Introduction

For many years, veterinarians have had an interest in the therapeutic benefits of specially formulated foods—foods that optimize health (Dzanis, 1998), improve animal production (van’t Klooster, 1999; Teferedegne, 2000; van Houtert and Sykes, 1999), and maximize performance (Keisler et al., 1999; Galyean et al., 1999; Parsons and Allison, 1991). Proper nutrition is considered to be the foundation of optimal health. Further, whole food nutrition is considered to be the most beneficial. Techniques for production of whole food nutritional products for humans have been pioneered and utilized by Standard Process Inc. (Palmyra, WI) for over 70 years. Veterinarians have successfully utilized these human products for many years. However, it has always been clear that products formulated for humans do not fully address the unique requirements of other species.

Each species has unique nutritional and physiological requirements (Hayes et al., 1975; Hill, 1998; Case et al., 2000). Cats, for example, are strict carnivores, have a strict need for taurine and preformed vitamin A in their diets, and have highly efficient renal concentrating abilities. Dogs are more versatile with their diet, have less stringent requirements, and have an incredible diversity in size and conformation among breeds. Optimal nutritional support requires recognition of the myriad of species-specific requirements.

In addition, disease etiology and pathogenesis must be understood for each species. For example, canine hypoadrenocorticism is commonly caused by adrenocortical destruction mediated through an autoimmune process (Smallwood and Barsanti, 1995; Greco and Harpold, 1994). Also, large dogs commonly develop osteoarthritis (Hoskins and Kerwin, 1997) more often than small dogs or cats.

The products under evaluation here are a unique combination of Protomorphogen™ and Cytosol™ extracts, tissue concentrates, whole foods, and botanicals. Each ingredient was selected for its physiological benefit and lack of detrimental side effects. Ingredient combinations were individualized for each species based on specific factors associated with targeted organs, glands, and other tissues. This was determined by a combination of literature review, experience with the clinical application of nutritional principles gleaned from the literature, and experience with the clinical use of Protomorphogen™ and Cytosol™ extracts.

Following development of the formula ingredients it was essential to establish a baseline of efficacy, palatability, safety, and compatibility with commonly used supplements, pharmaceuticals, and other therapies. A limited study was developed to assess these factors along with evaluating client perception and acceptance. Further, integration into clinical practice was observed and assessed.
Methods

Patient selection

Canine and feline patients with naturally occurring disease were included if they had disease affecting the following tissues or were in need of general nutritional support:

<table>
<thead>
<tr>
<th>Canine</th>
<th>Feline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal</td>
<td>Cardiac</td>
</tr>
<tr>
<td>Cardiac</td>
<td>Hepatic</td>
</tr>
<tr>
<td>Dermal</td>
<td>Immune system</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Intestine</td>
</tr>
<tr>
<td>Immune system</td>
<td>Renal</td>
</tr>
<tr>
<td>Intestine</td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td></td>
</tr>
</tbody>
</table>

These patients were presented in a routine fashion for standard veterinary care. Patient evaluation included history, physical examination, complete blood count, serum chemistry profile, urinalysis, and radiographs as indicated by the case. Not all procedures were performed in all patients. Patients were excluded only if the owner was unable to participate through the first month of product administration or could not ensure that product was being administered to the patient (compliance).

Owner Informed Consent

The study protocol and goals were discussed with the owner. Information concerning the study product ingredients was given to the owner. An informed consent was signed by the owner prior to enrollment of their pet in the study.

Product selection

Study product was selected based on the results of the initial clinical evaluation. In the majority of patients, a single product was selected for administration. However, some patients received multiple products simultaneously. Pharmaceuticals and other concomitant products were continued during the nutritional product evaluation. Canine products were provided in powdered form and feline products were provided as tablets that were easily crushed into powder for mixing with food, if needed.

Patient evaluation

The study evaluation period was a minimum of one month and included the following:

Initial evaluation, including

- History
- Physical examination
- Laboratory testing as indicated

Telephone report at one week, including questions to determine

- Ease of compliance with product administration
- How the product was being administered
- If the owner had observed anything unusual with the patient
- If the owner had any questions or concerns

Physical examinations at monthly intervals for the first three months, including

- Clinical history
- Routine physical examination

Owner surveys at monthly intervals for the first three months, including questions concerning

- Any observations made by the owner
- Method of administration
- Ease of administration
- Any problems experienced by the patient
- Any new problems since the previous evaluation
- Any concomitant medications

Owner exit interview, inquiring

- If the owner felt that the product was beneficial
- If the owner would continue to administer the product based on patient response
- How easy the product was to administer

Additionally, the owner was asked to give comments and suggestions during all phases of the study.
**Data recording**

All patient data was compiled in a study notebook that was maintained at one location for completeness and ease of retrieval. Simultaneously, data was recorded in the permanent patient record.

