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A systematic review of the evidence of reduced allergenicity and clinical benefit of food hydrolysates in dogs with cutaneous adverse food reactions

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Abstract

Several hydrolysate-based diets have been commercialized for helping diagnose or treat dogs with cutaneous adverse food reactions (CAFR). This systematic review was performed to examine the evidence in favour of reduced immunological and clinical allergenicity of hydrolysates in dogs with CAFR. Citation databases, meeting abstracts and article bibliographies were scanned for relevant citations, and companies were contacted to provide unpublished reports. Eleven studies relevant to this study were identified. Some evidence of reduced serum IgE binding to a soy hydrolysate (1 study) and decreased intradermal test reactivity to hydrolysed proteins (three studies) was found. In four reports, the feeding of dogs suspected of having CAFR with hydrolysate-based diets reduced or eliminated clinical signs in a variable proportion of subjects. The percentage of dogs with CAFR that still reacted to these hydrolysate-based diets could not be assessed, however. Importantly, up to 50% of dogs with CAFR enrolled in three controlled studies exhibited increases in clinical signs after ingesting partial hydrolysates derived from foods to which they were hypersensitive. In conclusion, the limited number of studies undertaken point to reduced – but not eliminated – immunological and clinical allergenicity of hydrolysate-based commercial diets. A variable proportion of dogs with CAFR will exhibit a worsening of clinical signs when fed partial hydrolysates. Clinicians must weigh the clinical benefit of these diets versus their high cost and low risk of reduced appetence or gastrointestinal sign development. At this time, hydrolysate-containing diets are probably best used in dogs suspected not to be hypersensitive to their individual components.

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Introduction

In dogs, adverse food reactions (AFR) are relatively common causes of nonseasonal pruritus with or without accompanying skin lesions.[1–7] Based on the type of disease pathogenesis, cutaneous AFR have been subdivided in either immunological food allergies or non–immune-mediated food intolerances.[7,8] To date, results of studies on the mechanism underlying experimental or naturally occurring cutaneous AFR (CAFR) in dogs have uncovered the presence of food-specific serum IgE reaginic antibodies,[9–15] food allergen-induced leucocyte histamine release,[16] food allergen intradermal immediate reactivity[9,13,16] and activated food allergen-specific T-lymphocytes.[17,18] These findings suggest that canine AFR might often be, *in fine*, food allergies.

In humans with 'classic' type I food hypersensitivities, serum IgE usually bind allergenic epitopes on proteins weighing more than 10 kDa (for an updated list of food allergens in humans, see[19]). Only rare food allergens have been defined in dogs, but so far, all recognized allergic proteins also have weighted more than 20 kDa.[20,21]

Taking advantage of the knowledge that IgE epitopes in food allergens usually are born by large proteins, the concept of hydrolysing them into smaller fragments that do not cross-link IgE molecules on the surface of mast cells was set forth decades ago for use in children with cow's milk allergy (CMA). In infants with a high risk of development of CMA, practice guidelines from several paediatric associations have recommended the use of formulas with reduced allergenicity (reviewed in[22]). This recommendation is supported by the findings of a systematic review that compared the efficacy of amino-acid-based formulas to that of hydrolysed milk or nondigested soy formulas in patients with proven CMA.[23] While amino-acid-based and extensively hydrolysed formulas seem equally effective at relieving signs of CMA, patients drinking partially hydrolysed formulas appear to remain at risk of development of clinical signs of allergy. In contrast, a 2006 Cochrane systematic review found that there was no evidence to support a higher benefit of feeding a hydrolysed formula over exclusive breast feeding for the prevention of food allergy and intolerance in children.[24] In summary, studies of children with CMA have established that only amino-acid-based and extensively hydrolysed formulas (i.e. those with peptides weighing less than 3000 kDa) might be considered truly hypoallergenic, and this reduced allergenicity

might solely apply to IgE-based immediate hypersensitivities. Importantly, partially hydrolysed formulas (i.e. those with peptides weighing 3000–10 000 kDa) can lead to development of clinical signs in a substantial fraction of hypersensitive infants.[25,26]

As an aid for diagnosis or treatment of AFR, dogs are fed homemade or commercial diets that usually contain novel ingredients.[7] If a diet that had inherent hypoallergenic properties were to be developed, it would be of additional value compared to novel ingredient-based ones, as allergic subjects would have a lower risk of developing reactions to it, even if they were hypersensitive to one or more of its components. For these reasons, diets containing hydrolysates have been commercialized for several years assuming the theoretical postulate that such foods would be of reduced allergenicity compared to non-digested ones.[27]

The main objectives of this systematic review were to answer the following two questions related to the hypoallergenicity of hydrolysate-containing diets:

1. In dogs with experimental or spontaneous food allergy, do hydrolysed proteins exhibit reduced immunological allergenicity (e.g. decreased IgE binding or intradermal reactivity) compared to their native nonhydrolysed precursors?
2. Does the administration of hydrolysate-containing diets lead to reduced pruritus or skin lesions in dogs with CAFR, and especially in dogs allergic to the native nonhydrolysed proteins?

Materials and methods

Search strategy for identification of studies

Relevant experimental or clinical studies were identified by searching two databases twice, on 31 March and 6 June 2008: MEDLINE (from 1966) and ISI's (Thomson) Science Citation Index Expanded (from 1945). The following search strategy was used for both databases:

1: dog or dogs or canine
2: food or diet*
3: allerg* or hypersensitiv* or reaction
4: hydroly*
5: 1 AND 2 AND 3 AND 4

To identify additional relevant studies, other searches were done: the bibliography of all selected articles was scanned for possible relevant references, companies marketing canine hydrolysate-based diets were contacted to provide citations and details of any relevant studies, and published abstracts from annual meetings of the European Society of Veterinary Dermatology, European College of Veterinary Dermatology, American Academy of Veterinary Dermatology, American College of Veterinary Dermatology or World Congresses of Veterinary Dermatology between 1995 and 2008 were hand-searched.

There were no restrictions on years considered, publication status or language of the works.

Criteria for considering studies for this review

This review includes reports of experimental studies and clinical trials, open or blinded, and randomized or not. Study participants could be laboratory dogs with experimentally induced or spontaneous food hypersensitivity, or client-owned dogs suspected of, or proven as, having pruritus or skin lesions exacerbated by their diet (e.g. dogs with CAFR).

Experimental studies had to report either the comparison of *in vitro* IgE binding to hydrolysed food proteins in serological tests, or the results of *in vivo* reactivity to hydrolysed food extracts in intradermal tests (IDT). Clinical studies had to test the variation of pruritus and/or skin lesions after feeding a hydrolysate-containing diet.

