverse effects of omega-3 fatty acid supplementation include altered platelet function, gastrointestinal adverse effects, detrimental effects on wound healing, lipid peroxidation, potential for nutrient excess and toxin exposure, weight gain, altered immune function, effects on glycemic control and insulin sensitivity, and nutrient-drug interactions

Antioxidants

- Anti-oxidants are used to decrease the damaging effects of free radicals and reactive oxygen species
- Most data suggest that a balance of antioxidants is more important than any single antioxidant
- Many of these products are used as adjunct treatment for hepatic disorders

The natural activities of cells, the role of reactive oxygen species, and their relation to antioxidants, nutraceuticals, botanicals, and other biologic therapies

- Vet Clin North Am Small Anim Pract. 2004 Jan;34(1):39-66.

- Mandelker L.
- **Source**
- Community Veterinary Hospital, 1631 W. Bay Drive, Largo, FL 33770, USA. lestervet2@aol.com

- **Abstract**
- There have been remarkable advances in molecular and cell biology that define the mechanisms of how various supplements function in and around cells
- Current evidence strongly supports the probability that cellular functions and cellular responses that pertain to inflammation, disease, and life and death activity can be modulated with supplementation; however, the complexity of each individual's reaction and the vast differences in physiologic influences makes clinical research difficult in regard to clinical studies using antioxidant and biologic therapies

The natural activities of cells, the role of reactive oxygen species, and their relation to antioxidants, nutraceuticals, botanicals, and other biologic therapies

- Not enough is known specifically about each supplement and its interactions with cells, nor is enough understood about how the body compensates or reacts to such applications
- What works well in one individual or species might work differently in another

The natural activities of cells, the role of reactive oxygen species, and their relation to antioxidants, nutraceuticals, botanicals, and other biologic therapies

- In addition, not all antioxidants are created equally, and discrepancies in purity and absorption can occur
- It must also be determined whether or not less than optimum levels or infrequent usage will produce the same physiological effects
- Not everyone--nor every species of animal--responds in the same manner to supplements, which might account for the variations in clinical research

The natural activities of cells, the role of reactive oxygen species, and their relation to antioxidants, nutraceuticals, botanicals, and other biologic therapies

- The cellular effects of antioxidants and other supplements are well defined and meaningful, and their clinical application looks promising despite individual variations
- Combinations of antioxidants are synergistic and support cellular functions, effects that are often not apparent with individual agents

The natural activities of cells, the role of reactive oxygen species, and their relation to antioxidants, nutraceuticals, botanicals, and other biologic therapies

- Such combinations offer a variety of mechanisms for reducing oxygen metabolites in tissues, altering signaling pathways, and modulating transcription factors, and they might play key roles in reducing the damage afforded by ROS
- It is the author's opinion that combinations of antioxidants are best suited for clinical application in modulating disease and reducing premature aging when caused by excessive free radical accumulation
- Clinicians should approach clinical application of these supplements based on the best available scientific research and species-specific information available

Prebiotics and Probiotics

- Prebiotics and probiotics are used for support of gastrointestinal health
- **Probiotics** are the naturally-occurring bacteria in each species that generally are inhabitants of the large bowel
- **Probiotics** have been shown to have a number of important functions, from normalizing immune system function, to protecting against renal disease

Prebiotics and Probiotics

- Prebiotics and probiotics are used for support of gastrointestinal health
- **Prebiotics** are the substances which maintain normal and stable populations of probiotic bacteria in the bowel: they feed probiotic bacteria
- **Prebiotics** are generally insoluble and partially insoluble fibres that are not digested in the small intestine
- FOS's or fructooligosaccharides are one example

Feline gastrointestinal microbiota

- Anim Health Res Rev. 2012 Jun;13(1):64-77. doi: 10.1017/S1466252312000060.
- Minamoto Y, Hooda S, Swanson KS, Suchodolski JS.
- **Source**
- Gastrointestinal Laboratory, Texas A and M University, 4474 TAMU, College Station, TX 77843-4474, USA.
- **Abstract**
- The close relationship between gastrointestinal (GI) microbiota and its host has an impact on the health status of an animal that reaches beyond the GI tract
- A balanced microbiome stimulates the immune system, aids in the competitive exclusion of transient pathogens and provides nutritional benefits to the host