**Adverse events**

At each evaluation, owners were queried verbally and on the various owner survey forms to determine if any adverse events had occurred during the previous time period. Adverse events were defined as anything unusual for that patient that could be related directly to the study product.

**Results**

Sixty-one canine and 23 feline patients with naturally occurring disease were selected for inclusion if the owner was able to participate for the minimum period of time. Forty-seven canine patients received only one study nutritional product while 14 received multiple study nutritional products simultaneously. Twenty feline patients received only one study nutritional product while three feline patients received multiple study nutritional products simultaneously.

Evaluation of owner survey responses and physical examination findings provided results that are summarized in Tables 1 and 2. Each individual owner provided the definition and criteria for determining palatability. For feline patients, a number of owners routinely administered the product by pilling and thus were unable to assess palatability. Determination of product benefit was made by the owner based on observable changes in the patient and the occurrence of apparent side effects (negligible). Responses to questions concerning continued product use were based on observable benefits, lack of side effects, and ease of administration. Assessment of ease of administration was relative to the level of difficulty typical of that individual patient. Occurrences of adverse events were recorded and then compared to historical patterns of that patient. For example, one canine patient had an episode of increased flatulence. Further questioning of the owner revealed that this episode followed feeding of table scraps and thus was not clearly attributable to the study product, a criterion for an adverse event. Only those adverse events that could be clearly correlated with study product are included in Tables 1 and 2.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Feline - Single Products</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>Palatable</td>
<td>75.00%</td>
</tr>
<tr>
<td>Beneficial</td>
<td>95.00%</td>
</tr>
<tr>
<td>Adverse Events</td>
<td>5.00%</td>
</tr>
<tr>
<td>Continue Use</td>
<td>90.00%</td>
</tr>
<tr>
<td>Easy to Administer</td>
<td>85.00%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Canine - Single Products</th>
<th>Canine - Multiple Products</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Palatable</td>
<td>78.72%</td>
<td>21.28%</td>
</tr>
<tr>
<td>Beneficial</td>
<td>95.74%</td>
<td>0.00%</td>
</tr>
<tr>
<td>Adverse Events</td>
<td>0.00%</td>
<td>91.49%</td>
</tr>
<tr>
<td>Continue Use</td>
<td>95.74%</td>
<td>0.00%</td>
</tr>
<tr>
<td>Easy to Administer</td>
<td>89.36%</td>
<td>10.64%</td>
</tr>
</tbody>
</table>
Table 3 presents results of owner responses concerning study product administration by method used. It was determined that the majority of canine and feline patients received their product mixed with their regular food: 87.23% for single canine products, 78.57% for multiple canine products, and 45% for single feline products. However, it should be noted that administration by pilling (40%) in cats was almost equal to those receiving product with food.

Information in Table 4 summarizes the results of owner observations and veterinary evaluations concerning resolution of the patient’s clinical signs. The majority of feline patients (83.33% and 80.00% for owner and veterinarian, respectively) had resolution by two months. For canine patients, the majority had resolution by two months based on owner observation (82.22% for single products and 84.38% for multiple products) or three months based on veterinary evaluation (86.20% for single product and 75.00% for multiple products). A minority of patients did not experience resolution as observed by the owner and veterinarian.

### Table 3 - Methods of Administration

<table>
<thead>
<tr>
<th></th>
<th>Mix in Food</th>
<th>Place on Food</th>
<th>Pilling/Orally</th>
<th>Treat</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Feline Single</strong></td>
<td>45.00%</td>
<td>0.00%</td>
<td>40.00%</td>
<td>15.00%</td>
<td>20</td>
</tr>
<tr>
<td><strong>Canine Single</strong></td>
<td>72.34%</td>
<td>14.89%</td>
<td>10.64%</td>
<td>2.13%</td>
<td>47</td>
</tr>
<tr>
<td><strong>Canine Multiple</strong></td>
<td>57.14%</td>
<td>21.43%</td>
<td>14.29%</td>
<td>7.14%</td>
<td>14</td>
</tr>
</tbody>
</table>