Outcome measures

In view of the anticipated variability in study designs and outcome assessment, there were no strict standardized outcome measures. Instead, for each study the experimental design and arguments in favour of any reduced allergenicity of the tested hydrolysates were evaluated. In general, the evidence for the following three points was examined:

a. decreased IgE binding to hydrolysed extracts compared to their native parent in serological tests, or
b. decreased IDT reactivity to hydrolysed extracts compared to their native parents, or
c. decreased pruritus and skin lesions after feeding hydrolysate-containing diets to hypersensitive laboratory dogs or client-owned dogs with suspected or proven CAFR.

Data abstraction

The searches were done by one of the authors (TO); data were extracted and presented in tabular form. Study assessment and detailed outcome measures were verified independently by the second author (PB). Discrepancies were resolved by consensus. Because of heterogeneity of study designs and outcome measures, as well as the scarcity of controlled studies, data were not pooled together and statistical analyses were not performed.

Results

Searches and characteristics of included studies

The results of the study search are summarized in Figure 1. Studies were identified in either database searches, meeting abstracts, bibliographies or after contacting technical veterinarians associated with commercial dog food companies. In total, 11 relevant studies that reported results of experiments performed using laboratory dogs (five studies)[13,28–31] or findings from clinical trials (six studies) were selected.[32–37] We excluded four reports that either did not provide relevant data using hydrolysates[38,39] or that described results of IgG but not IgE binding to intact and hydrolysed proteins.[40,41] The latter two references, however, appear to correspond to the same set of experiments. The summary of the characteristics of the included studies can be found in Table 1.

Studies of serum IgE binding to hydrolysed and intact proteins

Only one study testing the binding of serum IgE to intact and hydrolysed proteins was identified by our search strategy (Table 2).[30] In this experimental study, six laboratory beagles were sensitized against native soy proteins by repeated subcutaneous injections of proteins in alum. When the subjects were 2 years old, serum IgE from sensitized dogs identified soy allergens varying between 20 and 75 kDa. When whole hydrolysed soy (Nurish 1500, Solae, Iper, Belgium) was used as a substrate for immunoblotting, only two low-intensity diffuse bands were recognized by serum IgE from one of six dogs. Immunoblotting performed using the whole soy hydrolysate fractionated by ultrafiltration revealed that the circulating IgE from that particular dog only bound to soy allergens in the fraction containing proteins greater than 50 kDa. IgE binding to lower molecular weight fractions was not detected.

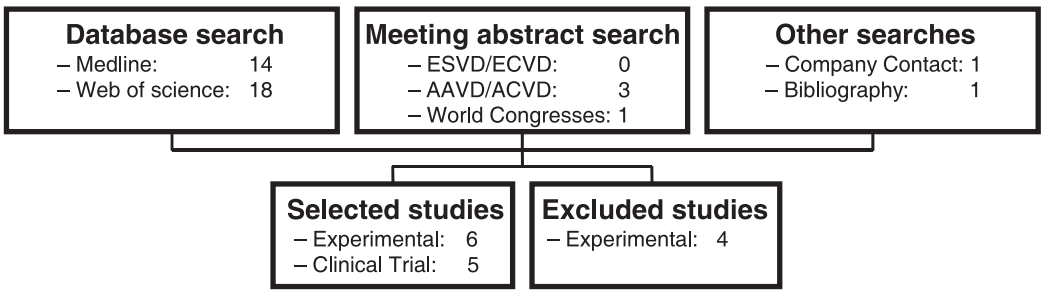

Figure 1. Search strategy diagram.

Table 1. Characteristics of included studies

Study	Reference	Sponsor	Experimental or spontaneous sensitizations	Subjects	Relevant outcome measures
Groh and Moser 1998	32	Not specified	Spontaneous	29 client-owned dogs with pruritus suspected of having cutaneous adverse food reactions	Unclear
Olson *et al.* 2000	28	Iams	Experimental	14 laboratory dogs: 11 sensitized to casein, soy and chicken liver + 3 controls	IDT, skin lesions, pruritus
Sousa *et al.* 2000	33	Purina	Spontaneous	24 client-owned dogs with signs of cutaneous adverse food reaction	Pruritus
Beale and Laflamme 2001	34	Purina	Spontaneous	10 client-owned dogs with corn or soy sensitivity	Pruritus
Jackson *et al.* 2003	13	Purina	Spontaneous	14 laboratory dogs hypersensitive to corn and soy	Skin lesions*
Biourge *et al.* 2004	35	Royal Canin	Spontaneous	60 client-owned dogs with pruritus suspected of having skin hypersensitivity	Pruritus
Loeffler et al. 2004	36	Hill's	Spontaneous	63 client-owned dogs suspected of allergic skin or ear diseases	Pruritus
Loeffler *et al.* 2006	37	Hill's	Spontaneous	181 client-owned dogs with nonseasonal pruritus (includes those of Loeffler *et al.* 2004)	Pruritus
Puigdemont *et al.* 2006	29	Royal Canin	Experimental	12 laboratory dogs: 9 sensitized to soy + 3 controls	IDT, skin lesions, pruritus*
Serra *et al.* 2006	30	Royal Canin	Experimental	8 laboratory dogs: 6 sensitized to soy + 2 controls; same dogs as in Puigdemont *et al.* 2006	IDT, immunoblotting
Ricci *et al.* 2006	31	Purina	Spontaneous/ Experimental	26 (phase I) or 12 (phase II) laboratory dogs with clinical response to intact soy or chicken	Skin lesions, pruritus†

*ELISA tests for soy IgE were performed, but not with the soy hydrolysed proteins. The results, therefore, were not considered relevant to this review.
†ELISA tests for chicken IgE were performed, but not with the chicken hydrolysed proteins. The results, therefore, were not considered relevant to this review. IDT, intradermal test.

Studies of intradermal tests with hydrolysed and intact proteins

Three reports of IDT reactivity to intact and hydrolysed extracts in experimentally sensitized dogs were found.[28–30]

In the first study,[28] 11 crossbred sled dogs were sensitized to casein, chicken liver and soy proteins by repeated subcutaneous injections of antigen in alum. At the end of the sensitization period, when the dogs were approximately six months of age, IDT were performed using decreasing amounts of extracts made from intact or 1, 2, 5 10, 20 and 50% hydrolysed casein, intact or hydrolysed chicken liver, intact soy or three test diets: Exclude (DVM Pharmaceuticals, St Joseph, MO, USA; a hydrolysed casein and chicken liver-containing diet), HA-Formula (Nestle-Purina, St Louis, MO, USA; a hydrolysed soy-containing diet) or a proprietary hydrolysed chicken liver test diet (unknown name, Iams, Lewisburg, OH, USA) (Table 2). Of note is that electrophoresis of the various hydrolysed casein fractions still revealed some nondigested proteins except for the 50% hydrolysed sample, which did not contain any.

