THESIS

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Comparative dietetics of Home Curated Diet versus Commercial Food Diets and their effects on Canine Atopic Dermatitis

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1. List of Abbreviations

AD	Atopic Dermatitis
CAD	Canine Atopic Dermatitis
CAFR	cutaneous adverse food reactions
FIAD	food-induced allergic dermatitis
NFIAD	Non-food-induced allergic dermatitis
Ig	Immunnoglobulin
ALD	Atopic-like dermatitis
ICADA	International Committee and Allergic disease of Animals
ACVD	American College of Veterinary Dermatology
CADESI	Canine Atopic Dermatitis Extent and Severity Index
CADsl	canine atopic dermatitis sensu lato
CADLI	Canine Atopic Dermatitis Lesion Index
TEWL	Transpidermal water loss
AMPs	antimicrobial peptides
BDS	β-defensins
Caths	cathelicidins
ASIT	Allergen-specific immunotherapy
IDT	Intradermal testing
PUFA	Polyunsaturated Fatty Acids
Vit	Vitamin
TAC	Total antioxidant capacity
IMID	Immune-mediated inflammatory disease

2. Introduction

Canine Atopic Dermatitis (AD) is the most common pruritic skin disease in our world today. It is a very hard clinical disease to diagnose, mainly because it is a multifactorial disease associated with exposure to various offending agents (eg. environmental and food allergens). Even to this day, its pathogenesis has not been fully understood. The clinical manifestation of AD varies among different dogs. However, based on personal experience volunteering and interning at different clinics in different geological regions of the world, one thing they all had in common is the amount of dogs that suffer from AD. On a personal note, my dogs have also been victims to this disease. It is costly to rectify and oftentimes overwhelming trying to find a way to relieve our furry companions from this misery.

Even though various extensive and expensive tests are done, the results lack specificity and sensitivity to determine the specific AD allergens. We try elimination diets but the process is slow and the results are late to produce. We buy the most expensive hypoallergenic commercial food diets on the market in hopes of curing AD but oftentimes the foods appear unappealing to our dogs and we can observe their displeasure when it comes to meal time. We curate our dogs' raw food diet or cooked meals but are never certain if these diets provide the best nutritional value. We spent money on expensive dog shampoos and bathed our dogs regularly. Regular applications of medicated ear drops are needed to prevent otitis. Tying to pill our dogs with glucocorticoids or antihistamines can be a struggle.

After all that effort, the results are often disappointing and the best that we can achieve is to keep AD at bay. The process is never-ending and the battles are seldom won. This is one of the most disheartening aspects of AD.

Knowledge is a powerful tool. With the internet in our hands and information right at our fingertips, we have to be weary that not all information on the internet is scientifically accurate. Many research, papers, articles and books have been published about AD throughout the years. But due to its complexity, numerous of these published works provide conflicting information. To help navigate through this limitless amount of material, literature and references will be based on the guidelines provided by the International Committee and Allergic Diseases of Animals (ICADA). Almost all of the references in this thesis will be articles that have been approved by the ICADA.

This thesis hopes to be able to provide the most scientifically accurate data concerning AD in terms of its diagnosis, prevention and treatment. We will explore which diet is best in controlling AD flares be it commercial diet or home curated meal, along with finding the best, most practical and economical strategy to curb this disease. Much has been discovered about AD but more studies need to be done to further understand the disease. It will certainly be an adventure and life long journey in the discovery of this complex disease currently known as canine atopic dermatitis.

3. Literature review

The earliest documentation of canine atopic dermatitis (AD) was described by Wittich in 1941 and 20 years later (1960), Patterson described another case of a dog with allergic conjunctivitis with increased tear production and pruritus. But it was Halliwell and Schwartzman who pioneered the study of canine atopic dermatitis and its clinical manifestation in 1971. Countless articles, textbooks and studies have been published since then to try and understand this challenging disease. But most of the clinical trials from these published papers are conducted with biased information (eg. owners conflicting information about their pets), uncontrolled standard groups (eg. various breeds of dogs), fewer patients (eg. dogs from the same litter), and the pathogenic data are often conflicting. These lead to poorly verified dogmas with partially tested hypotheses and therapeutic recommendations that lack sufficient evidence. To avoid such conflicting information, the American College of Veterinary Dermatology (ACVD) created the Task Force on Canine Atopic Dermatitis and in 2010 the name was changed to International Committee and Allergic diseases of Animals (ICADA)

As of today, canine AD is defined by ICADA as "A genetically predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features associated with immunoglobulin (Ig) E antibodies most commonly directed against environmental allergens. Canine atopic-like dermatitis (ALD): An inflammatory and pruritic skin disease with clinical features identical to those seen in canine atopic dermatitis in which an IgE response to environmental or other allergens cannot be documented." [1] Due to these two diseases being difficult to definitively distinguish clinically, they will be collectively referred to as canine atopic dermatitis (CAD) throughout this thesis.

Although this thesis would like to focus mainly on food-induced allergic dermatitis (FIAD), due to the intricate nature of AD, there is no sufficient scientific evidence or clinical test/manifestation to prove definitively the differences between CAD, CAD *sensu stricto* (sensitization to environmental), ALD, FIAD and also non-food induced atopic dermatitis (NFIAD). And thus, the same criteria will be used to diagnose all these disease.[2]

4. Scientific goals

There are 3 main purposes of this thesis.

1. Gather as much current knowledge on CAD to better understand the disease and in hopes of treating it. (Its histology, pathogenesis, clinical manifestation etc.)
2. Collect and provide additional data on clinical cases of CAD from around the world.
3. Analyze the collected date to determine the best diet to prevent flare-ups of FIAD.
4. Determine which diet is best between commercial food diet vs home curated meals.

5. Histopathological manifestations of canine atopic dermatitis

In 1981, Scott DW gave a detailed description of the histological features of CAD reporting epidermal hyperplasia, orthokeratotic and parakeratotic hyperkeratosis, hypergranulosis, spongiosis, melanosis and leucocyte exocytosis as the most common histological findings. He was also able to observe the appearance of mast cells and eosinophils in 15% of evaluated cases [3]. Since then, only a handful of research focused on the histopathological aspects of AD.

In 2001, with the help of histological and immunohistochemical stains, Olivry T was able to further characterize the cell types of the inflammatory infiltrate involved in CAD. The study expressed that the perivascular infiltrate seen in canine AD was mixed, composed of T cells, dendritic cells, eosinophils and hyperplastic mast cells. Epidermal infiltrate was composed of T cells, Langerhans cells and some eosinophils [4].

In the article "Review: Clinical and histological manifestations of canine atopic dermatitis" Bizikova best summarized the histopathological manifestation of CAD as follows, "the late-phase skin reaction was characterized by an inflammatory pattern consisting of superficial perivascular to interstitial mononuclear dermatitis with neutrophils and eosinophils. Degranulation of mast cells and eosinophils was reported upon allergen challenge. An irregular epidermal hyperplasia with lymphocytic and eosinophilic exocytosis resulting in an occasional formation of eosinophilic micro-abscesses and infiltration of the lesional skin with epidermal and dermal dendritic cells were also reported." [5].

6. Pathogenesis of canine atopic dermatitis.

6.1 Skin barrier dysfunction

A study done by Santoro et al., in 2015 determined that the skin barrier between humans and canine are not so different after all [6]. In his study, he showed the correlation between the skin barrier dysfunction and the cutaneous microbes (bacteria and yeasts) and the host (antimicrobial peptides). He cited the works of Inman et al., from 2001 which proved that the ultrastructure of canine epidermis lacked in thickness and length of the stratum corneum lipid deposits in nonlesional skin of dogs with CAD [7]. With the help of electron microscopy, Inman was also able to identify the disrupted lipid lamellae even if impaired extrusion of lamellar bodies could not be demonstrated [7].

Likewise similar studies were done to investigate the plasma and cutaneous lipid profile of dogs with AD. The study in 1990 by Van den Broek demonstrated the decreased serum triglyceride levels were found in atopic dogs after corn oil was administered, which in turn suggested a primary defect in lipid absorption or metabolism [8]. A second study showed that canine (and human) patients with AD had slightly higher plasma levels of linoleic acid and lower levels of dihomo-γ-linolenic acid and arachidonic acid than normal patients [9], further supporting Santoro's study between the similarity of canine and human dermatology. However, findings obtained from the studies of Van den Broek [8] and Horrobin [9] were either not replicated or hard to demonstrate. Taugbøl's study in 1998 demonstrated significantly greater levels of serum dihomo-γ-linolenic acid in dogs with AD in comparison to healthy dogs [10]. Campbell's findings in 1995 further complicated the relationship between serum and skin lipids as they were significantly influenced by the fatty acid source obtained by the dog's diet. [11] In 2000, Marsh published an article that further proves the influence of dietary fatty acid composition to canine epidermal barrier function. The study demonstrated significant decreases in transepidermal water loss (TEWL) in dogs supplemented with linoleic acid [12].