Feline gastrointestinal microbiota

- With recent rapid advances in high-throughput sequencing technology, molecular approaches have become the routinely used tools for ecological studies of the feline microbiome, and have revealed a highly diverse and complex intestinal ecosystem in the feline GI tract
- The major bacterial groups are similar to those found in other mammals, with Firmicutes, Bacteroidetes, Actinobacteria and Proteobacteria constituting more than 99% of intestinal microbiota

Feline gastrointestinal microbiota

- Several nutritional studies have demonstrated that the feline microbiota can be modulated by the amount of soluble fibers (i.e., prebiotics) and macronutrients (i.e., protein content) in the diet
- Initial clinical studies have suggested the presence of a dysbiosis in feline inflammatory bowel disease (IBD)

Feline gastrointestinal microbiota

- Recently, metagenomic approaches have attempted to characterize the microbial gene pool
- However, more studies are needed to describe the phylogenetic and functional changes in the intestinal microbiome in disease states and in response to environmental and dietary modulations
- This paper reviews recent studies cataloging the microbial phylotypes in the GI tract of cats

Companion animals symposium: microbes and gastrointestinal health of dogs and cats

J Anim Sci. 2011 May;89(5):1520-30. doi: 10.2527/jas.2010-3377. Epub 2010 Nov 12. Suchodolski JS.

Source

Gastrointestinal Laboratory, Department of Small Animal Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX 77843-4474, USA. jsuchodolski@cvm.tamu.edu

Abstract

- Recent molecular studies have revealed complex bacterial, fungal, archaeal, and viral communities in the gastrointestinal tract of dogs and cats
- More than 10 bacterial phyla have been identified, with Firmicutes, Bacteroidetes, Proteobacteria, Fusobacteria, and Actinobacteria constituting more than 99% of all gut microbiota
- Microbes act as a defending barrier against invading pathogens, aid in digestion, provide nutritional support for enterocytes, and play a crucial role in the development of the immune system

Companion animals symposium: microbes and gastrointestinal health of dogs and cats

- 0f significance for gastrointestinal health is their ability to ferment dietary substrates into short-chain fatty acids, predominantly to acetate, propionate, and butyrate
- However, microbes can have also a detrimental effect on host health
- Specific pathogens (e.g., Salmonella, Campylobacter jejuni, and enterotoxigenic Clostridium perfringens) have been implicated in acute and chronic gastrointestinal disease

Companion animals symposium: microbes and gastrointestinal health of dogs and cats

- Compositional changes in the small intestinal microbiota, potentially leading to changes in intestinal permeability and digestive function, have been suggested in canine small intestinal dysbiosis or antibiotic-responsive diarrhea
- There is mounting evidence that microbes play an important role in the pathogenesis of canine and feline inflammatory bowel disease (IBD)
- Current theories for the development of IBD favor a combination of environmental factors, the intestinal microbiota, and a genetic susceptibility of the host

Companion animals symposium: microbes and gastrointestinal health of dogs and cats

- Recent studies have revealed a genetic susceptibility for defective bacterial clearance in Boxer dogs with granulomatous colitis
- Differential expression of pathogen recognition receptors (i.e., Toll-like receptors) were identified in dogs with chronic enteropathies
- Similarly to humans, a microbial dysbiosis has been identified in feline and canine IBD

Companion animals symposium: microbes and gastrointestinal health of dogs and cats

- Commonly observed microbial changes are increased Proteobacteria (i.e., Escherichia coli) with concurrent decreases in Firmicutes, especially a reduced diversity in Clostridium clusters XIVa and IV (i.e., Lachnospiraceae, Ruminococcaceae, Faecalibacterium spp.)
- This would indicate that these bacterial groups, important short-chain fatty acid producers, may play an important role in promoting intestinal health

Metabolic diseases and pro- and prebiotics: Mechanistic insights

- Nutr Metab (Lond). 2012 Jun 19;9(1):60. doi: 10.1186/1743-7075-9-60. Nakamura YK, Omaye ST.

- **Source**

- Department of Agriculture, Nutrition, and Veterinary Sciences, University of Nevada Reno, Reno, NV, 89557, USA. omaye@unr.edu.

