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Moderate dietary supplementation with vitamin E enhances lymphocyte functionality in the adult cat

Teresa O'Brien [a], David G. Thomas [b], Patrick C.H. Morel [b], Kay J. Rutherfurd-Markwick [c,*]

[a] Institute of Food, Nutrition and Human Health, Massey University, Palmerston North, New Zealand
[b] Institute of Veterinary, Animal and Biomedical Sciences, Massey University, Palmerston North, New Zealand
[c] Institute of Food, Nutrition and Human Health, Massey University, Albany, New Zealand

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ABSTRACT

This study aimed to determine the effects of supplemental Vit E and/or Se on selected parameters of the immune system of the cat. Nine diets were fed in a 3 × 3 factorial design with no supplementation (control (C)); and either moderate (M); or high (H) levels of Vit E (0, 225 or 450 mg/kg DM diet) and/or Se (0, 2 or 10 mg/kg DM diet) added to a complete and balanced basal diet. After 28 days of feeding, enhanced lymphocyte proliferative responses to Concanavalin A and phytohaemagglutinin were observed ($P < 0.05$) in cats fed diets containing supplemental Vit E, irrespective of whether they also contained Se. Cats in the MVitE, HVitE, MVitE + MSe, HVitE + MSe, and HVitE + HSe groups all showed enhancement of phagocytic activity compared to control animals ($P < 0.001$). Our results indicate that a supplemental level of 225 mg/kg DM diet Vit E appears to have beneficial effects on immune function in the cat.

1. Introduction

Vitamin E (Vit E) and selenium (Se) are essential for immune function and are known to have immune-enhancing effects when supplemented in the diets of various animals including humans (Chew, 1996; Meydani et al., 2005; Sharadamma et al., 2011; Wu and Meydani, 2014). Combined supplementation of Vit E and Se has also been found to produce a greater enhancement of immune function in some species; an effect that is thought to be due to the synergistic antioxidant effects of Vit E and Se in the cell membrane and their control of arachidonic acid metabolism (Liu et al., 2014). However, there has been very little published on the effects of Vit E on feline immune function, and there is no available information on the effects of dietary supplementation of Se, or a combination of Vit E and Se on immune function in cats.

The antioxidant activity of Vit E explains a great deal of its protective effects on immune function (Bendich, 1990; Meydani et al., 2005). Free radicals and lipid peroxidation have a suppressive effect on the immune system and the antioxidant activity of Vit E is thought to reduce these effects and enhance the immune response (Chew, 1996). Vitamin E may also regulate immune function by reducing the activity or synthesis of immunosuppressive compounds, such as prostaglandin E_2 (Hayek et al., 2000; Wu and Meydani, 2014), and the cell signalling molecule, nuclear factor κB (Rooke et al., 2004). Some immune enhancing effects of Vit E may also be related to its stimulation of interleukin-2 production (Meydani et al., 2005). Vitamin E supplementation enhances the production of interleukin-2 by T helper 1 cells, and is an important promoter of T and B cell proliferation and differentiation (Beharka et al., 1997).

The effects of Vit E supplementation on immune cell function and resistance to pathogens in various production animals, laboratory animals and humans (Liu et al., 2014; Meydani et al., 2005), have shown that Vit E supplementation can influence both the innate and acquired immune systems. It has been suggested that phagocytic activity may be enhanced by Vit E supplementation, which is likely to be due to the effects of Vit E on the production of immunosuppressive compounds such as free radicals and prostaglandin E_2 (Beharka et al., 1997; Wu and Meydani, 2014).

While many positive effects of Vit E supplementation on immune function have been reported, other studies have reported mixed results, with either little or no significant improvements, or with only some immune parameters enhanced (Kelleher, 1991; Meydani et al., 2005). Several studies of the effects of Vit E supplementation on phagocytic activity in humans have reported a reduction in free radical production and killing of pathogens (Kelleher, 1991; Meydani and Beharka, 1996), with excessive Vit E supplementation neutralising the free radicals produced by the cell to fight infection (Erickson et al., 2000).

There are limited data available regarding the effect of Vit E on immune function in cats. Both 250 IU/kg DM (225 mg/kg DM) and 500 IU/kg DM Vit E (450 mg/kg DM) were shown to increase the lymphocyte proliferative response to concanavalin A, but not

* Corresponding author. Institute of Food, Nutrition and Human Health, Massey University Albany, Private Bag 102 904, North Shore City 0745, New Zealand. Tel.: +64 9 414 0800; fax: +94439640.
E-mail address: K.J.Rutherfurd@massey.ac.nz (K.J. Rutherfurd-Markwick).

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Table 1
Number of male and female cats and average age of cats (years) in each group (±SEM).

	C	MVitE	HVitE	MSe	HSe	MVitE + MSe	MVitE + HSe	HVitE + MSe	HVitE + HSe
Male	1	4	3	6	7	4	8	5	1
Female	7	4	5	2	1	4	0	3	7
Average age (years)	8.48 ± 0.83	3.31 ± 0.52	2.83 ± 0.43	2.94 ± 0.51	6.33 ± 1.72	3.31 ± 0.67	4.90 ± 0.80	5.10 ± 0.91	5.22 ± 1.24

Diet key: C = Control (63.2 mg/kg DM Vit E and 0.38 mg/kg DM Se); MVitE (225 mg/kg DM); HVitE (450 mg/kg DM); MSe (2 mg/kg DM); HSe (10 mg/kg DM).

