Veterinary Immunology and Immunopathology 152 (2013) 333–340

Contents lists available at SciVerse ScienceDirect

Veterinary Immunology and Immunopathology

journal homepage: www.elsevier.com/locate/vetimm

Research paper

The potential for enhancement of immunity in cats by dietary supplementation

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ARTICLE INFO

Article history:
Received 16 October 2012
Received in revised form
19 December 2012
Accepted 10 January 2013

Keywords:
Feline
Cat
Immune function
Dietary supplementation

ABSTRACT

This study was conducted to examine the potential benefits of dietary supplementation on the feline immune system. Forty three cats (8 or 9 per group) were fed a low protein control diet (22.7% DM basis), the same diet supplemented with yeast-derived nucleotides, salmon oil or L-arginine or a commercial moist high protein diet (53.0% DM basis) for a period of five weeks. The low protein diets were formulated using a commercial moist diet base with added fat and starch and fed *ad libitum*, along with water. Specific immune assays showed that supplementation with arginine caused a significant enhancement of lymphocyte proliferative responses to the T-cell mitogen PHA after 35 days ($P = 0.018$), while supplementation with either nucleotides or salmon oil resulted in significant enhancement after both 14 ($P = 0.0048$, $P < 0.0001$ respectively) and 35 days (both $P < 0.0001$). Dietary supplementation with arginine, nucleotides or salmon oil each led to significant increases in blood leucocyte phagocytic activity after both 14 ($P = 0.0003$, $P = 0.0077$, $P < 0.0001$ respectively) and 35 days ($P < 0.0001$). This indicates that a number of dietary ingredients have the ability to modulate the immune system of healthy cats possibly resulting in a greater ability to fight infection and disease.

1. Introduction

The increased importance of functional foods to improve and maintain human health over the past few decades has led to an increasing interest in the use of dietary components. With the increasing humanisation of pets, this interest has been utilised by pet food manufacturers to find alternative and more consumer friendly methods of maintaining and optimising companion animal health.

Dietary components can impact the health of companion animals in two ways, firstly by supplying the necessary nutrients required to maintain bodily functions, and secondly by acting as bioactive molecules which for example can influence digestive, gut-related or cognitive functions, antioxidant status, or modulate the immune system. Recent evidence suggests that while healthy pets fed a good quality complete and balanced diet are unlikely to experience nutritional deficiencies, the macro-addition of certain dietary ingredients can significantly enhance immunity, while excessive intakes of other nutrients, can result in immunodeficiency and disease (Bradley and Xu, 1996; Lessard et al., 1997; Chandra, 1997; Field et al., 2002; Schwartz et al., 2012; de Heredia et al., 2012). Therefore, while pets may be adequately nourished, their immune systems may not be operating at optimum levels.

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http://dx.doi.org/10.1016/j.vetimm.2013.01.007

Information on the potential benefits of feed ingredients and pro-nutrients in companion animals is scarce, especially in the scientific literature. Metabolic differences between species may mean that there is the potential for dietary ingredients and supplements to have species specific effects. As such, caution should be taken to ensure that data is not extrapolated from one species to another (NRC, 2008), and it is important that information on the efficacy and safety of putative nutraceuticals is determined on the individual animal species.

The cat is widely recognised as having a unique and highly specialised metabolism (National Research Council (NRC) 2006, 2008). Arginine, is considered a conditionally essential amino acid in most mammals, but is essential in the diet of the carnivorous cat due to its inability to synthesise citrulline as a result of the low activity of two enzymes in the arginine synthesis pathway; Δ^1-pyrroline-5-carboxylate synthase and ornithine aminotransferase (Morris and Rogers, 1978a, 1978b; Rogers and Phang, 1985). The essentiality of arginine is further demonstrated by the fact that a single arginine free meal fed to cats can result in death within 2 h due to hyperammonemia (Morris and Rogers, 1978b).

Arginine plays a key role in both innate and acquired immunity in other species, with a deficiency of arginine in the diet leading to impaired NO synthesis and immune suppression (Li et al., 2007). A number of *in vitro* and *in vivo* studies carried out primarily in rodents and humans have demonstrated that arginine is able to stimulate the immune system (enhancing T-lymphocyte proliferation, increasing IL-2 production, improving cytotoxicity of macrophages, NK cells and T lymphocytes), accelerate wound healing and reduce morbidity and mortality (Li et al., 2007; Wu et al., 2009).

