

A Double-Blind, Placebo Controlled-Trial of a Probiotic Strain *Lactobacillus sakei* Probio-65 for the Prevention of Canine Atopic Dermatitis

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Canine atopic dermatitis (CAD) is a ubiquitous, chronic inflammatory skin disorder prevalent in dogs, which results in production of abnormal levels of IgE antibodies in reciprocation to an allergen challenge. In this study, administration of the probiotic strain *Lactobacillus sakei* probio-65 for 2 months significantly reduced the disease severity index in experimental dogs diagnosed with CAD. In addition, one month pre-medication of *L. sakei* probio-65 revealed significant difference in the PVAS score in experimental dogs for both probio-65 and placebo groups. However, post 2 months treatment resulted in a significant decrease in the CASESI score values in the probio-65-treated group ($p < .0.06$).

Keywords: Canine atopic dermatitis, *Lactobacillus sakei*, probiotics, skin disorder

Atopic dermatitis is a common inflammatory skin disorder, marked by a heightened predisposition for the development of allergic reactions following exposure to several antigenic factors. Canine atopic dermatitis (CAD), is a prevalent dermatosis and is recognized as one of the frequent diagnosis in veterinary practice, which predominantly results from the heightened Th2 inflammatory response over Th1 response. Moreover, CAD pathogenesis and development are mediated through several genetic and environmental factors [4, 6]. Reports suggest that owners and their CAD-afflicted dogs suffer through lower standard of life [7, 9]. CAD influences 10% of canine populations; therefore, it exhibits a large impact on canine health worldwide [3, 5, 13]. The designation of CAD as a syndrome rather than a simplistic disease limits researchers from its complete understanding and successful management.

Over the course of time, the most efficacious and routinely

followed treatments for the management of CAD have included broad-targeting therapies such as allergen-specific immunotherapies, steroids such as glucocorticoids, immunosuppressant drug such as cyclosporins, antiallergic drugs such as antihistamines, and essential fatty acids. These agents effectively suppress a multitude of inflammatory mediators, and therefore assist in subsiding the allergic response in most CAD patients. Traditionally, CAD has been treated mainly through the glucocorticoid approach; however, the treatment suffers from severe limitation, as over time the efficacy of the drug tends to diminish and, adverse side-effects may become intolerable. Therefore, there is a need of alternate treatment options. The novel treatment procedure for CAD should comprise long-term strategies to combat aggravating factors such as acute flare-ups and instillation of secondary infections. The patient suffering with CAD develops increased susceptibility to

staphylococcal colonization [2] and conventionally antibiotics are used as the instantaneous first line of defense. The continued and unregulated use of antibiotics has increased the prevalence of antibiotic resistance in the field of medicine [1], which further escalates the challenge in devising treatment strategies for controlling CAD and secondary opportunistic infections. In contrast to the traditional “monotherapy” mode of treatment, the updated approval of the International Task Force on CAD emphasis on the concept of ‘multimodal’ management technique that intervenes at different targeting nodes along the pathway [10]. Probiotic therapy, as highlighted by previous studies [8], could be considered as an integral part of the multimodal therapy that may help in the long-term efficient management of CAD. Specifically, the novel treatment patterns for CAD should consider strategies that aim at abating conditions such as pruritus and skin lesions. Hence, a double-blind placebo study, an innovative approach of using probiotics, was applied on experimental dogs suffering from CAD, in order to confirm the probiotic potential of probio-65 in terms of its efficacy for the treatment of CAD.

A total of 42 dogs confirmed with CAD diagnosis were admitted from Haemaru Referral Animal Hospital in a double-blinded, placebo-controlled trial. Dogs of age 2 to 8 years with atopic dermatitis were randomly selected to be administered a probiotic strain, *L. sakei* probio-65 ($n = 32$), or placebo supplementation ($n = 10$) once a day continuously for 8 weeks.

Numerical tools such as the canine atopic dermatitis extent and severity index scoring system (CADESI-03) were used to evaluate the severity of clinical signs [11]. CADESI-03 is based on a human scoring system that numerically evaluates the size and severity of dermatitis lesions, and thereby facilitates the measurement of changes in disease severity. Higher scores correspond to more severe skin disease. Changes in CADESI-03 were used to assess lesion severity. CADESI-03 is a validated assessment of clinical lesions (erythema, excoriation, lichenification, and self-induced alopecia) at 62 anatomical sites from 0 to 5 yielding a score of 0–1,240.

A second visual tool, Pruritus Visual Analogue Scale (PVAS), evaluated according to Reich *et al.* [12] was utilized, which allowed the dog owner to record a score for pruritus exhibited by the pet. The PVAS documents visual parameters such as the intensity and frequency of scratching at particular areas, repeated biting and licking of the particular area, and nibbling. These parameters are scored on a scale from normal to extremely severe/continuous. A

description is provided for each level to make scoring consistent, easy, and accurate. The procedure of scoring pruritus and owner satisfaction (5-point scale) were followed every 28 days. Pruritus was assessed using a 10-point scale and the owner’s compliance of administration and owner’s global evaluation score were also measured.