- **Abstract**

- Metabolic diseases, such as obesity and type 2 diabetes, are world-wide health problems
- The prevalence of metabolic diseases is associated with dynamic changes in dietary macronutrient intake during the past decades

Metabolic diseases and pro- and prebiotics: Mechanistic insights

- Based on national statistics and from a public health viewpoint, traditional approaches, such as diet and physical activity, have been unsuccessful in decreasing the prevalence of metabolic diseases
- Since the approaches strongly rely on individual's behavior and motivation, novel science-based strategies should be considered for prevention and therapy for the diseases

Metabolic diseases and pro- and prebiotics: Mechanistic insights

- Metabolism and immune system are linked
- Both overnutrition and infection result in inflammation through nutrient and pathogen sensing systems which recognize compounds with structural similarities
- Dietary macronutrients (fats and sugars) can induce inflammation through activation of an innate immune receptor, Toll-like receptor 4 (TLR4)
- Long-term intake of diets high in fats and meats appear to induce chronic systemic low-grade inflammation, endotoxicity, and metabolic diseases

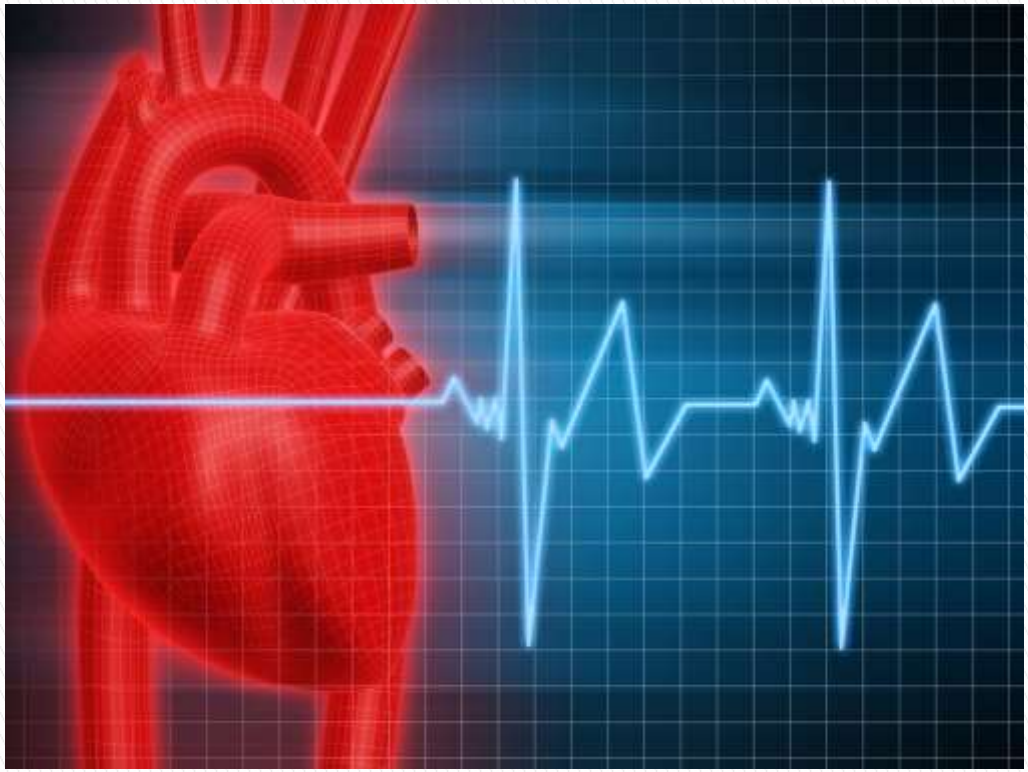
Metabolic diseases and pro- and prebiotics: Mechanistic insights

- Recent investigations support the idea of the involvement of intestinal bacteria in host metabolism and preventative and therapeutic potentials of probiotic and prebiotic interventions for metabolic diseases
- Specific intestinal bacteria seem to serve as lipopolysaccharide (LPS) sources through LPS and/or bacterial translocation into the circulation due to a vulnerable microbial barrier and increased intestinal permeability and to play a role in systemic inflammation and progression of metabolic diseases

Metabolic diseases and pro- and prebiotics: Mechanistic insights

- This review focuses on mechanistic links between metabolic diseases (mainly obesity and type 2 diabetes), chronic systemic low-grade inflammation, intestinal environment, and nutrition and prospective views of probiotic and prebiotic interventions for the diseases

Botanicals



Organ Specific

System Specific

Renal disease in small animals: a review of conditions and potential nutrient and botanical interventions