Lipid metabolism in cats also differs from that of other mammalian species, with the cat having limited liver Δ^6 desaturase activity, resulting in a restricted ability to convert linoleic acid to arachidonic acid and α-linolenic acid to eicosapentaenoic (EPA) and docosahexaenoic acid (DHA) in that tissue (NRC, 2006). It does appear that the cat has sufficient Δ^6 desaturase activity in tissues such as the brain and retina to meet tissue requirements for DHA (Filburn and Griffin, 2005), and it has been suggested that cats may use an alternate pathway *via* Δ^8 and Δ^5 desaturase to synthesise fatty acids in the *n*-6 family (Morris, 2004). In cats, EPA and DHA are of great scientific interest due to their apparent ability to decrease the risk of cardiovascular disease, lower blood pressure, decrease risk of certain cancers and modulate immune function (Chew et al., 2000; Plantinga and Beynen, 2003; Park et al., 2011).

Dietary supplementation with fish oil (a rich source of EPA, DHA and other *n*-3 fatty acids) is thought to result in altered platelet function in a number of species including cats (Saker et al., 1998). Decreased concentrations of pro-inflammatory prostaglandin E_2, and increased lymphocyte proliferation and modulation of γ-IFN production (Trebble et al., 2003) have also been reported. However, conflicting results have been obtained, and some studies have shown that supplementation with *n*-3 PUFAs results in immunosuppression (Chew et al., 2000; Calder et al., 2006). A study in cats showed consumption of fatty acids derived from fish oil at an *n*-6:*n*-3 ratio of 5:1 resulted in decreased lymphocyte proliferation to pokeweed mitogen and a reduction in the numbers of a subpopulation of B cells (Chew et al., 2000).

Nucleotides have been commercially used in human infant formulas for many years, as a way of improving gastric development and early immune function, and there are data reporting reduced digestive disorders post-weaning in other species, including pigs (Helembai et al., 2006; Ruihua et al., 2006). Nucleotide supplementation has been shown to enhance a range of immune functions in humans (Martinez-Augustin et al., 1997; Gil, 2002) and mice (Navarro et al., 1996; Jyonouchi et al., 2003). Nucleotide-free diets have been shown to impair cell-mediated and humoral immune responses; which include decreased macrophage and natural killer (NK) cell activity, delayed type hypersensitivity responses, cytokine levels, lower antibody production, all of which may lead to an increased susceptibility to infection (Gil, 2002; Sanchez-Pozo and Gil, 2002). These changes can be reversed by supplementation with nucleotides (Gil, 2002; Navarro et al., 1996). A number of animal studies suggest that nucleotide supplementation of diets can affect immune function by enhancing mitogen-induced lymphocyte proliferation, interleukin-2 production, cell-mediated immunity, and enterocyte and lymphocyte maturation and improving resistance to infection (Gil, 2002; Jyonouchi et al., 2003; Yamauchi et al., 2002).

The objective of the current study was to examine the effects of feeding either nucleotides (in the form of an enriched preparation derived from yeast), salmon oil or arginine on the immune status of adult cats to ascertain if the immunomodulatory effects reported in other species also occur in cats.

2. Materials and methods

2.1. Animals

Forty three adult domestic short-haired cats (*Felis catus*), 32 castrated males and 11 intact females aged between 2.0 and 11.0 years (average 5.0 years) and weighing 2.2–5.9 kg from the Centre for Feline Nutrition, Massey University (Palmerston North, New Zealand) were used in this study as experimental animals. Cats were housed (8 or 9 cats/pen; 1.4 m × 4.4 m × 2.4 m) in a natural light and temperature environment with access to shelter. All cats had been vaccinated against feline rhinotracheitis, calicivirus and panleukopenia using a modified live vaccine (Felocell CVR, Norden Laboratories, München, Germany) as kittens, and received a booster vaccination every three years. Feline leukaemia and feline immunodeficiency virus have not been detected in the colony since its establishment in 1992. The study was approved by and conformed to the requirements of Massey University Animal Ethics Committee (Anonymous, 2003).

2.2. Experimental design and diets

The cats were divided into 5 groups of 8 or 9 animals (43 in total), comprising mixed groups of castrated males