6.2 Transpidermal water loss

Santoro studied the skin barrier functions by evaluating the TEWL as it is a good indicator on the integrity of the skin [6]. Shimada demonstrated in 2008 that the removal of the stratum corneum leads to increased TEWL in dogs and subsequently the increase in TEWL is directly proportional to the severity of damage to the stratum corneum [13].

6.3 Ceremides and Lipids

Ceramides are waxy lipid molecules composed of one sphingosine and one fatty acid. These molecules are mainly located in the cellular lipid bilayer. Ceramides may be composed of a combination of different sphingosines and fatty acids. They make up to 50% of the skin composition to form the natural skin barrier. Uchida discovered in 2014 that ceramide not only acts as a skin barrier, but is also involved in cellular signaling [14]. Decreased ceramide levels have been associated with Increased TEWL in dogs with AD [15]. It is important to note that time and again, studies like Santoro [6] and Popa show that even in healthy dogs of different breeds; there is a wide quantitative variation in the patterns of stratum corneum ceramides [16].

6.4 Filaggrin

Filaggrin (filament aggregating protein) is a filament-associated protein that binds to keratin fibers in epithelial cells. An initial study done by Marsella in 2009 used anti-human filaggrin antibodies in an experimental model of CAD and revealed the decreased expression in atopic skin. However, the use of this reagent was limited due to cross-reactivity with other epidermal proteins [17]. In 2013 Kanda further explored this research and discovered the unique gene structure of canine filaggrin, which results in production of filaggrin monomers larger than those of humans or mice [18]. Although many studies were conducted, Santoro concluded that it is unclear whether these abnormalities in filaggrin expression are due to primary triggers or the consequence of AD [6].

6.5 Role of infections in canine atopic dermatitis

Due to the complexity of AD, it is good to evaluate the possible relationship between cutaneous infections and the clinical signs of AD. Santoro's article states as follows "The relationship between cutaneous infections and exacerbation of the clinical signs of AD is complex and not completely elucidated. However, many studies in humans have shown a correlation between cutaneous skin infections and severity of AD, suggesting a direct effect of micro-organisms on the immune system [19]. This may also be true in CAD, although there have been fewer studies and the situation is less clear" [6].

In 2001, many studies established that dogs with AD would commonly suffer from recurrent bacterial infections of the skin and otitis [20]. Staphylococcus intermedius (now reclassified as S. pseudintermedius) was the species of bacterial most commonly associated with bacterial folliculitis, however, Mason was not able to establish definitively whether this organism was part of the normal cutaneous resident microflora or not. [21] A comparative study of Mason's [22] McEwan's [23] and Harvey's [24] articles demonstrated that dogs with AD compared to healthy dogs had increased staphylococcal adherence and colonization of both lesional and nonlesional skin but the number of bacteria present diminished when the AD went into clinical remission. DeBoer's hypothesis concerning the relevance of bacterial colonization to the pathogenesis of pruritus was supported when he demonstrated that antibiotic treatment alone could improve the clinical signs of AD in many cases. Even in nonatopic dogs, staphylococcal infections could induce cutaneous inflammation and pruritus [20].

DeBoer also established that cutaneous infections with yeast (specifically Malassezia pachydermatis) were more common in dogs with AD [20]. Morris conducted a study in 1998 to determine if Malassezia proteins could act as allergens in atopic dogs. He introduced Malassezia extracts with the intradermal injection to induce the development of significantly greater wheal-and-flare reactions in atopic dogs with cytological evidence of yeast dermatitis than was seen in atopic dogs without yeast. His hypothesis was further supported when Nuttall showed that dogs with AD, regardless if they had or did not have Malassezia overgrowth would exhibite higher levels of anti-Malassezia IgE compared to healthy dogs or nonatopic dogs with Malassezia dermatitis in 2001 [26]. Based from the study done by Bond in 1998 [27], Santoro summarises the article as such "The ability of Malassezia to induce systemic humoral immune responses was also confirmed by the demonstration of significantly higher serum titres of anti-Malassezia immunoglobulin G (IgG) and immunoglobulin A (IgA) in dogs suffering from yeast dermatitis compared with healthy dogs" [6].

In 2009, Fazakerley's study demonstrated that up to 91.7% of dogs with AD are colonized by a heterogeneous population of coagulase-positive staphylococci (90% S. pseudintermedius and 4% S. aureus) compared with only 39.5% of healthy dogs (84% S. pseudintermedius and 8% S. aureus) [28]. Although atopic dogs were more prone to suffer from S.pseudintermidius or other wide varieties of clonal groups compared to healthy dogs, there is no specific bacteria that can be associated with AD, pruritic dogs, or even healthy dogs [28][29].

Due to the misuse of antibiotics, the prevalence of bacterial resistance continues to increase both in human and veterinary medicine. This presents a potential risk for recurrent pyoderma in dog with AD as the conventional treatments may be ineffective in the future. There is currently no study comparing canine AD with the prevalence of secondary staphylococcal infections, the frequency of antibiotic usage and the increasing prevalence of meticillin- or multidrug-resistant S. pseudintermedius in veterinary practice [6].

6.6 Antimicrobial peptides, β-defensins and cathelicidins.

There are several researches done on the potential importance of antimicrobial peptides (AMPs), particularly β-defensins (BDs) and cathelicidins (Caths) and their functions in skin barrier and innate immunity in human and CAD [30]. A recent article

written by Valdez-Miramontes in 2021 discusses the importance of AMPs and their applications in veterinary medicine. Here is how he defines AMPs, “Antimicrobial peptides (AMPs) are molecules with a broad-spectrum activity against bacteria, fungi, protozoa, and viruses. These peptides are widely distributed in insects, amphibians and mammals. Indeed, they are key molecules of the innate immune system with remarkable antimicrobial and immunomodulatory activity. Besides, these peptides have also shown regulatory activity for gut microbiota and have been considered inductors of growth performance.” [31]

Figure 1: A) Three-dimensional representation of the antimicrobial peptides: α-defensins, β-defensins, and cathelicidins. [31]

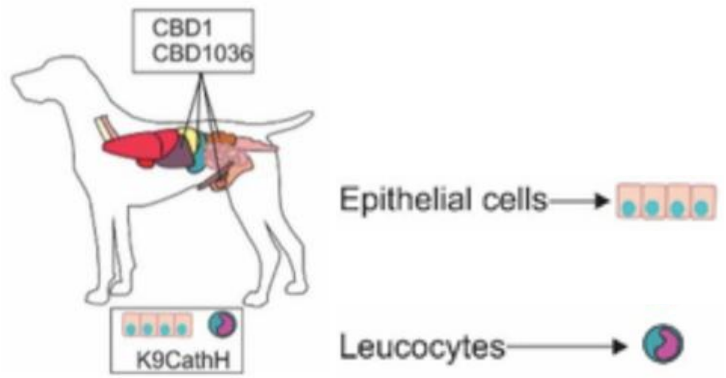

Figure 2: B) Distribution of antimicrobial peptides in dogs. The lines indicate the main source of production. [31]

Sang’s paper identified that most of the AMPs identified in canines are β-defensins BDs. “Comparative genome analysis of the dog has identified 43 - β defensin genes and pseudogenes, which are codified in the canine chromosome 16” (Sand et al. 2005) [32]. Patil expressed in his research that the first canine defensing gene was named canine β-defensin-1 which is codified by CBD1 gene. The mature peptide region of CBD2

and CBD3 has broad antimicrobial activity, particularly against pathogens of the urogenital tract [33]. Direct quote from Valdez-Miramontes' article "Regarding localization, canine skin highly expresses β-defensins CBD1 and CBD1036, the putative orthologous of hBD-1 and hBD-3 in humans, respectively. Their expression has also been detected in the testes, kidney, palatine tonsil, trachea, lung, gastrointestinal tract, liver, spleen, peripheral blood mononuclear cells, bone marrow and skin" [31] Erles was also able to determine that CBD1036 has antimicrobial activity against *Bordetella bronchiseptica* which is a respiratory pathogen [34]. CBD1036 was identified in the duodenal mucosa of healthy dogs but a noticeable increase in numbers were present when a dog suffered from inflammatory bowel disease [35].

Table 1, Antimicrobial peptides activity against canine pathogens [31].

Peptide	Antimicrobial activity	Minimal inhibitory concentration (μg/mL)
K9CATH	*Neisseria gonorrhoeae*	50
	M. tuberculosis	10.66
	B. abortus	8
	B. melitensis	128
	S. aureus	5.66
	E. coli	21

Canines express a single cathelicidin known as K9CATH and can be found in the epithelial cells and leukocytes [36]. Santoro pointed out that higher levels of K9CATH can be expressed in the bone marrow, whereas lower levels are present in the gastrointestinal tract, liver, testes, spleen and skin [36].