- Altern Med Rev. 2001 Sep;6 Suppl:S46-61. Pollen SM.
- **Source**
- Coleman Animal Healing Center, 631 W. Clark St., Pasco, Washington 99301, USA.
- **Abstract**
- Nutritional and botanical approaches that may benefit small animals diagnosed with renal disease are considered with regard to their effects on renal physiology and ability to ameliorate specific pathologies

Renal disease in small animals: a review of conditions and potential nutrient and botanical interventions

- Suggestions are made for water- and fat-soluble vitamins, mushrooms, quercetin, and Western and Chinese herbs, based on their activities as free-radical scavengers, immune modulators, antimicrobials, anti-emetics, and erythrocyte production stimulators
- Attention is focused on omega-3 fatty acids from fish and flaxseed, in addition to several other nutrients and botanicals
- Renal anatomy and physiology is reviewed, as well as the etiology of chronic renal disease in small animals, its symptomatic presentation, and progression

Anti-inflammatory and anti-apoptotic effects of Crataegus oxyacantha on isoproterenol-induced myocardial damage

- Mol Cell Biochem. 2012 Aug;367(1-2):1-8. doi: 10.1007/s11010-012-1251-9. Epub 2012 Feb 15.. Vijayan NA, Thiruchenduran M, Devaraj SN.

- **Source**
- Department of Biochemistry, University of Madras, Guindy Campus, Chennai, Tamil Nadu, India. avnavin@gmail.com

- **Abstract**
- This study was designed to evaluate the anti-inflammatory and anti-apoptotic effects of the alcoholic extract of the berries of Crataegus oxyacantha (AEC), a medicinal herb, on isoproterenol-induced myocardial infarction (MI) in a rat model
- Three groups of Wistar albino rats, each comprising six animals, were selected for this study
- Group I rats served as control
- Group II rats were given isoproterenol (85 mg/kg body weight) subcutaneously on 59th and 60th days

Anti-inflammatory and anti-apoptotic effects of Crataegus oxyacantha on isoproterenol-induced myocardial damage

- Group III rats were given AEC (0.5 ml/100 g body weight/day), orally on a daily basis for 60 days, and isoproterenol (85 mg/kg body weight, subcutaneously) was given on 59th and 60th days
- On the 61st day, the animals were sacrificed, and marker enzymes like lactate dehydrogenase (LDH) and creatine kinase (CK) were estimated in serum
- In the heart tissue sample, antioxidant status, lipid peroxidation and anti-inflammatory properties of AEC were determined
- Isoproterenol significantly increased the release of LDH, CK in serum, decreased the antioxidant status in the heart along with an increase in lipid peroxidation

Anti-inflammatory and anti-apoptotic effects of Crataegus oxyacantha on isoproterenol-induced myocardial damage

- Nitritive stress and apoptosis were seen in isoproterenol-induced rat heart
- Pre-treatment with the AEC for 60 days had a significant effect on all the above factors and maintained near normal status
- The study confirms the protective effect of AEC against isoproterenol-induced inflammation and apoptosis-associated MI in rats

The effect of crataegus fruit extract and some of its flavonoids on mitochondrial oxidative phosphorylation in the heart

Phytother Res. 2009 Dec;23(12):1701-7. doi: 10.1002/ptr.2815.

Bernatoniene J, Trumbeckaite S, Majiene D, Baniene R, Baliutyte G, Savickas A, Toleikis A.

Source

Department of Drug Technology and Social Pharmacy, Kaunas University of Medicine, A. Mickeviciaus str.9, LT-44307 Kaunas, Lithuania.

Abstract

Crataegus (Hawthorn) fruit extracts (CE) are widely used for the treatment of various cardiovascular diseases (arrhythmias, heart failure, myocardial weakness, etc)

Despite the fact that many of these diseases are associated with disturbances of the mitochondria, no data have been found on the effect of CE on their function

The effect of crataegus fruit extract and some of its flavonoids on mitochondrial oxidative phosphorylation in the heart

- The aim of this study was to perform an oxygraphic investigation of the effect of CE (in concentration range from 70 ng/mL to 13.9 microg/mL of Crataegus phenolic compounds (PC)) and its several pure flavonoids on isolated rat heart mitochondria respiring on pyruvate+malate, succinate and palmitoyl-L-carnitine+malate
- CE at doses under 278 ng/mL of PC had no effect on mitochondrial functions
- At concentrations from 278 ng/mL to 13.9 microg/mL of PC, CE stimulated State 2 respiration by 11%–34% with all used substrates, and decreased the mitochondrial membrane potential by 1.2–4.4 mV measured with a tetraphenylphosphonium-selective electrode and H2O2 production measured fluorimetrically