The sensitization protocol induced highly variable serum allergen-specific IgE in the study subjects, with two, five and four dogs having elevated IgE levels specific for three, two or one sensitizing antigens, respectively. In contrast, at the end of the sensitization period, all 11 dogs exhibited positive dose-dependent IDT reactions to the three immunizing antigens.

Intradermal reactivity to the 1, 2, 5, 10 and 20% hydrolysed casein were not significantly different from those of the intact proteins, and three dogs reacted 'more severely' to hydrolysates than to native protein extracts. 'Fewer dogs' (exact number unknown) reacted to the 50% casein hydrolysate, and the diameter of reactions was smaller with this extract than with the intact casein. Intradermal test reactions to Exclude, HA-Formula or the chicken hydrolysate test diet were usually smaller than

Table 2. Evidence of immunological hypoallergenicity

Study	Reference	Procedure	Relevant results
Olson *et al.* 2000	28	Intradermal injections of 100 μg, 10 μg, 1 μg and 1 ng of intact casein, 1, 2, 5, 10, 20 and 50% hydrolysed caseins, chicken liver, hydrolysed chicken liver, soy protein, Exclude*, HA-Formula† and a hydrolysed chicken liver test diet	Decreasing sizes of reaction with decreasing extract concentrations; fewer dogs reacted to 50% casein hydrolysate than to casein; reactions to 100 and 10 μg of commercial or test diets were smaller than corresponding intact proteins
Puigdemont *et al.* 2006	29	Intradermal injections of 4 μg, 400 ng and 40 ng of intact and hydrolysed soy proteins	Mean wheal areas of hydrolysed soy protein injections were smaller than those of the intact proteins
Serra *et al.* 2006	30	Same as Puigdemont *et al.* 2006	Mean wheal areas of hydrolysed soy protein injections were smaller than those of the intact proteins; no reaction to soy hydrolysate fractions < 10 kDa; increasing reactivity with fractions of increasing molecular weight
Serra *et al.* 2006	30	Immunoblotting	Sera from 6 of 6 sensitized dogs (100%) reacted to intact soy (5 reacted weakly), only 1 of these 6 dogs (17%) reacted weakly to hydrolysed soy

*Exclude, DVM Pharmaceuticals: hydrolysed casein and chicken, oats, pinto beans and tallow.
†HA-Formula, Nestle Purina: hydrolysed soy, cornstarch canola and coconut oil.

those with corresponding native protein sources, especially when injections were made with 100 and 1 μg of protein.

Although eight of the sensitized dogs (73%) were found to develop diarrhoea and weight loss with or without pruritus and alopecia when fed diets consisting of soy, casein and chicken liver at 11 months of age, the clinical effect of feeding hydrolysed test or commercial hydrolysate-containing diets was not investigated nor reported, regrettably.

The other two papers reported data from the same set of dogs sensitized as described in the preceding section.[29,30] In the first of these two reports,[29] IDT was performed 1 month after the end of sensitization to compare the reactivity to intact or whole soy hydrolysate (Nurish 1500, Solae, Iper, Belgium). Intradermal injections of whole hydrolysed soy still induced positive reactions in sensitized dogs, but the mean wheal surface areas after intradermal injections of 40 ng, 400 ng and 4 μg of whole hydrolysed soy were significantly smaller than reactions to corresponding amounts of native soy proteins.

In the second report of the same set of experiments, IDT was performed as described in the first paper, but the timing of the test was not specified.[30] The interpretation of IDT results was similar to that of the first paper, but mean wheal areas were reported to be markedly smaller than in the preceding study. Additionally, positive IDT reactions were observed in the three most sensitized dogs to hydrolysed soy fractions weighing more than 10 kDa. Intradermal test results were negative with the two fractions containing proteins less than 10 kDa.

Studies testing the clinical allergenicity of hydrolysate-containing diets

Nine studies that reported the variability of clinical signs after feeding hydrolysate-containing diets (Table 3) were identified.[13,29,31–37] There were four open trials that tested the effect of an hydrolysate in client-owned dogs suspected of having a CAFR,[32,35–37] one open and one blinded study that reported the use of one hydrolysate in dogs with a likely diagnosis of CAFR[33,34] and two trials testing the effect of various hydrolysed ingredients in dogs from a colony with spontaneous or induced food allergies.[13,31] One additional study reported the clinical effect of whole hydrolysed soy in six sensitized beagles.[29] In the last report,[28] a dietary challenge with intact ingredients was mentioned, but a similar provocation test with hydrolysates was not reported.

The four open clinical trials had a similar design (Tables 1 and 3).[32,35–37] The last report[37] included cases described in the preceding paper from the same group.[36] Study subjects generally consisted of dogs with pruritus, with or without ear or skin lesions, in which common ectoparasites or microbial infections had been ruled out. Of particular importance, the real proportion of dogs with CAFR in the tested populations was not known in any of these studies.

Altogether, the total number of dogs enrolled – omitting the first of the duplicate publications – was 270, of whom 198 ate a hydrolysate-based food. Study subjects were usually fed hydrolysate-containing diets as an exclusive food source for durations that varied between 6 and 8 weeks. In one study, the dietary trial was shorter if signs had subsided earlier.[32] In the largest open trial,[37] dog owners were asked to choose between one hydrolysate-containing commercial food (109 dogs, 60%) or a homemade diet with novel protein and carbohydrate ingredients (72 dogs, 40%). In three studies, a provocation test with the original diet was performed if signs had abated with the tested hydrolysate-containing foods.[35–37]

With any of the three tested hydrolysate-containing diets (DVM's Exclude, Royal Canin's hypoallergenic diet and Hill's z/d Ultra allergen free), clinical signs improved or disappeared in a proportion of enrolled dogs that varied between 18% (complete improvement in[37]) and 69% (total or partial resolution of signs in[32]); details are presented in Table 3. In only one study were dogs with nonresolving signs after eating the hydrolysed food subsequently fed a second homemade or commercial diet.[35] In this trial, two of 20 dogs (10%) with a final diagnosis of CAFR had had