"In humans, LL-37 expression is mainly regulated by vitamin D, through the interaction with vitamin D receptor (VDR), which subsequently promotes the activation of the cathelicidin promoter which contains three vitamin D response elements (VDREs), leading to the expression of LL-37. Although dogs and cats express VDR, the promoter region of K9CATH and eCATH do not contain VDRE sequences suggesting that these species do not produce this peptide in response to vitamin D" (Gombart et al. 2005) [37], (Cartwright et al. 2018) [38].

Although Valdez-Miramontes' research reviews many potential applications of AMPs in veterinary medicine, most of the research was gated towards bovine, small ruminants and pigs. No new research was conducted to determine the potential benefits of antimicrobial effects in the dermatology, immunology and/or nutrition of canine [31].

6.7 Environmental triggers to Canine Atopic Dermatitis.

Back in 2001, the ACVD compiled several studies that identified some common environmental allergens associated with allergic disease. With the help of serum and intradermal testing (IDT), Hill's review identified a number of commonly reported allergens, including storage mites (*Acarus siro* and *Tyrophagus putrescentiae*), house dust, house dust mites (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*), and epidermal allergens (human, horse, cat and dog) [39].

Pollens and molds were more variable potential allergens due to the varying geographical locations in which the research was conducted and their respective test subjects. However, Hill's review found that these individual studies achieved very different findings [39]. This may be due to the inconsistency between the studies. E.g, allergen concentrations or types were not standardized; allergen tests produced by different manufacturers with different precision content and biological potency; and *in vitro* assays may have varied with respect to specificity for canine IgE [39].

The ACVD concluded that even though much information was collected from those studies, future studies should use standardized allergen testing methods, standardized allergen extract preparation and more accurately identify the major allergens pertinent to canine dermatology [39].

7. Clinical Manifestation of Canine Atopic Dermatitis.

As early as 1986, Willemse [40] had proposed the clinical criteria for canine AD. It was later amended by Prélaud [41], in 1998 before the ACVD created the first validated scoring system used in clinical trials, called the Canine Atopic Dermatitis Extent and Severity Index (CADESI-03)[42]. This set of criteria showed 85% sensitivity and 79% specificity for the diagnosis of AD whereas criteria by Willemse and Prélaud *et al* were lower in sensitivity and specificity [2]. Since then, many other studies have been published. Which led to the developments of two additional validated scoring systems, Canine Atopic Dermatitis Lesion Index (CADLI) [43] and CADESI-04[44].

Criteria sets for the diagnosis of canine atopic dermatitis (All criteria are referenced from Bizikova P, 2015) [5]:

7.1 Age of Onset

Bizikova concluded that the majority of dogs developed signs of AD before the age of 3 years. One publication done by Wilhem in 2010 showed that French bulldogs and Shar-pei dogs seemed to develop AD earlier than other breeds [45]. The same population group was used to assess the differences in the age of onset between canine AD associated with environmental allergens and food-induced AD. It showed that dogs with food-induced AD were more likely to be very young (<1 year, 46.5 versus 38.6%) or older (>6 years, 8.7 versus 3.8%) in comparison to dogs with AD associated with environmental allergens [2].

7.2 Breed predisposition and breed-specific phenotypes

With minor geographical difference, most studies agreed that boxer, French bulldog, West Highland white terrier (WHWT), Labrador retriever, golden retriever, German shepherd and cocker spaniel dogs represented the most commonly affected breeds. But bear in mind that some breeds are more popular in different parts of the world and studies done in those respective areas showed more affected proportions of some particular breeds. For example, studies from Australia showed that the Cavalier King Charles spaniel, great Dane and silky terrier were breeds found to be predisposed to CAD and respectively, the French bulldog was exclusively predisposed in Hamburg [46].Whereas the Vizsla was one of the most commonly affected breeds in a study from Hungary [47].

7.3 Sex predilection

Although most research conclude that sex predilections does not occur in AD, it must be noted that the study done by Wilhem in 2011 showed that female boxers and male golden retrievers pertained AD more frequently [48].

7.4 Seasonality

FIAD does not present with seasonal signs, but seasonality can appear in some dogs with AD associated with environmental allergens. In many studies, there is scientific proof that in some dogs, seasonality can disappear as the disease progresses [49]. Comparative studies done by Bruet [48], Zur [50] and Picco [51] shows that the majority of seasonally affected dogs exhibited clinical signs in the spring and/or summer.

7.5 Anatomical location of pruritus

Pruritus is the most common feature of CAD and it responds to steroid treatments. By integrating date from various scientific articles , Petra was able to show that the most commonly affected body regions were the distal limbs (62–81% of dogs), face (27–57% of dogs), ventrum (39–66% of dogs) and ears (48–60% of dogs). Reportedly, 38% of dogs were affected in the flexural areas [5].

Along with pruritus, dogs with AD can also develop various primary and/or secondary skin lesions. Some of those lesions include erythema, erythematous macular or papular eruptions, self-induced alopecia, excoriations, hyperpigmentation and lichenification and on occasions, yeast and/or bacterial infection [49]. Some less significant clinical signs included urticaria (2–3%), hot spots (1–11%), hyperhidrosis (4–13%), interdigital fistulae (13–22%) and seborrhoea oleosa (8–14%) [5]. It is important to note that the study done by Picco in Switzerland in 2008 could not find any significant differences in clinical phenotypes between CAD *sensu stricto* and FIAD[48].

Jaeger conducted a study in 2010 with 552 dogs from 3 different continents (Australia, Germany and the United States). He concluded that lesions were present most commonly on the paws (62%), ventrum (51%), ears (48%) and face (39%). Bear in mind that various breeds had specific site predilections. In Jarger's study, he emphasizes that breed predispositions can vary greatly between continents and also within different locations in the same continent. He advises that information regarding breed predilections should be obtained locally or regionally and the results should be interpreted cautiously [54].

Table 2 is examples of breed-specific clinical phenotypes in canine atopic dermatitis. Data is taken from study done by Wilhem S, 2011 [48].

Canine Breed	**Breed-specific distribution of clinical signs**	**Breed-specific clinical lesions**
Dalmations	Lips	decreased frequency of pruritus without lesions
German shepherd dogs	elbows, hindlimbs, thorax and generalized	increased seborrhoea oleosa with hyperhidrosis and pyotraumatic dermatitis (hot spots), decreased pruritus without lesions
Shar-peis	thorax, hindlimbs, flexor dermis and dorsolumbar skin	increased otitis and decreased pruritus without lesions
West Highland white terriers	dorsolumbar skin, forefeet, hindfeet, flexor skin, lips, face, genitals and generalized	increased seborrhea oleosa with hyperhidrosis, Malassezia dermatitis, decreased frequency of conjunctivitis
Labrador retrievers		increased dry skin and pyotraumatic dermatitis (hot spots), increased incidence of interdigital fistulae
Golden retrievers		increased pyotraumatic dermatitis
French bulldogs	axillae, eyelids and flexural surfaces	
Boxers		increased urticaria and otitis,

7.6 Non-cutaneous conditions associated with canine AD

Many researches over the years have concluded that CAD can be presented together with non-dermatological symptoms, for instance rhinitis or conjunctivitis. One study done by Lourenco-Martins in 2011 demonstrated how concurrent signs of conjunctivitis were presented in 21–30% of dogs with AD, while rhinitis was recorded in ~7% of included dogs [52]. On top of that, another study done by Furiani in 2011 showed that bacterial colonization of the conjunctival sac with dogs suffering from AD were more persistent compared to that of healthy dogs. The most frequently cultured bacteria were *Staphylococcus pseudintermedius*. Moreover, in the aspect of cytology, atopic dogs had significantly higher numbers of keratinized epithelial cells and lymphocytes from the conjunctival sac, and eosinophils that could only be observed in dogs with AD [53].

8. Methods and Materials

8.1 Definitions

As previously stated, CAD is a multifactorial complex disease and there is not sure way to define the disease. Therefore, for the purpose of this study we will define CAD as cases with clinical features of atopic dermatitis irrespective of the offending agents (i.e. seasonal/non-seasonal, environmental or food allergens). The diagnosis of CAD was not based on the fulfillment of any criteria but on the exclusion of any resembling disease and on the clinical judgment of each investigator. In this study, CAD will contain five possible diagnoses:

1. Food-induced atopic dermatitis (FIAD): Dogs with clinical features of atopic dermatitis and a positive response to a six- to eight-week elimination diet and subsequent challenge.
2. Undetermined atopic dermatitis (UAD): Dogs with clinical signs of atopic dermatitis never subjected to an elimination diet.
3. Non–food-induced atopic dermatitis (NFIAD): Dogs with clinical signs of atopic dermatitis and negative response to an elimination diet.
4. Canine atopic-like dermatitis (ALD): Dogs with inflammatory and pruritic skin disease with clinical features identical to those seen in canine atopic dermatitis in which an IgE response to environmental or other allergens cannot be documented.
5. Canine atopic dermatitis *sensu lato* (CADsl): Dogs with clinical signs of atopic dermatitis in response to environmental factors and a negative response to an elimination diet.