The effect of crataegus fruit extract and some of its flavonoids on mitochondrial oxidative phosphorylation in the heart

- Similar uncoupling effects on mitochondrial respiration were observed with several pure CE flavonoids
- The highest CE concentration also slightly reduced the maximal ADP-stimulated and uncoupled respiration, which might be due to inhibition of the mitochondrial respiratory chain between flavoprotein and cytochrome c
- Whether or not the uncoupling and other effects of CE on mitochondria may be realized in vivo remains to be determined

Milk thistle and its derivative compounds: a review of opportunities for treatment of liver disease

- J Vet Intern Med. 2013 Jan-Feb;27(1):10-6. doi: 10.1111/jvim.12002. Epub 2012 Nov 9. Hackett ES, Twedt DC, Gustafson DL.

- **Source**

- Department of Clinical Sciences, Colorado State University, Fort Collins, CO 80523, USA. Eileen.Hackett@colostate.edu

- **Abstract**

- Milk thistle extracts have been used as a "liver tonic" for centuries
- In recent years, silibinin, the active ingredient in milk thistle extracts, has been studied both in vitro and in vivo to evaluate the beneficial effects in hepatic disease

Milk thistle and its derivative compounds: a review of opportunities for treatment of liver disease

- Silibinin increases antioxidant concentrations and improves outcomes in hepatic diseases resulting from oxidant injury
- Silibinin treatment has been associated with protection against hepatic toxins, and also has resulted in decreased hepatic inflammation and fibrosis
- Limited information currently is available regarding silibinin use in veterinary medicine
- Future study is justified to evaluate dose, kinetics, and treatment effects in domestic animals

Pharmacokinetics and safety of silibinin in horses

Am J Vet Res. 2013 Oct;74(10):1327-32. doi: 10.2460/ajvr.74.10.1327.

Hackett ES, Mama KR, Twedt DC, Gustafson DL.

Source

Department of Clinical Sciences, College of Veterinary Medicine and Biological Sciences, Colorado State University, Fort Collins, CO, 80523.

Abstract

Objective-To determine the oral bioavailability, single and multidose pharmacokinetics, and safety of silibinin, a milk thistle derivative, in healthy horsesAnimals-9 healthy horses

Procedures-Horses were initially administered silibinin IV and silibinin phospholipid orally in feed and via nasogastric tube

Pharmacokinetics and safety of silibinin in horses

- Five horses then consumed increasing orally administered doses of silibinin phospholipid during 4 nonconsecutive weeks (0 mg/kg, 6.5 mg/kg, 13 mg/kg, and 26 mg/kg of body weight, twice daily for 7 days each week)
- Results-Bioavailability of orally administered silibinin phospholipid was 0.6% PO in feed and 2.9% via nasogastric tube
- During the multidose phase, silibinin had nonlinear pharmacokinetics

Pharmacokinetics and safety of silibinin in horses

- Despite this, silibinin did not accumulate when given twice daily for 7 days at the evaluated doses
- Dose-limiting toxicosis was not observed
- Conclusions and Clinical Relevance-Silibinin phospholipid was safe, although poorly bio-available, in horses
- Further study is indicated in horses with hepatic disease

Milk thistle and its derivative compounds: a review of opportunities for treatment of liver disease

- J Vet Intern Med. 2013 Jan-Feb;27(1):10-6. doi: 10.1111/jvim.12002. Epub 2012 Nov 9. Hackett ES, Twedt DC, Gustafson DL.

- **Source**

- Department of Clinical Sciences, Colorado State University, Fort Collins, CO 80523, USA. Eileen.Hackett@colostate.edu

- **Abstract**

- Milk thistle extracts have been used as a "liver tonic" for centuries
- In recent years, silibinin, the active ingredient in milk thistle extracts, has been studied both in vitro and in vivo to evaluate the beneficial effects in hepatic disease

Milk thistle and its derivative compounds: a review of opportunities for treatment of liver disease

- Silibinin increases antioxidant concentrations and improves outcomes in hepatic diseases resulting from oxidant injury
- Silibinin treatment has been associated with protection against hepatic toxins, and also has resulted in decreased hepatic inflammation and fibrosis
- Limited information currently is available regarding silibinin use in veterinary medicine
- Future study is justified to evaluate dose, kinetics, and treatment effects in domestic animals

Scientific evidence and rationale for the development of curcumin and resveratrol as nutraceutricals for joint health

Int J Mol Sci. 2012;13(4):4202-32. doi: 10.3390/ijms13044202. Epub 2012 Mar 30. Mobasheri A, Henrotin Y, Biesalski HK, Shakibaei M.