Table 3. Evidence of clinical hypoallergenicity

Study	Reference	Tested interventions	Duration of diet trials	Relevant results
Groh and Moser 1998	32	Open trial with Exclude*	8 weeks	20 of 29 dogs (69%) showed clinical improvement
Olson *et al.* 2000	28	Challenges with intact casein, soy, chicken liver; 1–50% casein hydrolysates; Exclude*, HA-Formula†, hydrolysed chicken liver test diet	Not specified	8 sensitized dogs (73%) developed pruritus and alopecia after eating diet with intact ingredients; data were not reported for hydrolysates
Sousa *et al.* 2000	33	Open trial with HA-Formula†	1 week	2 dogs (8%) experienced worsening in pruritus after eating HA-Formula
Beale and Laflamme 2001	34	RCT with positive and negative control diets or HA-Formula†	2 weeks	Veterinarian- and owner-assessed pruritus scores increased by more than 60% and 20% over baseline diet scores in soy-sensitive dogs eating HA-Formula; no such increase in corn-sensitive dogs
Jackson *et al.* 2003	13	Challenges with positive and negative control diets, intact corn, cornstarch, intact soy, HA-Formula†	2 weeks	3 dogs (21%) developed increases in lesional scores after eating HA-Formula, all of whom had reacted to intact soy and corn
Biourge *et al.* 2004	35	Open trial with hypoallergenic diet‡	8 weeks	20 of 58 dogs (34%) were diagnosed with uncomplicated adverse food reactions; in 2 of these dogs (10%) signs did not improve with hypoallergenic diet but improved after second dietary trial
Loeffler *et al.* 2004	36	Open trial with Canine z/d ULTRA§	6 weeks	Adverse food reaction diagnosed as sole cause of pruritus in 9/46 dogs (20%), concurrent atopy and adverse food reaction diagnosed in 9 other dogs (20%)
Loeffler *et al.* 2006	37	Open trial with Canine z/d ULTRA§ or homemade diets with novel proteins	6 weeks	Adverse food reaction diagnosed as sole cause of pruritus in 15 of 82 dogs (18%) eating z/d ULTRA, concurrent atopy and adverse food reaction diagnosed in 16 other dogs (20%) eating this diet
Puigdemont *et al.* 2006	29	Challenges with intact and hydrolysed soy	Up to 3 hours	3 dogs (50%) developed: vomiting (1 dog), soft faeces – diarrhoea (3 dogs) or erythema/ pruritus (1 dog) after eating intact soy, none of these dogs reacted to hydrolysed soy
Ricci *et al.* 2006	31	Open trial with intact chicken and HA-Formula (phase I) or blinded crossover RCT with hydrolysed chicken and hydrolysed soy (phase II)	2 weeks per challenge	Phase I: clinical scores increased by more than five points in 10 dogs (38%) fed HA-Formula – Phase II: similar clinical score increases in 6 dogs (50%) fed hydrolysed chicken and in 4 dogs (33%) fed hydrolysed soy; pruritus scores > 3 of 5 in 5 dogs (42%) fed hydrolysed chicken and in 6 dogs (50%) fed hydrolysed soy (phase II)

*Exclude, DVM Pharmaceuticals: hydrolysed casein and chicken, oats, pinto beans, tallow.
†HA-Formula, Nestle Purina: hydrolysed soy, cornstarch canola and coconut oil.
‡Hypoallergenic DR21 Formula, Royal Canin: soy isolate hydrolysate, rice, poultry fat, beet pulp, poultry liver hydrolysate, vegetal and fish oils.
§Canine z/d ULTRA Allergen-Free, Hill's Pet Nutrition: hydrolysed chicken, modified cornstarch, vegetable oil.
RCT, randomized controlled trial.

no reduction in signs following the hydrolysate-based diet, but their condition had responded favourably to the second elimination diet.

In two of these trials, the palatability of the tested hydrolysate-containing diets was assessed favourably in 80% of dogs.[32,37] Regrettably, adverse effects were not discussed in three papers.[32,35,37] Gastrointestinal signs consisting of either constipation, soft stools and flatulence were reported in six of 63 dogs (10%) in the only trial reporting adverse events.[36] In the largest report,[37] five of 109 dogs (5%) did not eat the hydrolysate-containing diet, and the overall dropout rate in this group was nearly 25%. In another trial, two of 29 dogs (6%) refused to eat the hydrolysate-based food.[32] Finally, it is worth noting that the owners of 24 of 63 dogs (38%) mentioned cost as a concern with feeding the tested hydrolysates.[36]

There were two trials that evaluated the effect of the same hydrolysed soy-containing diet (HA-Formula) in dogs with a tentative diagnosis of CAFR[33] or in dogs with previously diagnosed corn or soy hypersensitivity (Table 3).[34] In the first open study,[33] 24 dogs with signs that had abated following a previous dietary restriction–provocation test were fed the hydrolysate-based diet for 1 week. Pruritus increased in two of 24 dogs (8%) with the hydrolysed diet.

The second study was a blinded crossover randomized controlled trial that enrolled 10 corn or soy hypersensitive dogs, of whom nine completed the experiment.[34] Subjects were randomly assigned to eat successively, for 2 weeks

each, either a 'positive control' diet (i.e. a diet with intact corn or soy depending upon the dog's hypersensitivity), a 'negative control' diet (one without the known provocative ingredient) or the hydrolysate-based test diet. The authors reported that the mean scores of veterinary assessed skin lesions (erythema, excoriations, otitis externa, pruritus and pyoderma) were similar between baseline and negative control diets; in contrast, they were higher with positive control diets compared to baseline ones. Including all dogs together, mean scores of all parameters but erythema were nearly identical between negative and hydrolysed test diets. Similar observations could be made for owner-assessed outcome measures (pruritus, inflammation, stool character and frequency of defecation). In soy-hypersensitive dogs fed the hydrolyzed soy-containing test diet, however, veterinary- and owner-assessed pruritus scores were reported to increase over pretrial values by more than 60% and 20%, respectively. In contrast, pruritus scores did not increase in corn-sensitive dogs fed the test diet. The exact number of corn and/or soy hypersensitive dogs that had mild to moderate clinical reactions to the soy hydrolysate and cornstarch-containing diet could not be assessed from the poster data provided by the study sponsor. However, four (44%), two (22%) and two of nine dogs had to discontinue eating the positive, negative or test hydrolysate-based diets, respectively, because of development of adverse reactions that were not described in detail.

Fourteen Maltese–beagle crossbred dogs with historical hypersensitivity to corn and soy were entered in an open dietary trial (Table 3).[13] These dogs were fed a 'positive challenge' diet for the first day and a 'negative' diet to which they did not react for 5 months. After 3 months of feeding the 'negative' diet, dogs were challenged – at 2 weeks intervals – with 200 mg/kg of cornstarch, corn and soy for 2 days each and, finally, a soy hydrolysate and cornstarch-containing diet (HA-Formula) for 14 days. Ten (71%), 11 (79%), three (21%) and three of 14 dogs (21%) exhibited CAFR to corn, soy, cornstarch and the tested hydrolysate-based diet, respectively. All three hydrolysate-reacting dogs had had worsening of clinical signs after eating both corn and soy, and two of them also had reacted to cornstarch. As a result, three of 11 soy-reacting dogs (27%) exhibited cutaneous clinical score increases after ingesting the soy-based hydrolysate.