L. sakei probio-65 was previously isolated from the Korean traditional fermented food *kimchi* by proBionic. The test group was orally administered for 2 months with 1 g (< 5 kg BW) or 2 g (> 5 kg BW) of freeze-dried powder containing *L. sakei* probio-65 (2×10^9 CFU/g) and the control group received the same amount of placebo treatment.

Statistical analysis was performed using SPSS ver. 12.0 software and considering a p -value cutoff of <0.05 as statistically significant. Means and standard deviation were used to describe continuous variables. Non-parametric methods were used for univariate analyses due to dependent variables of the non-Gaussian distribution, which were treated as continuous variables. Therefore, comparisons between groups have been tested using the non-parametric Mann-Whitney test.

The study was performed on a group of 42 dogs with confirmatory clinical diagnosis of canine atopic dermatitis. However, four dogs were excluded from the final study owing to mismanagement in monitoring the diet intake.

The pre-treatment average CADESI score for the 28 dogs in the test group and 10 dogs in the placebo group was 577.18 and 427.70, respectively. The score decreased to 8.7% and 5.14% after 1 month of *L. sakei* probio-65 administration in the test group and placebo group, respectively ($p = 0.06$). Post 2 months, the CADESI score decreased further to 16.36% in the *L. sakei* probio-65 administration test group and 7.27% in the placebo group ($p = 0.006$). No significant difference was observed in between pre-treatment values and 1 month treatment CADESI scores; the mean or percentage difference between pre-treatment values and post 2 months CADESI values significantly increased in the *L. sakei* probio-65 administration test group (Fig. 1).

In contrast to the CADESI values, the PVAS values showed significant differences in between pre-treatment PVAS values and 1 month PVAS treatment values. The average PVAS score values for the 28 dogs in the test group and 10 dogs in the placebo group at the pre-treatment visit were found to be 7.04 and 4.50, respectively. Administration of *L. sakei* probio-65 exhibited a significant reduction in pruritus scores at 1 month post therapy compared with the placebo group ($p = 0.045$). The score decreased to 24.43% at 1 month in the *L. sakei* probio-65 group and 15.55% in the

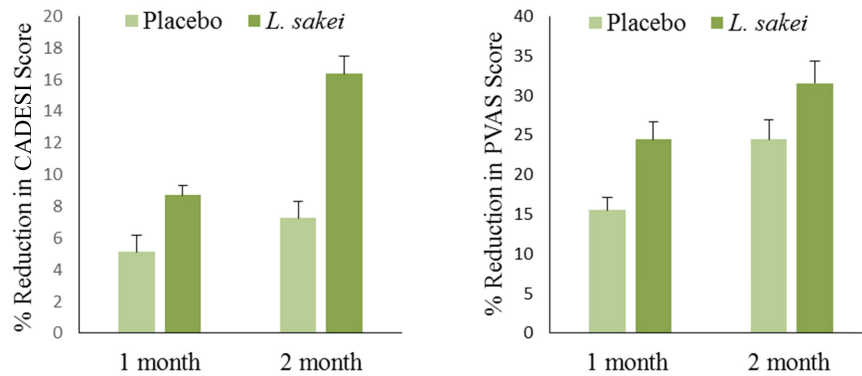


Fig. 1. Percent reduction in CADESI and PVAS scores throughout the study.

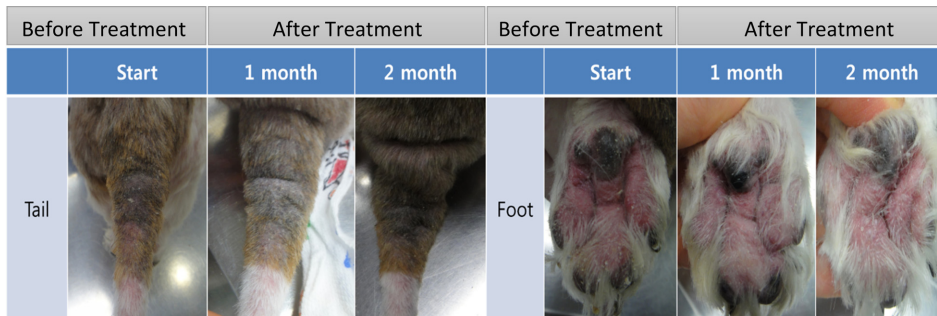


Fig. 2. Improvements in atopic dermatitis-affected dog skin by oral administration of *L. sakei* probio-65.

placebo group. However, there was no significant difference for post 2 months treatment. As shown in Fig. 1, the score in the *L. sakei* probio-65 group and placebo group decreased to 31.53% and 24.44%, respectively ($p = 0.069$).

The owners responded to the treatment tolerated by dogs to be reasonably straightforward and simple to administer, as well as slightly improved the skin problem associated with CAD. Fig. 2 shows the tail and foot before and after the treatment, which clearly indicates the efficacy of *L. sakei* probio-65 against CAD symptoms. Based on the above findings, it could be concluded that the administration of *L. sakei* probio-65 resulted in improvement of the symptoms of CAD in all experimental dogs. The treatment reduced the CADESI and PVASI scores following 2 months of treatment without any adversary side effects. These findings reinforce the suggestions that *L. sakei* probio-65 may act as part of a “combined treatment strategy” for CAD in dogs.

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