8.2 Citation

Citations databases, abstracts and proceedings from international meetings published between the years 2001 to 2021 were reviewed in this thesis. Wherever necessary, older articles were included for background information. Almost all referenced citations are approved by the ACVD.

8.3 Study population via surveys and record of data.

An online survey was created for the purpose of this thesis. A sample of the survey can be obtained from Appendix 1. In the survey, owners were asked to the

following information: sex and breed of canine, history and severity of the AD and diets that the dog took and is currently taking.

Candidates of the survey were evaluated and selected based on criteria proposed by Willemse [40] and/or Prélaud [41].

I. <u>Willemse</u>

Major criteria:	Minor criteria:
• Pruritus • Typical morphology and distribution: Facial and/or digital involvement or lichenification of the flexor surface of the tarsal joint and/or the extensor surface of the carpal joint • Chronic or chronic relapsing dermatitis • Individual or family history of atopy and/or breed predisposition	• Onset of signs before 3 years • Facial erythema and cheilitis • Bilateral conjunctivitis • Superficial staphylococcal pyoderma • Hyperhidrosis • Immediate positive intradermal test to inhalants • Elevated serum allergen-specific IgE • Elevated serum allergen-specific IgG

II. <u>Prélaud:</u>

- Cortico-steroid-sensitive pruritus
- Erythema of the pinnae
- Bilateral cranial erythematous pododermatitis
- Cheilitis
- Appearance of first signs between the ages of 6 months to 3 years

Sensitivity and specificity were calculated using either 1 of 2 sets of criteria (Appendix 2). The clinical examination was done using CADESI-4 lesion grading atlas (Appendix 3), CADESI-4 grading sheet (Appendix 4) or Canine Atopic Dermatitis Lesion Index (CADLI) (Appendix 5).

9. Results

A total of 52 dogs participated in the online survey. Geographically, 29 dogs were from Asia, 13 from Europe, 6 from Australia and 4 from Africa. 61.54% (32) were neutered females, 23.08% (12) were neutered male, and 7.69% (4) were unneutered female and male respectively. Of those that took the survey, only 14 of those 52 dogs have ever been on a home curated meal for more than 3 months. And currently, only 3 remain on that home curated meal.

Table 3: Date on the sex of dogs that participated in the survey.

Country of origin	Neutered female	Neutered male	Unneutered female	Unneutered male
Malaysia	16	4	3	2
Japan	2	0	0	0
Korea	1	0	1	0
Norway	2	2	0	1
Hungary	3	2	0	0
Ireland	1	1	0	1
Australia	5	1	0	0
Africa	2	2	0	0

Table 4: Data on dogs that were on a home curated meal for more then 3 months collected from the survey.

Continent	No. of dogs	No. of dogs that were on a home curated meal for more than 3 months.	No. of dogs remaining on a home curated meal.
Asia	29	5	2
Europe	13	4	1
Australia	6	3	0
Africa	4	2	0

Table 5: Data on the types of dog breeds collected from survey.

Country of origin	Mixed breed	Specific breed
Malaysia	18	7
Japan	0	2
Korea	0	2
Norway	0	5
Hungary	1	4
Ireland	0	3
Australia	2	4
Africa	3	1

28 test subjects have specific breeds and 24 are mixed breed. Dogs from the specific breed category are not necessarily certified pure breed.

List of dog breed participated in the survey:

- Jack Russell terrier (4) [Malaysia, Norway, Hungary, Australia]
- Golden retriever (3) [Japan, Ireland, Norway]
- French bulldog (3) [(Malaysia, Norway, Hungary]
- Collies (2) [Malaysia, Korea]
- Shih Tzu (2) [Malaysia, Australia]
- Bichon Frise (2) [Malaysia, Korea]
- Pomeranians (2) [Malaysia, Australia]
- German shepherd (2) [Japan, Ireland]
- Labrador retriever (2) [Malaysia, Norway]
- Staffordshire bull terrier (1) [Norway]
- American Staffordshire bull terrier (1) [Hungary]
- Pugs (1) [Ireland]
- Kelpi (1) [Australia]
- Viszla (1) [Hungary]
- Pitbull (1) [Africa]

Table 6: Breeds of dogs that tried a home curated diet for at least 3 months.

Location	Breed of dog	Type of home curated meal.	Are they currently on a home curated meal?
Malaysia	Mixed	Buffalo meat	Yes
	Mixed	Mix meats	Yes
	Mixed	Fish meats	No
	Shih Tzu	Mix meats	No
Japan	German Shepherd	Mix meats	No
Hungary	American Staffordshire bull terrier	Pet shop curated diets	Yes
	Jack Russell terrier	Mix meat	No
	French	Mix meat	No
Ireland	Pug	Mix meat	No
Australia	Mixed	Mix meat	No
	Kelpi	Kangaroo meat	No
	Jack Russell terrier	Kangaroo meat	No
Africa	Mixed	Mix meat	No
	Pitbull	Pet shop curated diets	No

Mixed meats are defined as recipes that are curated by the owner with any mixture of meats including but not limited to chicken, pork, beef, turkey, duck, rabbit, etc.

*Due to the varying geological location, age and breed difference, unique and special cases will be outline in this study.

<u>Case 1: 6 year old mixed breed neutered female, located in Malaysia.</u>

History:

She was on chicken kibbles from birth to the age of 6 month when she first showed signs of AD. She had severe scratching until the point of alopecia and damaged bleeding and darken dermis in her hind limbs. Local veterinarian diagnosed patient with FIAD and/or CADsl without IDT or elimination diet but based on Willemse [40] and/or Prélaud [41]'s criteria. Her CADLI score was 31 out of 50. Patient's AD lesions were localized at the ear pinna, forepaws, and abdomen; especially in the hind limbs. Throughout the years, the owner had switched to various different commercial food diets but was unsuccessful in preventing AD. Medicated shampoo was used on average once a

week. There was severe otitis that lasted for 2 months. Doctors prescribed antihistamine for 2 weeks with ear cleaning solutions. Since then, the owner cleaned the patient's ear regularly. In the month of September 2021, the owner curated a diet consisting of a small portion of commercial foods and non-commercial food diets. Owner got the recipe from online sources [56].

Diet:

Breakfast: Origi-7 Advanced Soft Organic Dog Food Lamb

Dinner (main): Cooked food that contains Buffalo meat, broccoli, carrot, capsicum, pumpkin, French bean, tomato, rosemary, turmeric, ginger powder, kelp and blueberry powder, grounded egg shell, rice. No additional supplements are given.

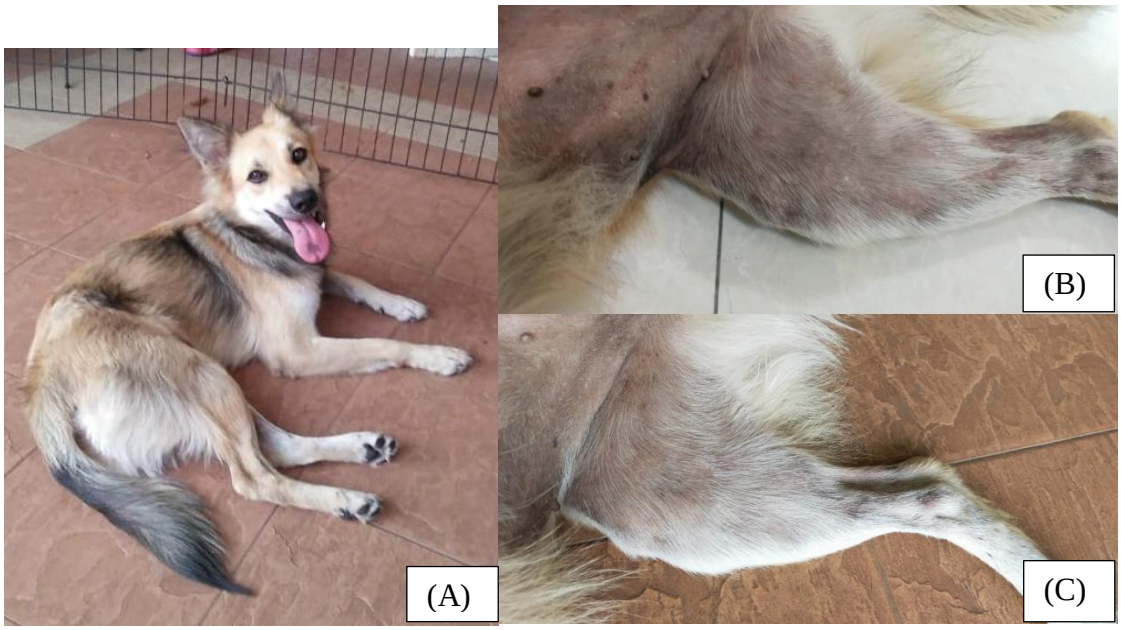

Figure 3: A) Picture of patient. B) Picture was taken in September 2021 before the patient was put on the buffalo meat diet. C) Picture was taken on December 5th, about 3.5 months into the buffalo meat diet.