A related study[31] used soy or corn-allergic Maltese–beagle dogs from the same colony; the information presented herein was extracted from data provided by the senior author (H. Jackson, personal communication). In the first phase, 26 dogs were challenged with intact chicken and HA-Formula. In the second phase, 12 of these dogs were later selected because they had had increases in skin lesions after ingesting chicken. These dogs were challenged successively, in a blinded fashion, with hydrolysed chicken (< 10 kDa peptides) or hydrolysed soy for 2 weeks each. In the first set of challenges, clinical score increases of five points or more – at least mild reactions – were observed in 10 of 26 dogs (38%) eating HA-Formula. In the second phase of the study, clinical score increases of similar magnitude were observed in six (50%) and four of 12 chicken-sensitive dogs (33%) eating hydrolysed chicken or hydrolysed soy, respectively. Similarly, pruritus scores increased to at least three of five grades in five (42%) and six of 12 chicken hypersensitive dogs (50%) fed hydrolysed chicken or hydrolysed soy, respectively.

Finally, in one of the previously described experiments,[29] six soy-sensitized dogs (of whom three had high soy-specific IgE serum levels) were fed increasing amounts of native or whole hydrolysed soy. Oral challenge with intact soy led to the development of vomiting, pruritus and erythematous pododermatitis in one dog, and soft faeces or diarrhoea in all three subjects with high soy-specific IgE serum levels. Importantly, none of these three dogs reacted to oral challenges with six increasing doses (total dose: 17.75 g) of the whole soy hydrolysate.

Discussion

In this systematic review, 11 reports that studied the *in vitro* or *in vivo* effect of hydrolysed ingredients or hydrolysate-containing diets in dogs with experimental or suspected or proven spontaneous CAFR were identified. Clinical inferences based on the conclusions of this paper must be made after assessment of internal and external validities of this review's methodology and included studies.

Validity of this systematic review

Internal validity

Selection, detection, performance and attrition are biases that will diminish the validity of randomized controlled trials.[42] In this review, there were only two studies that were randomized and controlled, one with client-owned pets[34] and one with laboratory dogs (second phase).[31] Even though details on the process of randomization and masking could not be extracted from the abstracts or study data provided by the authors, there is no information to suspect that selection or detection bias could have taken place in these two small studies. Performance bias also is unlikely to have occurred as both randomized controlled trials were of crossover design, thereby ensuring that all dogs received the same intervention at some point in the study. Finally, attrition bias was minimal: one dog was enrolled in the small clinical trial[34] but it did not appear to complete the study; details about this withdrawn dog were unavailable.

External validity

The selection of subjects, the nature and duration of interventions administered and the outcome measures constitute the main factors to be evaluated for assessment of the external validity of included studies.[42]

The main goal of this systematic review was to select studies that enrolled two types of subjects: (i) laboratory dogs that were either spontaneously or experimentally hypersensitive to native (i.e. nonhydrolysed) food ingredients; and (ii) dogs that had suspected or proven CAFR. Dogs from the first category were included because of their known IgE-mediated hypersensitivity to specific native food items. Such dogs are of great value to study the immunological and clinical effect of foods containing hydrolysates derived from the parent nondigested proteins to which they are sensitive. Unfortunately, it is not known whether experimental sensitizations mirror, immunologically, the situation that occurs in the general population of dogs with food allergy. Moreover, such canine experimental models

of IgE-based food allergies are unlikely to provide relevant information for dogs with non–IgE-mediated AFR.

In this review, four open studies that enrolled pruritic dogs suspected of having CAFR were included.[32,35–37] Although these trials enrolled subjects representative of the population of dogs likely to benefit from the commercialization of hydrolysate-containing diets, they all had the flaw of not knowing beforehand the exact proportion of enrolled dogs with CAFR. Although clinical signs improved partially and completely in a variable fraction of dogs eating the hydrolysate-based diets, the number of dogs having CAFR that did not respond to the dietary intervention could not be assessed with the proposed design.

In only four studies were dogs with known food hypersensitivity challenged orally with relevant hydrolysates.[13,29,31,34] Only one of these four studies[34] had enrolled client-owned dogs with hypersensitivity to relevant food items, but the number of dogs that completed the trial was very low (nine subjects), and the differences in outcome measures between groups were so small that the study probably was underpowered.

Overall, the nature and duration of the interventions used in these studies were consistent with current practice guidelines: when the diets were given with the aim to improve signs of CAFR, the trials usually lasted 6 to 8 weeks. When the hydrolysates were given to provoke the recurrence of signs, the designs called for 2-week challenges, a duration that would permit the development of IgE-mediated reactions, the mechanism suspected to underlie most canine CAFR.[9–15]

Finally, outcome measures selected in this review were relevant to the aim of studying the hypoallergenicity of hydrolysate-based ingredients. Indeed, the effect of IgE binding to the hydrolysed items, *in vitro* in serological assays or *in vivo* in IDT, or the effect of oral challenges with hydrolysed food items on pruritus or skin lesions was described.

Evidence of reduced immunological allergenicity of hydrolysates

Altogether, some evidence suggesting the reduced, but not the abolition of, immunological allergenicity of several different hydrolysates was found.

In one study,[30] serum IgE from soy-sensitized dogs recognized several proteins in immunoblotting performed with native soy extract while the IgE binding to hydrolysed soy was reduced and altered. It was not abolished, however. IgE binding was still detected against some high molecular weight fractions present in the hydrolysate, thereby suggesting that the tested item was only partially hydrolysed.

The effect of IDT with hydrolysates in experimentally sensitized dogs appeared to be more variable. Intradermal reactivity was either unchanged, increased or decreased depending on the hydrolysed extract.[28] In two other studies using the same dogs,[29,30] IDT with the tested whole soy hydrolysate still yielded immediate reactions, but the wheal surface areas were reduced with the hydrolysed compared to the native soy. When IDT was performed with hydrolysate fractions weighing less than 10 kDa, results became negative. These observations suggested a reduced, but not abolished immunological allergenicity of the tested food hydrolysates that still contained some high molecular weight fractions. Only extensive hydrolyzation yielding very low molecular weight fragments therefore appears to provide minimal allergenicity. These IDT results are, altogether, very similar to those of skin prick (i.e. puncture) tests performed with cow's milk hydrolysates in children with CMA.[25,26,43] Indeed, in these studies, many infants with CMA and concurrent positive prick test to cow's milk still reacted to partially digested hydrolysates, while fewer of them had positive reactions to extensively hydrolysed formulas.

Evidence of reduced clinical allergenicity of hydrolysates

This review uncovered some evidence suggesting reduced – but not eliminated – clinical allergenicity of hydrolysate-based foods in dogs with proven CAFR.

Clinically, the feeding of dogs suspected of having CAFR with hydrolysate-based diets reduced or eliminated clinical signs in a variable proportion of dogs.[32,35–37] How many dogs with CAFR still reacted to these hydrolysate-based 'elimination diets', and therefore were misdiagnosed as not having such condition, unfortunately could not be determined with such study design. In other words, if a dog still had clinical signs after eating these hydrolysates, they could have been diagnosed as not having a CAFR, when, in fact, they could have suffered from this disease but had reacted to the hydrolysate-containing diet.