phytohaemagglutinin, in aged cats (Hayek et al., 2000). However, a study into the Vit E requirements of cats found no enhancement in lymphocyte proliferation to concanavalin A when over 1000 IU/kg DM Vit E (>900 mg/kg DM) was fed for 26 weeks (Hendriks et al., 2002). In young cats, supplementation of Vit E at 250 IU/kg DM (225 mg/kg DM) had no effect on T or B cell proliferation, but a significant increase in the response to pokeweed mitogen was seen with a 500 IU/kg Vit E (450 mg/kg DM) supplemented diet in comparison to age-matched controls (Hayek et al., 2000). In addition, prostaglandin E_2 production was reduced in these cats. The minimum Vit E requirement for cats is 30 IU/kg DM (27 mg/kg DM) (Hayek et al., 2000; Hendriks et al., 2002; NRC, 2006), well below the amount thought to be required for optimal immune response in this species (Hayek et al., 2000). It has been suggested that the level of Vit E supplementation required to enhance the immune system is around 4–10 fold greater than the maintenance requirement (Hendriks et al., 2002).

Selenium is thought to modulate immune function and reduce inflammation by a number of mechanisms (Mocchegiani et al., 2014). These include incorporation into glutathione peroxidase, which performs antioxidant removal of immunosuppressive radical peroxides and regulation of the lipoxygenase and cyclo-oxygenase pathways of the arachidonic acid cascade, which in turn controls the synthesis of leukotrienes, thromboxanes, prostaglandins and lipoxins and modulates the products of the respiratory burst of phagocytes (Rooke et al., 2004; Spallholz et al., 1990). Selenium also increases expression of the high-affinity interleukin-2 receptor on T cells, thereby increasing T cell activity (McKenzie et al., 1998). Selenium containing enzymes control the production of pro-inflammatory cytokines such as interleukins-1 and 6 and tumour necrosis factor-α, and prevent the activation of the pro-inflammatory nuclear factor κB cascade by the removal of free radicals from the cell (Rooke et al., 2004).

Various studies in animals and humans have shown that both Se deficiency and toxicity suppress immune function, while adequate and supplementary Se can improve immune function (Hoffman and Berry, 2008; Rooke et al., 2004; Spallholz et al., 1990). However, no information is available regarding the optimum level of Se intake to enhance immune function in the cat.

The minimum Se requirement for the cat is 0.3 mg/kg DM (NRC, 2006), which is based on studies in other animal species (NRC, 2006; Wedekind et al., 2000). Studies to determine the requirement for Se in growing kittens suggest that diets must contain a minimum of 0.4 mg/kg DM (Wedekind et al., 2000) or 0.5 mg/kg DM to account for low bioavailability (Wedekind et al., 2003). There are no data available describing Se deficiency or toxicity in the cat (Simcock et al., 2004), however deficiency appears to be uncommon and has not been observed in cats (NRC, 2006).

The cat has evolved as an obligate carnivore and has developed several metabolic adaptations that result in it having differing nutritional requirements to other species (Morris, 2002). We therefore hypothesised that Vit E and Se may not have the same effects on immunity that have been reported in other species. We investigated selected immunological parameters (cell marker expression, lymphocyte proliferation and phagocytosis) in the cat in response to the dietary supplementation of Vit E and/or Se.

2. Materials and methods

2.1. Animals

Seventy two short-haired domestic cats (39 castrated male and 33 intact female) from the Centre for Feline Nutrition (Massey University, Palmerston North, New Zealand) were selected for this study. Cats ranged from 1.5 to 10 years of age and weighed between 2.36 and 6.86 kg (3.99 ± 0.12 kg, mean ± SEM). Average age and sex distribution of the cats within each group are shown in Table 1. Each cat had been vaccinated against feline rhinotracheitis, calicivirus and panleukopenia using a modified live vaccine Felocell (CVR; Norden Laboratories, Munich, Germany). One week before the trial, all cats were fed a basal diet *ad libitum* to standardise VitE and Se intake. The basal diet was a commercial moist (canned) feline diet (Heinz Wattie's Ltd, Hastings, New Zealand) that had passed a minimum adult maintenance feeding protocol (AAFCO, 2006) (Table 2) and had an analysed Vit E (total alpha tocopherol) and Se content of 63.2 mg/kg DM and 0.38 mg/kg DM respectively. This study was approved by and conformed to the requirements of the Massey University Animal Ethics Committee (Anonymous, 2007).

2.2. Experimental design and diets

Each cat was randomly allocated to one of nine dietary groups (n = 8), which included the basal diet, and eight treatment diets in

Table 2
Analysed composition of the basal diet.

Component	Amount
Dry matter (g/100 g as is)	23.8
Crude protein (g/100 g DM)	52.8
Crude fat (g/100 g DM)	28.5
Ash (g/100 g DM)	9
Crude fibre (g/100 g DM)	2.3
NFE[a] (g/100 g DM)	7.4
Metabolisable energy[b] (kcal/100 g DM)	453
Amino acid	(g/100 g DM)
Taurine	0.26
Aspartic acid	5.01
Threonine	2.29
Serine	2.51
Glutamic acid	7.06
Glycine	4.32
Alanine	3.52
Lysine	3.57
Valine	2.66
Methionine	1.19
Isoleucine	1.87
Leucine	4.23
Tyrosine	1.76
Phenylalanine	2.57
Histidine	1.48
Arginine	3.41

DM, dry matter.
[a] Nitrogen free extractables calculated by difference (100-crude protein-crude fat-ash-fibre).
[b] Determined using modified Atwater factors of: crude protein – 3.5, crude fat – 8.5, NFE – 3.5 kcal ME/g D.