There is a clear difference between the hind limbs before and during the buffalo meat diet. Fur had started to grow back and erythema, lichenification and hyperpigmentation has decreased noticeably. It is important to note that the patient was not on any medication or antihistamines and the curated diet was not always consistent in each meal. Owner would prepare a big batch for 10 days and the following batch would have different concentrates of buffalo meat, broccoli, carrot, capsicum, pumpkin, French bean, tomato, rosemary, turmeric, ginger powder, kelp and blueberry powder, grounded egg shell and rice.

Case 2: 3 year old mixed breed neutered female, located in Malaysia.

History:

Patient showed signs of AD at 6 months of age. Local veterinarians diagnosed with non-seasonal, FIAD. No IDT or elimination diet was done. Patient suffered from Demodex when she was about 1 years old. After that, the owner described that her pet suffers from pruritus, sometimes self-inflicted redness and lesions on the rib cage area. All 4 limbs had open wounds. Owner observed tail biting, ear infections, chin starching and pyoderma localizing near the ventral thorax. Her CADLI score was 35 over 50. A year ago, cream corticosteroids were taken for a month to help keep AD under control and allow time for the skin wound to heal. Treatment was effective. Owner uses antihistamine occasionally when there is an appearance of open lesions. Medicated shampoos are applied on a weekly basis. Owner had been switching between commercial foods diets before landing on the current mixture between commercial and non-commercial food diets. The new diet started in August 2021. Recipes of non-commercial food diets were taken off the internet.

Diet:

Morning breakfast: Pero fish.

Dinner: cooked meals, fish, pork, beef, rice, spinach, carrots, purple cabbage, regular cabbage, bell peppers coconut oil, turmeric powder. spirulina powder.

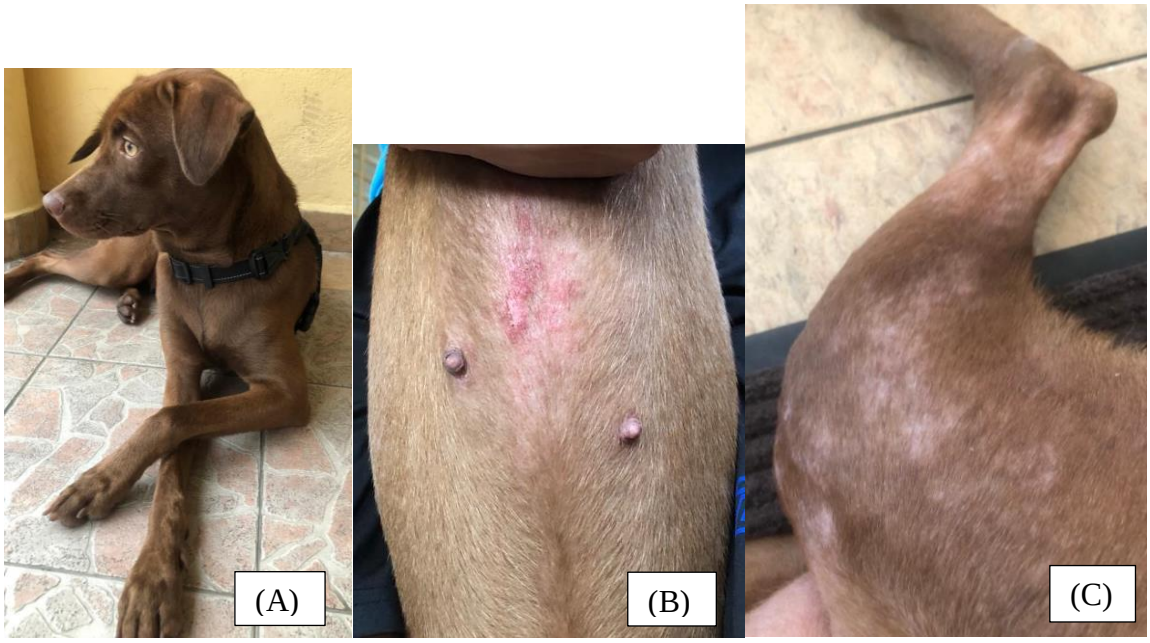

Figure 4: A) Picture of patient. B) Picture was taken in October 2021 before the patient started the home curated meal. C) Picture was taken in November 2021, about 3 months into the non-commercial diet.

Owner did not document the before-and-after process of the raw food diet but claims that the lesions have minimized significantly since starting this new diet. It is important to note that the patient takes antihistamines occasionally when there are open wounds on the chest area. Owner would prepare a weekly batch and switch between the main sources of proteins which are fish, pork and beef. The rest of the ingredients only vary in specific quantities between batches.

Case 3: 8 year old neutered female Kelpi located in Australia.

History:

Patient was first diagnosed with AD when adopted at 1.5 years old. Patient was diagnosed with non-seasonal AD, FIAD and chicken meal allergy through elimination diets. Occasional otitis externa would be observed throughout the years. The last occurrence was about a year ago and it lasted for about 1 month. At the beginning of AD, pruritus of medium severity, bites and minimal alopecia was present around the fore and hind paws. Her CADLI score was 19 over 50. Local veterinarian prescribed antihistamines to control the initial pruritus.

Diet:

Owner initially gave kangaroo meat with sweet potatoes and the AD was under control for about 3 years. Due to it being expensive, difficult to get as well as time consuming to make, the owner switched to Royal Canin Hypoallergenic diet and the results remained the same. So the patient has been on this diet ever since.

It is worth noting that medicated shampoo 'Malaseb' is used regularly. Along with the shampoo, Mometamax ointment which is an anti-inflammatory, anti-fungal and antibacterial ointment for the treatment of acute and chronic canine otitis externa associated with yeast (*Malassezia canis*) and/or bacteria susceptible to gentamicin is used when there is a flare up of CAD.

Case 4: 8.5 year old neutered male pitbull from Africa.

History:

Patient was first diagnosed with AD when adopted at 8 months old from Africa. With the process of elimination diet, the patient was diagnosed with non-seasonal AD, FIAD. There were some flare-ups of otitis externa but it was minimal. At the beginning of AD, pruritus and alopecia were severe around the fore and hind paws. Owner

observed frequent scratching of the ventral abdominal area. Noticeable alopecia occurred around the ears and head. The patient's CADLI score was 26 over 50.

Diet:

In 2018, the owner moved to Hungary with the patient and continued searching for a commercial food diet that would help with CAD. In December 2020, the owner found a local pet supplier that curated raw food diets. A box would contain 500g of raw meat (deboned chicken thigh or sternum, duck neck, heart, liver.) with a mixture of grinded up rabbit/beef meat and bones with minced carrots, cabbage and other veggies. Sometimes beef/lamb liver was also used [57]. The owner noted that the AD was under control and the patient's skin condition improved.

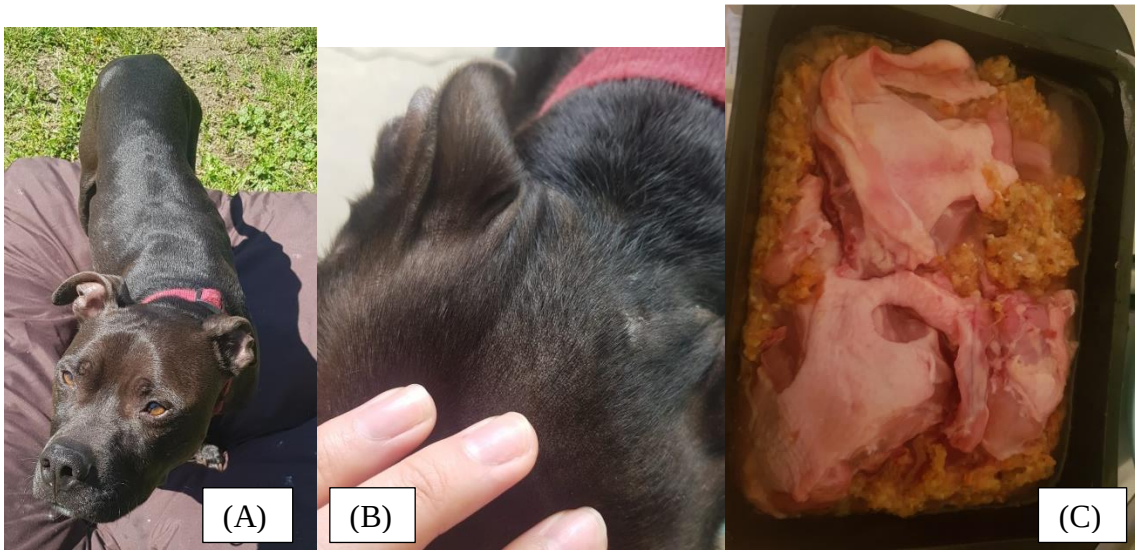

Figure 5: A) Picture of patient. B) Picture was taken in May 2021 of the patient's head during the 6 months into the raw food diet. C) Picture of raw food diet containing minced rabbit, carrots, cabbage, with chicken sternum curated by Fanni's Barfshop [57].