Some dogs with CAFR to undetermined food items had their signs recur following the ingestion of hydrolysate-containing diets.[33] Finally, between 20% and 50% of dogs ingesting partial hydrolysates derived from food items to which they were spontaneously hypersensitive exhibited increases in clinical signs of CAFR.[13,31,34] In all, the proportion of hypersensitive dogs reacting to the tested partial hydrolysates is nearly identical to those of children with CMA challenged with partially hydrolysed whey formulas.[25,26] In such children, clinical immediate reactions to partially hydrolysed formulas also can be severe (e.g. leading to asthma and urticaria).[25] Although these reactions were not reported in the studies involving dogs.

Risk of feeding hydrolysates to dogs with suspected or proven food hypersensitivity

This review found little information on the risk of feeding hydrolysed food items to dogs.

Approximately 10% of dogs fed hydrolysate-based diets will experience variable gastrointestinal signs, from constipation to diarrhoea.[36] Moreover, a small proportion of dogs refused to eat hydrolysate-containing diets, but most dogs were rated as finding these foods palatable.

Implications for clinical practice

To the authors' knowledge, there are only three hydrolysate-based diets currently available in multiple countries: Purina's HA-Formula, Hill's z/d ULTRA and Royal Canin's Hypoallergenic HP19/DR21 formula. This systematic review found that the limited number of studies undertaken point to reduced, but not eliminated, clinical hypoallergenicity of hydrolysates in dogs with proven CAFR. While most of the testing of hydrolysate-based diets in dogs with known CAFR was done for Purina's HA-Formula (four studies), only very limited information on the testing of Royal Canin's

Hypoallergenic DR21 Formula in known hypersensitive dogs (only three dogs clinically reactive to soy) was found. Moreover, the search strategy used could not identify any published reports of clinical testing of Hill's z/d ULTRA in dogs with proven CAFR, and particularly, in dogs hypersensitive to chicken.

Because studies performed in dogs with spontaneously arising CAFR established that a variable proportion of animals exhibited reactions to partially hydrolysed commercial dog foods, veterinarians must assume that an unknown fraction of the population of dogs with suspected or proven CAFR will react clinically – and sometimes severely – to these currently marketed diets. As a result, clinicians must weigh the modest benefit of using these partial hydrolysates against the low risk of gastrointestinal disturbances, low risk of refusal to eat and higher cost of the partial hydrolysed commercial dog foods. This benefit versus risk analysis of using hydrolysates also must be compared to similar assessments of other modalities available for restriction–provocation dietary interventions (e.g. feeding novel and limited ingredient-based commercial or homemade diets). Importantly, clinicians must also remember that hydrolysed proteins will, theoretically, have no additional benefit compared to intact proteins in dogs affected with CAFR not mediated by IgE.

In light of the currently available evidence, partially hydrolysed diets are probably of best benefit in dogs suspected not to be hypersensitive to their ingredients (protein and carbohydrate) in native form.

Implication for research

This systematic review confirms the scarcity of high quality investigations available to support the benefit of hydrolysate-based diets in dogs with known AFR.

It is recommended that several steps be performed before introducing future hydrolysates to the veterinary market. Such steps should include: (i) the demonstration of enhanced protein hydrolyzation compared to that of current products; (ii) the demonstration of markedly or completely reduced allergic patient serum IgE-binding to hydrolysed compared to native parent proteins (e.g. ELISA inhibition); (iii) the proof of markedly or completely reduced IDT reactivity of hydrolysates in dogs known to react to intact proteins and, most importantly, (iv) the blinded and randomized feeding of both hydrolysed and intact ingredients to dogs with known CAFR, especially to patients clinically hypersensitive to the native ingredients. A crossover design may be most appropriate for such testing.

In these randomized actively controlled trials, outcome measures must be clinically relevant and include, at least, an assessment of skin lesions and pruritus using published validated scales (e.g. CADESI-03[44] and composite pruritus scale[45]). The most important primary outcome measure should be the determination of the proportion of enrolled dogs exhibiting visible clinical reactions (i.e. those with changes in skin lesion and/or pruritus scores) after feeding either hydrolysed or intact ingredient-based diets.

Conclusions

The small number of studies reported so far point to reduced, but not eliminated, immunological and clinical allergenicity of currently marketed hydrolysate-based commercial diets. A variable proportion of dogs with CAFR will exhibit a worsening of clinical signs when fed partial hydrolysates. Clinicians must weigh the small clinical benefit of these diets versus their high cost and low risk of reduced appetence or gastrointestinal sign development. At this time, these hydrolysate-containing diets are probably best used in dogs suspected not to be hypersensitive to their individual components.

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References

1. White SD. Food hypersensitivity in 30 dogs. Journal of the American Veterinary Medical Association 1986; 188: 695–8.
2. Carlotti DN, Remy I, Prost C. Food allergy in dogs and cats. A review and report of 43 cases. Veterinary Dermatology 1990; 1: 55–62.
3. Harvey RG. Food allergy and dietary intolerance in dogs: a report of 25 cases. Journal of Small Animal Practice 1993; 34: 175–9.
4. Paterson S. Food hypersensitivity in 20 dogs with skin and gastrointestinal signs. Journal of Small Animal Practice 1995; 36: 529–34.
5. Chesney CJ. Systematic review of evidence for the prevalence of food sensitivity in dogs. Veterinary Record 2001; 148: 445–8.
6. Chesney CJ. Food sensitivity in the dog: a quantitative study. Journal of Small Animal Practice 2002; 43: 203–7.
7. Verlinden A, Hesta M, Millet S *et al*. Food allergy in dogs and cats: a review. Critical Reviews in Food Science and Nutrition 2006; 46: 259–73.
8. Hillier A, Griffin CE. The ACVD Task Force on Canine Atopic Dermatitis (X): Is there a relationship between canine atopic dermatitis and cutaneous adverse food reactions? Veterinary Immunology and Immunopathology 2001; 81: 219–26.
9. Ermel RW, Kock M, Griffey SM *et al*. The atopic dog – a model for food allergy. Laboratory Animal Science 1997; 47: 40–9.
10. Teuber SS, del Val G, Morigasaki S *et al*. The atopic dog as a model of peanut and tree nut food allergy. Journal of Allergy and Clinical Immunology 2002; 110: 921–7.
11. Buchanan BB, Frick OL. The dog as a model for food allergy. Annals of the New York Academy of Sciences 2002; 964: 173–83.
12. Jackson HA, Hammerberg B. Evaluation of a spontaneous canine model of immunoglobulin E-mediated food hypersensitivity: dynamic changes in serum and fecal allergen-specific immunoglobulin E values relative to dietary change. Comparative Medicine 2002; 52: 316–21.
13. Jackson HA, Jackson MW, Coblentz L *et al*. Evaluation of the clinical and allergen specific serum immunoglobulin E responses to oral challenge with cornstarch, corn, soy and a soy hydrolysate diet in dogs with spontaneous food allergy. Veterinary Dermatology 2003; 14: 181–7.
14. Foster AP, Knowles TG, Moore AH *et al*. Serum IgE and IgG responses to food antigens in normal and atopic dogs, and dogs with gastrointestinal disease. Veterinary Immunology and Immunopathology 2003; 92: 113–24.
15. Day MJ. The canine model of dietary hypersensitivity. The Proceedings of the Nutrition Society 2005; 64: 458–64.
16. Ishida R, Masuda K, Sakaguchi M *et al*. Antigen-specific histamine release in dogs with food hypersensitivity. Journal of Veterinary Medical Science 2003; 65: 435–8.
17. Ishida R, Masuda K, Kurata K *et al*. Lymphocyte blastogenic responses to inciting food allergens in dogs with food hypersensitivity. Journal of Veterinary Internal Medicine 2004; 18: 25–30.

