Plenary Session Abstracts: Friday afternoon, 27th August
Theme: NUTRITION

State of the Art Address

The role of reactive oxygen species and antioxidants in dermatology

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2500 million years ago, oxygen accumulated in the Earth's atmosphere as a result of the evolution of algae capable of photosynthesis. The enormous benefit of oxygen utilization for obtaining energy led to the rapid expansion of aerobic organisms. However, the high reactivity of the oxygen was coupled with the danger of oxidation of important cell components. Roughly 2% of electrons are lost during electron transport in mitochondrial membranes, leading to the formation of reactive oxygen species. Some of these are free radicals, which are defined as atoms or molecules with an unpaired electron, like superoxide anion or the hydroxyl radical. These molecules are extremely chemically reactive and short-lived. Other reactive molecules such as singlet oxygen and hydrogen peroxide are not free radicals, but are as reactive and capable of initiating oxidative reactions. Together, these molecules are called reactive oxygen species. Cells have evolved various antioxidant and repair systems for protection against metabolically produced reactive oxygen species. Antioxidant enzymes include superoxide dismutase, catalase, glutathione reductase and glutathione peroxidases, which collectively destroy superoxide, hydrogen peroxide and lipid hydroperoxides. Nonenzymatic small-molecular-weight antioxidants are no less important. They build up an effective antioxidant network, which includes glutathione (GSH) and ascorbic acid (vitamin C) in the aqueous phase, and tocopherol (vitamin E) and ubiquinol (coenzyme Q) in the lipid phase. Nevertheless, these systems can be overwhelmed in times of increased oxidative stress, e.g. high metabolic demands or outside forces such as sunlight, smoking or pollution. This then results in oxidative damage of cell components, like proteins, lipids or DNA. Good examples for the consequences of repeated oxidative stress to skin are the aging process and aging-associated skin cancers. There is much evidence that skin aging can be subdivided into intrinsic and extrinsic skin aging. Reactive oxygen species are not only involved in the metabolically induced intrinsic type of skin aging. Various exogenous sources of oxidative stress, in particular ultraviolet (UV)-irradiation, are believed to be responsible for the extrinsic type of skin aging, therefore also termed photoaging. Regarding photocarcinogenesis, shorter wavelength UVB light is important for tumour initiation, but UVA light, which generates more oxidative stress, predominantly causes tumour promotion in nonmelanoma skin cancer. It therefore seems reasonable from various standpoints to increase levels of protective antioxidant systems. One feasible approach is to increase low-molecular-weight antioxidants through a diet rich in fruits and vegetables, systemic supplements or by direct topical application. Indeed, various *in vitro* and experimental animal studies have proved that dietary low-molecular-weight antioxidants or supplements, especially ascorbate and tocopherol as well as polyphenols and flavonoids, exert protective effects against oxidative stress. However, controlled long-term studies on the efficacy of low-molecular-weight antioxidants in the prevention or treatment of skin aging in humans are still lacking.

Supporting Original Study 17

A randomized, double-blinded, placebo-controlled multicenter study on the efficacy of a diet with high levels of eicosapentaenoic acid and gamma-linolenic acid in the control of canine atopic dermatitis

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The purpose of this study was to evaluate the efficacy of a diet with high levels of eicosapentaenoic acid (EPA) (480 mg/megajoule) and gamma-linolenic acid (GLA) (50 mg/megajoule) in the control of clinical signs in dogs with atopic dermatitis. Selection of dogs with atopic dermatitis occurred according to a strict protocol; dogs with ectoparasites, endoparasites, dermatophytosis, *Malassezia* infection, active flea allergy dermatitis, hypothyroidism or food allergy were excluded, as well as dogs currently treated with hyposensitization, glucocorticoids, antihistamines, NSAIDs and dietary fatty acid supplements. Dogs were only selected if they met the diagnostic criteria for atopy and when atopy was confirmed by a positive intradermal test correlating with the history and clinical signs. During the entire study, flea control was applied and secondary pyoderma or *Malassezia* infections were controlled with antibiotics or topically applied lotions. The owners were informed that the diet and/or capsules might be treatment or placebo. The dogs received either a treatment with the test diet plus a daily placebo capsule, or the dog's usual diet plus a daily placebo capsule for a period of 10 weeks. The treatment diet provided 240 mg EPA/kg metabolic weight and 25 mg GLA/kg metabolic weight. Owners who judged that the treatment during the study had not been effective could participate in a double-blinded crossover period during which the dog received another treatment. At the start and end of the study, the severity of the following clinical signs was scored: pruritus, shedding, scaling, dry skin, erythema, smell of coat and alopecia. In total, 13 dogs received the control treatment and 15 dogs the test diet. Of the 13 control dogs, nine followed a crossover period on the test diet, which brought the total number of dogs on the diet to 24. The score after 10 weeks of treatment was expressed as percentage of the score at week 0. After 10 weeks of treatment, scores for intensity, frequency and total score for pruritus in dogs fed the test diet were significantly lower than scores for the control dogs ($P = 0.005$, $P = 0.013$, $P = 0.005$, respectively); the average score was reduced to 67, 65 and 53% of the

initial score, respectively. For dogs on the diet, the score for erythema was significantly lower than the score from the control dogs ($P = 0.019$) and was reduced to 66% of the initial score. Thirteen of the 24 owners of the dogs fed the test diet (54%) indicated that the skin and coat condition of their dog had improved compared to four of 13 control dogs (31%, $P = 0.030$). The dogs' plasma and cutaneous fatty acid compositions changed significantly on the test diet and were similar for responders and nonresponders. From this study, it can be concluded that a diet with high levels of EPA and GLA is effective in the reduction of pruritus and erythema in dogs with atopic dermatitis, but that not all dogs respond to the diet.
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