Owner noticed that even though the skin has improved, there is still slight alopecia around the head and ears. Owner also noticed that although the dog was eating well, he was progressively losing weight. Patient's activity level and behavior remained the same in spite of the weight loss. In mid-November 2021, the owner had to switch to normal kibbles as the patient had developed gastrointestinal problems. It is unclear if the gastrointestinal problems were caused by the raw food diet or age.

Case 5 : 3 year old neutered male Staffordshire bull terrier located in Norway.

History:

As early as 6 months old, the owner noticed that the patient started to develop severe purities on the 4 paws with slight alopecia around the ears, ventral abdominal and inguinal area. Aggressive form of otitis externa could be observed as well as frequent scratching and paw biting. Having done IDT, the chicken protein allergen of AD was identified but seasonal allergens (eg. pollen and mold) and environmental triggers (eg. dust mites, house mites, etc.) could not. Local veterinarian prescribed Apoquel and a commercial lamb based diet. The patient did try ASIT but the therapy was ineffective.

Diet:

The patient is currently on Eukanuba large breeds adult Lamb and Rice diet with Apoquel taken daily. Apoquel was taken on a daily basis since mid-2020. Once, the owner stopped the Apoquel for a few days and there was an aggressive AD flare-up. Owner went back to using Apoquel daily. Medicated baths would be given occasionally along with regular ear cleaning.

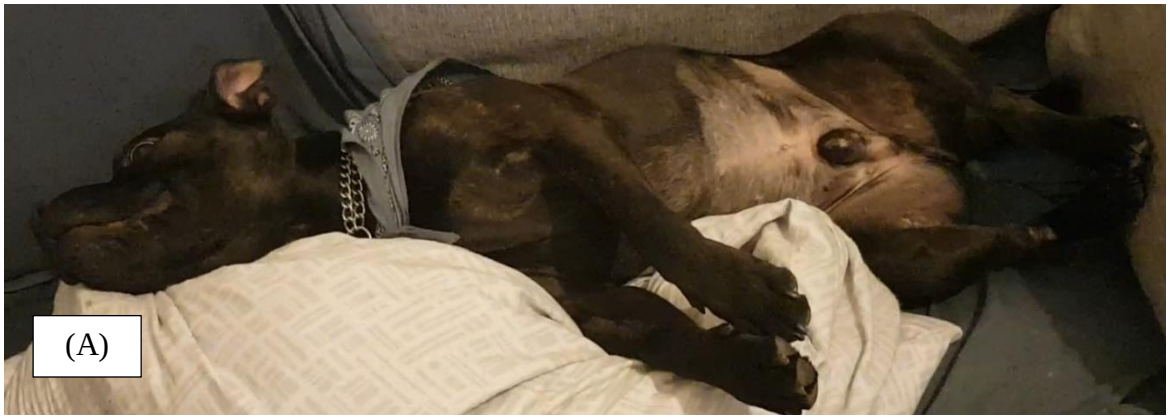

Figure 6: B) Picture was taken in February 2021 with barely noticeable ball spot in the ventral abdomen and inguinal area. There is a slight redness on the ears. This is 8 months into using Apoquel.

It is worth noting that around the 1 year mark of using Apoquel, the patient suffered from 5 spontaneous vomiting on 5 separate occasions. There was no conclusive diagnostics as to the cause of the vomiting but on all occasions stress was a factor (eg. travelling from Norway to Hungary and vice versa.)

10. Discussion

Out of 52 participants, only 3 (5.77%) dogs remain on a home curated diet. Although 14 dogs tried a non-commercial food diet, 2 dogs had to revert back to kibbles due to gastrointestinal related problems. One of the main concerns of the owners was that if they curated their own home-prepared meal, would it be a balanced diet with enough nutritional value for their dogs. Multi-faceted approach should be taken to treat dogs with AD.

"Prevention is better than cure"-Desiderius Erasmus

The best way to control any flares of CAD is:

(i) Re-establish the skin barrier function
(ii) Reduction in inflammation
(iii)Prevention and/or control of dietary hypersensitivity.

(i) <u>Reinforcement/reestablishing of the Skin Barrier Function</u>

Waltham Research Center conducted a study with keratinocytes cultures and discovered the nicotinamide (Vitamin B3), pantothenic acid, histidine, inositol and choline are good nutrients that help improve the structure and functions of the skin. Other nutrients like pyridoxine (Vitamin B6) and proline stimulates the synthesis of ceramides. [62]

Table 7: Concentrates of nutrients from different foods. Data taken from the US department of agriculture [63]

	Milligrams (mg) per 100g						
Foods	Vitamin B3	Pantothenic acid	Histidine	Inositol	Choline	Pyridoxine	Proline
Beef	6.88	0.552	0.79	37	56.4	0.4	0.948
Chicken	5.05	1.2	0.631	30	75.3	0.4	0.75
Turkey	8.09	0.845	0.584	23	52.3	0.6	0.562
Salmon	7.995	1.03	0.549	20	94.6	0.6	0.721
Tuna	9.92	0.28	0.688	15	65	1	0.827
Pork	7.914	0.86	0.917	42	73.4	0.5	1.499
Rabbit	6.5	0.8	0.82	-	0	0.47	1.42

Venison	6.6	0	1.49	-	0	0	1.56
Horse	4.6	0	1.08	-	0	0.33	1.31
Lamb	5.96	0.65	0.89	-	0	0.17	1.18
Duck	3.444	0.77	0.62	-	65	0.76	1.15
Brown rice	5.05	1.493	0.202	30	21.5	0.1	0.121
White rice	1.6	1.014	0.168	15	5.8	0.1	0.187
Broccoli	0.619	0.573	0.059	30	18.7	0.175	0.11
Carrots	0.465	0.273	0.04	12	8.8	0.12	0.034
Potatoes	1.4	0.56	0.04	50	14.5	0.3	0.07
Sweet potatoes	0.56	0.8	0.03	50	12.3	0.21	0.05

(ii) <u>Reduction in inflammation</u>

Polyunsaturated Fatty Acids (PUFA)

Lipids play an important role in preventing TEWL and inflammatory reactions. Omega 3 and omega 6 PUFA may be used to control skin inflammation, restore integrity of the hydrolipidic layer and limit the transcutaneous penetration of allergens, bacterial and fungal infections. It also helps with the maturation and differentiation of stratum corneum. [64] In 2004, Saevik, B.K found that PUFA could reduce the dose of long-term corticosteroid therapy. [65]

Table 8. Foods high in Omega 3 and Omega 6 PUFA. [63]

	Milligrams (mg) per 100g	
Food	Omega 3	Omega 6
Sunflower oil	0.192	3.606
Corn oil	1.161	53.515
Canola oil	9.137	19.005
Soybean oil	5.136	45.3
Olive oil	0.761	9.762
Palm oil	0.2	9.1

Beef	0.064	0.251
Chicken	0.104	7.421
Turkey	0.037	3.441
Salmon	0.047	0.081
Tuna	0.002	0
Pork	0.035	3.769

Essential vitamins and nutrients.

Vitamin E is a lipid-soluble non-enzymatic vitamin. Many studies have documented vitamin E as a highly efficient antioxidant and anti-inflammatory agent. [66], [67]. There are eight types of vitamin E (α-,β-,γ-, and σ-tocopherols and their related corresponding tocotrienols), γ-tocopherol being the most abundant tocopherol in diet, whereas α-tocopherol (α-Toc) is the most abundant vitamin E derivative in human tissues and sera. [68] Plevnik Kapun conducted a study in 2014 on twenty-nine dogs with CAD to determine the relationship between vit E supplements and their effect of CAD. Fourteen dogs received vitamin E (8.1 IU/kg once daily, orally) and 15 received mineral oil as placebo (orally). The results shows that significantly higher plasma levels of vit E and total antioxidant capacity (TAC) were observed in the vit E group compared to the placebo group. CADESI-03 scores determined throughout the treatment in the vit E group were significantly lower than in the placebo group. [69] Another study done by Teo in 2021 reviewed the benefits of vit E in CAD with more recent clinical data. [70] Vit E can be synthesized by plants and must be obtained through dietary sources. Richest sources are nuts, spinach, whole grains, olive oil, and sunflower oil.[68].

Table 9. Foods high in vitamin E. [63]

	Nuts	Spinach	Whole grain	Olive oil	Corn Oil	Sunflower oil
Milligrams (mg) per 100g	4.9-19	2.03	0.38 (bread)	14.35	22.6	41.08

Turmeric contains curcumin which can also benefit dogs suffering from AD, through mechanisms that are focused on the immune response (inhibition of mast cell activation, inhibition of lipoxygenase and cyclooxygenase synthesis, immunoglobulins, etc). [71]

Licorice root extract could provide an immunomodulatory benefit. A constituent of licorice, the triterpenoid saponin glycyrrhizin, has demonstrated the ability to suppress interleukin (IL)-4 levels and restore the immune balance of T helper (TH1/TH2) cells in a mouse allergy model. [72]

(iii) <u>Prevention or control of dietery hypersensitivity</u>

In the Encyclopedia of Canine Clinical Nutrition by Pascale [61], commercial diets labeled as "hypoallergenic" or "for allergic dermatitis" can be differentiated into 3 categories.