18. Olivry T, Kurata K, Paps JS *et al*. A blinded randomized controlled trial evaluating the usefulness of a novel diet (aminoprotect care) in dogs with spontaneous food allergy. The Journal of Veterinary Medical Science 2007; 69: 1025–31.
19. International Union of Immunological Societies. Allergen nomenclature. Available at: http://www.allergen.org. Accessed 7 January 2008.
20. Martin A, Sierra MP, Gonzalez JL *et al*. Identification of allergens responsible for canine cutaneous adverse food reactions to lamb, beef and cow's milk. Veterinary Dermatology 2004; 15: 349–56.
21. Ohmori K, Masuda K, Kawarai S *et al*. Identification of bovine serum albumin as an IgE-reactive beef component in a dog with food hypersensitivity against beef. The Journal of Veterinary Medical Science 2007; 69: 865–7.
22. Hays T, Wood RA. A systematic review of the role of hydrolyzed infant formulas in allergy prevention. Archives of Pediatrics and Adolescent Medicine 2005; 159: 810–6.
23. Hill DJ, Murch SH, Rafferty K *et al*. The efficacy of amino acid-based formulas in relieving the symptoms of cow's milk allergy: a systematic review. Clinical and Experimental Allergy 2007; 37: 808–22.
24. Osborn DA, Sinn J. Formulas containing hydrolysed protein for prevention of allergy and food intolerance in infants. Cochrane Database of Systematic Reviews (Online) 2006; 4: CD003664. Accessible at: http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD003664/pdf_fs.html.
25. Ragno V, Giampietro PG, Bruno G *et al*. Allergenicity of milk protein hydrolysate formulae in children with cow's milk allergy. European Journal of Pediatrics 1993; 152: 760–2.
26. Giampietro PG, Kjellman NI, Oldaeus G *et al*. Hypoallergenicity of an extensively hydrolyzed whey formula. Pediatric Allergy and Immunology 2001; 12: 83–6.
27. Cave NJ. Hydrolyzed protein diets for dogs and cats. The Veterinary Clinics of North America. Small Animal Practice 2006; 36: 1251–68.
28. Olson ME, Hardin JA, Buret AG *et al*. Hypersensitivity reactions to dietary antigens in atopic dogs. In: Reinhart GA, Carey, DP, eds. Recent Advances in Canine and Feline Nutrition, III. Wilmington, OH: Orange Frazer Press, 2000: 69–77.
29. Puigdemont A, Brazis P, Serra M *et al*. Immunologic responses against hydrolyzed soy protein in dogs with experimentally induced soy hypersensitivity. American Journal of Veterinary Research 2006; 67: 484–8.
30. Serra M, Brazis P, Fondati A *et al*. Assessment of IgE binding to native and hydrolyzed soy protein in serum obtained from dogs with experimentally induced soy protein hypersensitivity. American Journal of Veterinary Research 2006; 67: 1895–900.
31. Ricci R, Jackson HA, Paps JS *et al*. The magnitude of the clinical response to oral proteins in dogs with spontaneous chicken allergy is significantly reduced when the protein is hydrolyzed (abstract). Veterinary Dermatology 2006; 17: 210.
32. Groh M, Moser E. Diagnosis of food allergy in the nonseasonally symptomatic dog using a novel antigen, low molecular weight diet: a prospective study of 29 cases. Journal of Veterinary Allergy and Clinical Immunology 1998; 6: 5–6.
33. Sousa C, DeManuelle T, Power HT. Evaluation of the usefulness of purina CNM HA-formula in dogs with pruritic dermatosis that responds to a change in diet (Purina internal document). Nestlé Purina, St Louis, MO 2000; 1p.
34. Beale KM, Laflamme DP. Comparison of a hydrolyzed soy protein diet containing corn starch with a positive and negative control diet in corn- or soy-sensitive dogs (abstract). Veterinary Dermatology 2001; 12: 237.
35. Biourge BC, Fontaine J, Vroom MW. Diagnosis of adverse reactions to food in dogs: efficacy of a soy-isolate hydrolysate-based diet. Journal of Nutrition 2004; 134: 2062S–4S.
36. Loeffler A, Lloyd DH, Bond R *et al*. Dietary trials with a commercial chicken hydrolysate diet in 63 pruritic dogs. Veterinary Record 2004; 154: 519–22.
37. Loeffler A, Soares-Magalhaes R, Bond R *et al*. A retrospective analysis of case series using home-prepared and chicken hydrolysate diets in the diagnosis of adverse food reactions in 181 pruritic dogs. Veterinary Dermatology 2006; 17: 273–9.
38. Kennis RA, Tizard I, Hannah S *et al*. IgE antibodies to soy antigens, in sensitized and control dogs, detected by Western blot analysis and ELISA (abstract). Veterinary Dermatology 2001; 12: 232.
39. Kennis RA, Tizard I, Hannah S *et al*. Changes in IgE antibodies to soy in sensitized and control dogs after challenge using three diets in a crossover design (abstract). Veterinary Dermatology 2002; 13: 218.
40. Cave NJ, Guilford WG. *In vivo* assessment of antigenicity of a protein hydrolysate and characterization of a major antigen in chicken (abstract). In: Proceedings of the American College of Veterinary Internal Medicine (ACVIM) Forum. Seattle, WA: ACVIM, 2000: 147A.
41. Cave NJ, Guilford WG. A method for *in vitro* evaluation of protein hydrolysates for potential inclusion in veterinary diets. Research in Veterinary Science 2004; 77: 231–8.
42. Jüni P, Altman DG, Egger M. Systematic reviews in health care – assessing the quality of controlled clinical trials. British Medical Journal 2001; 323: 42–6.
43. Rugo E, Wahl R, Wahn U. How allergenic are hypoallergenic infant formulae? Clinical and Experimental Allergy 1992; 22: 635–9.
44. Olivry T, Marsella R, Iwasaki T *et al*. Validation of CADESI-03, a severity scale for clinical trials enrolling dogs with atopic dermatitis. Veterinary Dermatology 2007; 18: 79–96.
45. Hill PB, Lau P, Rybnicek J. Development of an owner-assessed scale to measure the severity of pruritus in dogs. Veterinary Dermatology 2007; 18: 301–8.