Source

Musculoskeletal Research Group, School of Veterinary Medicine and Science, Faculty of Medicine and Health Sciences, The University of Nottingham, Sutton Bonington, LE12 5RD, UK.

Abstract

Interleukin 1β (IL-1β) and tumor necrosis factor α (TNF-α) are key cytokines that drive the production of inflammatory mediators and matrix-degrading enzymes in osteoarthritis (OA)

These proinflammatory cytokines bind to their respective cell surface receptors and activate inflammatory signaling pathways culminating with the activation of nuclear factor κB (NF-κB), a transcription factor that can be triggered by a host of stress-related stimuli including, excessive mechanical stress and ECM degradation products

Scientific evidence and rationale for the development of curcumin and resveratrol as nutraceutricals for joint health

- Once activated, NF-κB regulates the expression of many cytokines, chemokines, adhesion molecules, inflammatory mediators, and several matrix-degrading enzymes. Therefore, proinflammatory cytokines, their cell surface receptors, NF-κB and downstream signaling pathways are therapeutic targets in OA
- This paper critically reviews the recent literature and outlines the potential prophylactic properties of plant-derived phytochemicals such as curcumin and resveratrol for targeting NF-κB signaling and inflammation in OA to determine whether these phytochemicals can be used as functional foods

Synergy between essential oil components and antibiotics: a review

- Crit Rev Microbiol. 2013 Feb 28. [Epub ahead of print]
- Langeveld WT, Veldhuizen EJ, Burt SA.
- **Source**
- Institute for Risk Assessment Sciences, Division of Veterinary Public Health, Faculty of Veterinary Medicine, Utrecht University , Utrecht , The Netherlands
- **Abstract**
- Abstract With the increase in antibiotic-resistant bacteria and the lack of new antibiotics being brought onto the market, alternative strategies need to be found to cope with infections resulting from drug-resistant bacteria

Synergy between essential oil components and antibiotics: a review

- A possible solution may be to combine existing antibiotics with phytochemicals to enhance the efficacy of antibiotics
- A group of phytochemicals that is said to have such effects, according to in vitro studies, is essential oils (EOs) and their components
- Amongst others, EOs containing carvacrol, cinnamaldehyde, cinnamic acid, eugenol and thymol can have a synergistic effect in combination with antibiotics

Synergy between essential oil components and antibiotics: a review

- Several modes of action have been put forward by which antibiotics and the essential oil components may act synergistically, such as by affecting multiple targets; by physicochemical interactions and inhibiting antibacterial-resistance mechanisms
- Many reported assays show additivity or moderate synergism, indicating that EOs may offer possibilities for reducing antibiotic use

Complex Botanical Formulae

- The history of Western Herbal Formulae has been destroyed at many levels by the persecution of knowledgeable individuals (e.g. witch hunts) as well as the destruction of written literature
- Traditional Chinese Veterinary Medicine has a long and continuous history of complex botanical medicines or herbal formulae
- We will speak about these formulae in a later lecture

Conclusion

- Many “non-drug” oral nutraceutical products are available to facilitate healing in our non-human patients
- These nutraceutical products tend to overlap those that are used in human Naturopathic Practice
- With a few exceptions, common nutraceutical interventions may be used to normalized health and well-being as well as prevent disease in our companion animals


RAZOR SHARP CORAL
CYCLONES
STINGRAYS
CROCODILES
SHARKS
STEVE IRWIN
ANGRY NATIVES
BACKPACKER MURDERERS
GIANT RATS
POISONOUS SNAKES
NOTHING
MANEATING KOALAS
SCORPIONS
MOSQUITOES
BABYKILLER DINGOS
SCORCHING DESERT
SHARKS
SHARKS
DANNI MINOGUE
FIRES
SHARKS WITH FRICKIN' LASERS
STINGING JELLYFISH
GIANT SPIDERS
CONVICTS
DERANGED GUNMEN