I. Diets with protein derived from selected sources are not suitable for elimination diet as the protein sources are highly diverse.
II. Diets with proteins deriving from selective sources are more suitable for elimination diets.
III. Curated diets with protein hydrolysates are in principle less allergenic than non-hydrolyzed preparations. The goal of hydrolysate is to fractionate the proteins into small peptides of low molecular weight, making the food intrinsic antigenic and easier to digest. This makes this diet the most suited as a commercial elimination diet.[59],[60]

" Let food be thy medicine and medicine be thy food"- Hippocrates (460-377BC)

By using the correct diet, we aim to re-establish the skin barrier function, reduce inflammation and prevent/control any hypersensitivity and AD flares. As was previously discussed, skin barrier function plays a pivotal role in the prevention of CAD flares. Intercellular cement formed by the ceramides is defected in dogs with AD. [7] This causes TEWL which subsequently causes an increased transcutaneous penetration by antigens; allowing increased adherence of bacteria to the surface of the corneocytes.

There are 2 examples of a non-commercial food diet in Appendix 6 suggested by Pibot. [61] In 2021, Watson conducted a study that lasted for 9 months on forty

privately owned dogs to evaluate the benefits of a therapeutic diet and its effects against pruritus of CAD. Those forty dogs were split at random into 2 groups. 1 group was given the test diet and the other was a placebo. Concentrates of the key nutrition from the 2 diets are located in figure 7. Pruritus of the dogs was evaluated using CADESI-04 at the beginning of the study, the subsequent 1st, 3rd, 6th and 9th month.

Figure 7. Concentrations of key nutritional components of the two diets fed during the study. Details of the diets are given for the proximates and a group of other ingredients which differed significantly between the Test (Flame) and Control (Ice) diets. [74]

	Units	Flame	Ice
Dry matter	%	90.50	90.51
Moisture	%	9.50	9.49
Protein	%	22.54	22.51
Fat	%	13.97	13.99
Ash	%	6.90	6.89
CFIB (crude fibre)	%	2.90	2.90
Linoleic acid	%	3.90	2.20
EPA+DHA	%	0.54	0.01
Vitamin E	mg/kg	900.64	162.14
Taurine	mg/kg	4500	600
Lutein	mg/kg	5	0.74
Curcuma extract	mg/kg	300	0
Licorice root extract	mg/kg	200	0

The results after the 9 month study showed that the dogs from the test group showed a significant decrease in the CADESI-04 score. Dogs from the control group had unchanged pruritus. This proves that with the right diet, CAD can be kept in check. [74]

11. Conclusion

Food plays a fundamental role in AD as it is the primary defense against any AD flares and immune-mediated inflammatory disease (IMID). Therefore the study of animal nutrition goes hand-in-hand when it comes to the treatment of dermatological diseases. Whether it is from a commercial food diet or a home curated meal, understanding and striking a balance in nutrition is vital in combating AD.

When asked for a reason as to why the owners switched back to commercial food diets, 9 of these owners gave almost the same answer as listed below:

1. It was time consuming to curate the diet.
2. Overall cost to curate the diet was expensive.
3. Owners were not confident that they were creating a balanced diet for their dogs.
4. Lack of animal nutritionists to guide these owners.
5. Modern medicine like Apoquel and Allergen-specific immunotherapy (ASIT) made controlling the AD flare-up much more effective.

Likewise, when asked about why they never put their dogs on a home curated meal, the other 38 participants gave the following answers.

1. Commercial food diets are balanced diets.
2. Although they are more expensive than regular dog kibble, it is still cheaper and less time consuming than making a home-curated meal.
3. Local veterinarians had recommended these commercial food diets along with medicine and ASIT.

The 3 remaining owners whose dogs are still on home curated meals were asked why they switched and remained on their current diet. Their reasons were:

1. Dogs reacted poorly to commercial food diets
2. Owners had their doubts that commercial hypoallergenic diets were providing enough nutritions and vitamins for their dogs.
3. Dogs preferred the home curated food compared to the commercial food diet.

With all these reasons in mind, it is essential that we continue to challenge the current therapeutic management of AD on a daily basis. That includes being aware of the nutritional content of commercial food diets, the importance of a balanced nutritional home

curated meal, the value of IgE doses of dietary allergens, the absence of flea/mites infestation opportunities, modern methods in AD diagnosis and treatment.

The course of action to prevent AD is a combination of good diagnostics of AD flares, eliminating and avoidances of AD trigger factors, optimizing skin care, reducing skin lesions and pruritus, and also the prevention of the reccurrence of AD after remission.

Selecting a good balanced diet is an essential part of managing AD. When selecting a commercial food diet, opt for diets that contain hydrolysed protein that makes the diet much easier to digest. If home curated meals are used, foods containing nicotinamide (Vitamin B3), pantothenic acid, histidine, inositol and choline are great as they help to restore the skin barrier function. Omega-3 and 6 PUFA are crucial to help suppress any inflammatory responses to AD. Additional foods containing Vit E, turmeric and licorice root are also very beneficial to the skin.

Although one of the goals of this thesis was to determine the best diet catered to AD prevention, based on data collected from this study, it is clear that the treatment of canine AD must be individualized for each patient. Not all interventions will work for every patient; drugs will not be equally effective for and/or tolerated by every dog. Veterinarians should treat each AD case based on medical principles recommended by the International Committee on Allergic Diseases of Animals (ICADA). At the same time, take into consideration the preference of the dog owner be it cost or ease of the various interventions. The quality of life of each patient is of utmost importance and it is our duty as veterinarians to provide the best solutions catering to each of their needs.

12. Summary

Atopic dermatitis (AD) is a common chronic relapsing pruritic skin disease of dogs. It is genetically inherited and remains with the dog throughout its life. Due to its complex pathogenesis, studies are constantly being conducted to further understand the disease. Its clinical manifestation is multifactorial and can be associated with exposure to food and/or environmental allergens. Each dog has its unique manifestation of the disease. Different veterinarians from different parts of the world use different approaches for treating AD. A multi-faceted approach should be taken to treat dogs with AD. That includes proper diagnostic guidelines provided by the ICADA, eliminating and avoidances of AD trigger factors, optimizing skin care, reducing skin lesions and pruritus, and also the prevention of the recurrence of AD after remission. Finding a balanced nutritious diet is crucial in combating AD. Many commercial hypoallergenic diets are being produced by many companies but not all dogs will respond favorably to the diet. Some owners resort to curating their own unique diets to keep AD at bay and in remission. These owners are willing to put in the extra effort, time and resources to help relieve their beloved pets of their suffering.

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16. Appendices

Appendix 1: Data Collection on Canine Atopic Dermatitis

1. Type of canine breed and country of origin.

   _____

2. Sex of the canine. [mark 'X']
   - ☐ Neutered Female
   - ☐ Unneutered Female
   - ☐ Neutered Male
   - ☐ Unneutered Male
3. Age of canine.

   _____

4. Severity of Atopic Dermatitis.
   - List as much information as possible about the canine AD.
   - Clinical symptoms.
   - Seasonal or non-seasonal AD?
   - Pruritis? Otitis externa? Conjunctivitis? Rhinitis? seborrhea sicca/oleosa? Pyoderma? Alopecia?

   _____

   _____

   _____

   _____

   _____

   _____

   _____

   _____

   _____

5. Any significant medical problems and history.
   - Current/past medication.eg. Cardiovascular disease? Liver problems?
   - Use of Corticosteroids? Antihistamine? Apoquel?

   _____

   _____

   _____

_____

_____

6. Type of Diet. [mark ‘X’]
   - □ Commercial dog food
   - □ Non-commercial food diet
7. Food brand/ Diet Content
   - Food brand of commercial diet (eg. Royal Canin hypoallergenic, Eukanuba Adult Small breed, etc)
   - Raw food content. Is the diet cooked or raw? “Boiled chicken? Carrots? Raw turkey neck? Etc.”
   - Are any additional supplements taken? Glucosamine? Multivitamins?

_____

_____

_____

_____

_____

_____

8. Any Additional information or comments you would like to add.

_____

_____

_____

_____

_____

Appendix 2: Sets of criteria and associated sensitivities and specificities.