Résumé Plusieurs aliments à bases de protéines hydrolysées ont été commercialisés dans le but d'aider à diagnostiquer et traiter les chiens présentant des réactions cutanées d'origine alimentaire (CAFR). Cette revue systématique a été réalisée pour évaluer l'efficacité des hydrolysats protéiques dans la diminution de l'allergénicité immunologique et clinique chez les chiens atteints de CAFR. Des bases de données regroupant publications et communications ont été étudiées pour déterminer leur validité et différentes compagnies ont été contactées afin de fournir des études non publiées. Onze études en rapport avec ce projet ont été identifiées. La diminution du taux d'IgE sérique avec un hydrolysat de sojat (1 étude) et une diminution de la réactivité des tests intradermiques à un hydrolysat de protéines (3 études) ont été trouvés. Dans 4 études, l'alimentation de chiens suspects de présenter une CAFR avec une alimentation à base de protéines hydrolysées a permis une diminution, voire une disparition des signes cliniques. Cependant, le pourcentage de chiens à CAFR réagissant à cette alimentation n'a pu être déterminé. Jusqu'à 50% de chiens à CAFR inclus dans trois études contrôlées ont présenté une aggravation de leurs signes cliniques après l'ingestion de nourriture à base d'une protéine hydrolysée à laquelle ils étaient sensibilisés. En conclusion, le nombre limité d'études mises en place suggèrent une diminution, mais pas une disparition, de l'allerginicité clinique et immunologique des aliments à base d'hydrolysats. Une proportion variable de chiens à CAFR présentera une aggravation des signes cliniques après avoir ingéré des hydrolysats partiels. Les cliniciens doivent peser le pour et le contre de ces aliments eu égard à leur prix élevé et au risque faible

d'appétence réduite ou de troubles gastro-intestinaux. A l'heure actuelle, les aliments à base d'hydrolysats sont probablement à réserver chez les chiens suspects de n'être pas allergiques à leurs composants individuels.

Resumen Varias dietas hidrolizadas se han comercializado para ayudar en el diagnóstico o tratamiento de perros con reacciones alimentarias adversas (CAFR). Esta revisión se realizó para examinar la evidencia en favor de una alergenicidad reducida de los hidrolizados en perros con CAFR. Se buscaron citas relevantes en bases de datos, resumenes de reuniones científicas y artículos, y se contactó con compañias para solicitar informes no publicados. Se identificaron once estudios clínicos relevantes para esta revisión. Se encontró evidencia de una reducción de la IgE en el suero a un hidrolizado de soja (1 estudio), y una reducción en las reacciones intradérmicas a hidrolizados proteicos (3 estudios). En cuatro publicaciones, perros sospechosos de CAFR alimentados con dietas hidrolizadas presentaron reducción o eliminación de los signos clínicos en una proporción variable de individuos. Sin embargo, el porcentaje de perros con CAFR que aún reaccionaron con la dieta hidrolizada no pudo calcularse. De relevancia resultó el hecho de que hasta un 50% de perros con CAFR embarcados en los estudios presentaron un incremento en los signos clínicos tras la ingestión de hidrolizados parciales derivados de alimentos a los que eran sensibles. Se concluye que, en el limitado número de estudios disponible, se observa una tendencia a la reducción -pero no eliminación- de la alergeniciad inmunológica y clínica con las dietas hidrolizadas comerciales. Una proporción variable de perros con CAFR pueden empeorar cuando se les alimenta con hidrolizados parciales. Los clínicos deben estimar el beneficio de estas dietas en relación con el alto coste y el bajo riesgo de reducción del apetito o de producir signos gastrointestinales. En estos momentos las dietas hidrolizadas parecen ser más adecuadas en perros no sospechosos de ser hipersensibles a sus componentes individuales.

Zusammenfassung Mehrere auf Hydrolysaten basierende Diäten, sind kommerzialisiert worden, um bei der Diagnose und Behandlung von Hunden mit kutanen Futtermittelallergien (CAFR) zu helfen. Diese systematische Review wurde durchgeführt, um die Evidenz, die für eine reduzierte immunologische und klinische Allergenität von Hydrolysaten bei Hunden mit CAFR spricht, zu untersuchen. Literaturdatenbanken, Meeting Abstracts, Bibliografien von Artikeln wurden auf relevante Zitate durchgesehen und Firmen wurden kontaktiert, um unpublizierte Berichte zur Verfügung zu stellen. Es wurden elf Studien, die für diese Studie relevant waren, gefunden. Eine gewisse Evidenz für eine reduzierte Bindung von IgE im Serum an Sojahydrolysat (eine Studie) und verminderte Reaktivität im Intradermaltest auf hydrolysierte Proteine (3 Studien) wurde gefunden. In vier Berichten wurde festgehalten, dass durch das Füttern einer auf Hydrolysat basierenden Diät an Hunde mit Verdacht auf CAFR die klinischen Symptome bei einer bedeutenden Anzahl an Individuen reduziert oder eliminiert wurde. Der Prozentsatz an Hunden mit CAFR, die weiterhin auf diese hydrolysierten Diäten reagierten, konnte jedoch nicht erfasst werden. Wesentlich war die Tatsache, dass bis zu 50% der Hunde mit CAFR, die an drei kontrollierten Studien teilnahmen, eine Zunahme an klinischen Symptomen zeigten, nachdem sie Teilhydrolysate, die aus Futter stammten, auf welches sie hypersensibel reagierten, aufgenommen hatten. Zusammenfassend kann man sagen, dass die limitierte Anzahl an durchgeführten Studien auf eine reduzierte – aber nicht eliminierte – immunologische und klinische Allergenität durch die auf Hydrolysat basierenden kommerziellen Diäten hinweist. Ein unterschiedlicher Anteil von Hunden mit CAFR wird eine Verschlechterung der klinischen Symptomatik zeigen, wenn ihnen Teil-Hydrolysate gefüttert werden. Die Kliniker müssen die klinische Unterstützung dieser Diäten versus der hohen Kosten und ihrem niedrigen Risiko, reduzierten Appetit oder die Entstehung von gastrointestinalen Symptomen zu verursachen, abwägen. Zu diesem Zeitpunkt werden auf Hydrolysat basierende Diäten vermutlich am besten bei Hunden verwendet, bei denen nicht der Verdacht besteht, dass sie hypersensitiv auf die individuellen Komponenten sind.