Set 1:

1. Age at onset <3 years
2. Mostly indoor
3. Corticosteroid-responsive pruritus
4. Chronic or recurrent yeast infections
5. Affected front feet
6. Affected ear pinnae

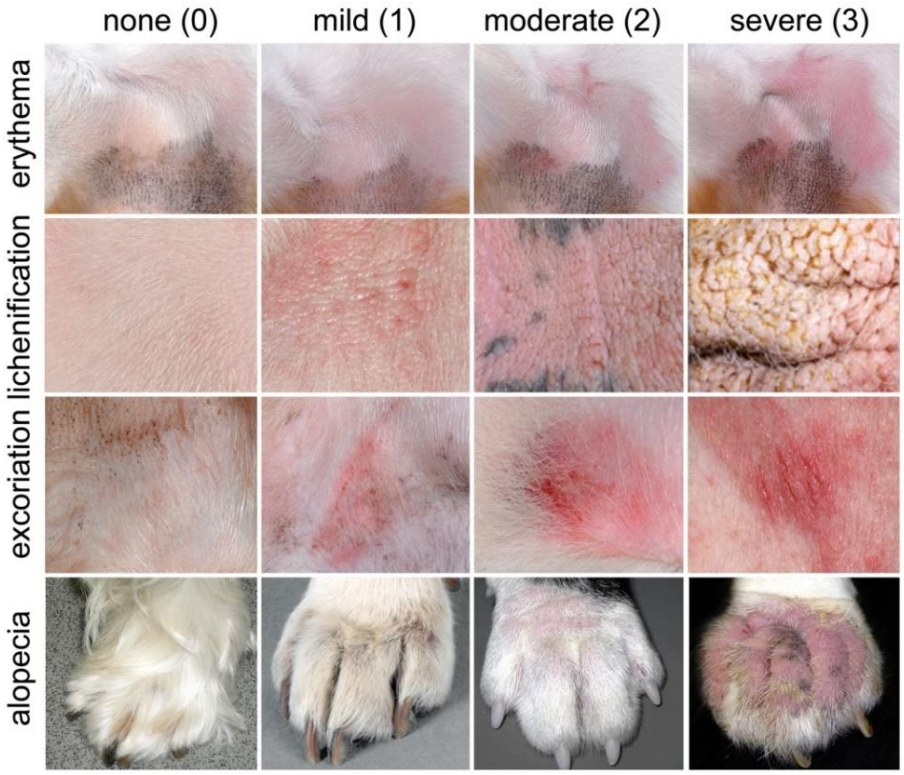
7. Non-affected ear margins
8. Non-affected dorso-lumbar area

Set 2:

1. Age at onset<3 years
2. Mostly indoor
3. Pruritus sine material at onset
4. Affected front feet
5. Affected ear pinnae
6. Non-affected ear margins
7. Non-affected dorso-lumber area

	CAD dogs				FIAD dogs			
	5 criteria		6 criteria		5 criteria		6 criteria	
	sens.	spec.	sens.	spec.	sens.	spec.	sens.	spec.
SET 1	0.854	0.791	0.582	0.885	0.802	0.857	0.541	0.857
SET2	0.772	0.83	0.42	0.937	0.703	0.857	0.355	1

Appendix 3 : CADESI-4 lesion grading atlas



Appendix 4 CADESI-4 grading sheet

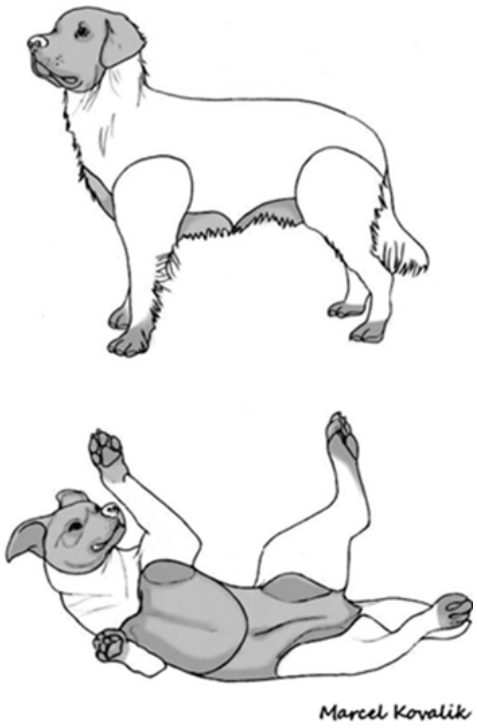
CADESI-04 (ICADA)			Erythema	Lichenification	Excoriations and/or Alopecia	TOTAL
Perilabial Area *(left and right combined)*		1				
Medial Pinnae (concave pinnae)	Left	2				
	Right	3				
Axillae	Left	4				
	Right	5				
Front Paws *(dorsal and palmar sides combined)*	Left	6				
	Right	7				
Hind Paws *(dorsal and plantar sides combined)*	Left	8				
	Right	9				
Cubital Flexor *(elbow folds)*	Left	10				
	Right	11				
Palmar Metacarpal *(from carpal to metacarpal pads)*	Left	12				
	Right	13				
Flanks	Left	14				
	Right	15				
Inguinal Areas *(groin)*	Left	16				
	Right	17				
Abdomen		18				
Perineum *(from vulva/scrotum to anus)*		19				
Ventral Tail *(proximal)*		20				
grade each site and each lesion type: *none: 0; mild: 1; moderate: 2; severe: 3*			**TOTAL Score** (20 x 3 x 3 = 180)			

Appendix 5 : Canine Atopic Dermatitis Lesion Index (CADLI) developed by Plant J.D in 2012 [55].

Canine Atopic Dermatitis Lesion Index (CADLI)

Score each of the indicated body regions, integrating the severity and extent of the lesion(s) in the area.
(0 = none; 1 = mild; 2, 3 = moderate; 4, 5 = severe and extensive lesions)
Consult the CADLI Guide for examples of lesion scoring.

Body region	Erythema excoriation erosion 0-5	Alopecia lichenification hyperpigmentation 0-5
Head & Pinnae		
Forefeet		
Hind feet		
Ventral thorax & Axillae		
Ventral abdomen & Inguinal		
Sub-totals 0-25		
Total 0-50		



Appendix 6 : Non-commercial elimination diet suggested by Pibot [61]

Example 1 of non-commercial ellimination diet.

COMPOSITION
(1000 g diet)

Venison, back ..... 475 g
Potato, cooked, with skin ..... 500 g
Rapeseed oil ..... 25 g

Add a well-balanced mineral and vitamin supplement.

ANALYSIS

The diet prepared in this way contains 27% dry matter and 73% water

	% dry matter	g/1000 kcal
Protein	43	102
Fat	16	37
Available carbohydrate	29	68
Fiber	3	7

Key Points

- **Control raw ingredients used**
  - Use of a single source of highly digestible proteins, against which the dog is not sensitized (i.e. has not previously consumed)
  - Use of a single source of extremely digestible carbohydrate
- **Palatability** to facilitate the strict observation of the diet

INDICATIVE RATIONING

Energy value (metabolizable energy) 1140 kcal/1000 g of diet prepared (4250 kcal/1000 g DM)

Dog's weight (kg)**	Daily amount (g)*	Dog's weight (kg)**	Daily amount (g)*
2	190	45	1980
4	320	50	2140
6	440	55	2300
10	640	60	2460
15	870	65	2610
20	1080	70	2760
25	1270	75	2910
30	1460	80	3050
35	1640	85	3190
40	1810	90	3330

**The rationing is offered in accordance with the dog's healthy weight. In case of obesity, the rationing must be prescribed in accordance with the ideal weight and not the real weight of the dog.*
***The quantities can be adapted as the dog's weight develops, but no other ingredients must be incorporated into the ration and no supplements must be given.*

Example 2 of non-commercial elimination diet.

COMPOSITION
(1000 g diet)

Duck	500 g
Rice, cooked	480 g
Cellulose	10 g
Rapeseed oil	10 g

Add a well-balanced mineral and vitamin supplement.

INDICATIVE RATIONING

Energy value (metabolizable energy) 1325 kcal/1000 g of diet prepared (4480 kcal/1000 g DM)

Dog's weight (kg)**	Daily amount (g)*	Dog's weight(kg)**	Daily amount (g)*
2	170	45	1700
4	280	50	1840
6	380	55	1980
10	550	60	2120
15	750	65	2250
20	930	70	2370
25	1100	75	2500
30	1260	80	2620
35	1410	85	2750
40	1560	90	2870

ANALYSIS

The diet prepared in this way contains 30% dry matter and 70% water

	% dry matter	g/1000 kcal
Protein	37	82
Fat	14	31
Available carbohydrate	43	95
Fiber	4	9

Contra-indications

For a puppy a commercial low-allergenic diet is preferable until the end of the growth phase

Appendix 7 Supervisor counter-signatute form

I hereby confirm that I am familiar with the content of the thesis entitled

Comparative Dietetics of Home Curated Diet versus Commercial Food Diets and their Effects on Canine Atopic Dermatitis

written by **Cheryl Ann Lim Chieh Yee** which I deem suitable for submission and defence.

Date: Budapest, 16. 12. 2021

ÁLLATORVOSTUDOMÁNYI EGYETEM
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