### Table 4 - Time to Resolution of Clinical Signs

<table>
<thead>
<tr>
<th></th>
<th>1 month</th>
<th>2 months</th>
<th>3 months</th>
<th>4 months</th>
<th>5 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Feline Single</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Client</td>
<td>55.56%</td>
<td>83.33%</td>
<td>88.89%</td>
<td>88.9%</td>
<td>94.44%</td>
</tr>
<tr>
<td>Veterinarian</td>
<td>50.00%</td>
<td>80.00%</td>
<td>90.0%</td>
<td>90.0%</td>
<td>90.00%</td>
</tr>
<tr>
<td><strong>Canine Single</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Client</td>
<td>64.44%</td>
<td>82.22%</td>
<td>91.11%</td>
<td>91.11%</td>
<td>91.11%</td>
</tr>
<tr>
<td>Veterinarian</td>
<td>62.07%</td>
<td>68.97%</td>
<td>86.2%</td>
<td>93.10%</td>
<td>93.10%</td>
</tr>
<tr>
<td><strong>Canine Multiple</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Client</td>
<td>53.13%</td>
<td>84.38%</td>
<td>84.38%</td>
<td>87.50%</td>
<td>87.50%</td>
</tr>
<tr>
<td>Veterinarian</td>
<td>39.29%</td>
<td>57.14%</td>
<td>75.00%</td>
<td>78.57%</td>
<td>85.71%</td>
</tr>
</tbody>
</table>

### Discussion

This pilot study was able to demonstrate the high level of palatability of the Standard Process® canine and feline nutritional products. While palatability is difficult to clearly define, the advantage of the method used here was that it was based on owner perception and meshed well with one of the goals of the study. As the individual responsible for product administration and the one most familiar with the patient, the owner was in the unique position of being best able to judge palatability. Interestingly, palatability was perceived to be higher in canine patients receiving multiple products even though these patients tended to have more significant health problems. Palatability was similar between the canine and feline patients receiving single products—78.72% and 75% palatable, respectively. It should also be recognized that palatability was assessed in patients with clinical disease states expected to cause a reduction in interest in a novel food based product.
Research

Owner responses to questions concerning the perceived benefits of the product and their desire to continue administering the product revealed that the owners felt the products were beneficial. There are multiple aspects to this issue. First, most owners were able to observe a positive change in their pets. These changes included increased activity, more alertness, improved hair coat, and a reduction in clinical signs. Second, the lack of side effects played an important role in owner perception. Third, owners expressed a desire to provide their pets with health care that was not reliant on pharmaceutical therapies or could adjunctively support pharmaceutical therapies. These factors played a role even in patients whose owners could not observe a physical change. Patients without an observable change tended to be those with a metabolic disturbance such as early kidney disease.

Ease of administration was based on owner perception as well. Owners were encouraged to utilize a variety of administration methods until they found the method that was most appropriate. Many cat owners selected the pilling method and did not attempt any other means of administration. It is interesting to note that administration was considered to be “easy” in a greater number of patients than were reported to show positive palatability. This brings into question how large a role palatability plays in administration ease, assuming palatability is at an acceptable level. Also, it is beneficial to recall that study participants were clinical cases with varying levels of illness.

Methods of administration varied according to individual owner choice. Ideally, product would be administered with the regular feeding. This has a number of physiological benefits in addition to owner convenience. Powder formulations were selected for canine products based on the assumption that dogs are more inclined to accept changes in their regular food. Also, these products are formulated with whole food ingredients including liver and kidney, foods that should be attractive to both dogs and cats. Tablets were selected for feline formulations in an effort to optimize administration options. These options included pilling, administering as treats, crushing or powdering and mixing with food, and even syringe feeding for anorexic patients. For the majority of owners, ease of administration with the variety of options available fostered long-term support with these products as is often needed in chronic cases.

Efficacy was not rigorously evaluated in this study and consisted of monitoring for improvement or resolution of the presenting clinical problem. Owners were queried concerning changes in the clinical picture:

- Physical examinations were performed
- Laboratory evaluations were completed by the veterinarian, as indicated

In the canine and feline studies, over 90% of the patients had resolution based on a combination of owner observation and veterinary evaluation. The time course of resolution is summarized in Table 4. Both the owner and veterinary results are shown. Previous experience with nutritional support in patients with chronic disease indicates that the majority shows improvement in 3-6 weeks depending on their clinical condition. This was confirmed in this study. Monthly examinations precluded a more precise understanding of the time course of improvement to resolution. However, by two months, over 80% of owners felt that their pets’ problems had been resolved. Owner observation and veterinary evaluation coincided well in the feline study, though this was not so in the canine study where veterinary evaluation of resolution lagged behind the owner observation. However, there was good agreement between owner observation and veterinary evaluation by four months with approximately 90% of single product feline and canine patients showing resolution. Resolution in canine patients receiving multiple study products was longer and likely reflects the increased chronicity and severity of their health problems.

A small percentage of patients did not have resolution. This could be related to a number of factors including improper product choice, incomplete understanding of the case history, a lack of product efficacy, inappropriate product dose, poor owner compliance, and/or severity and chronicity of the problem.

Adverse events related to study product administration occurred in one feline patient. The patient had a long-standing history prior to the study of vomiting 5-6 times per week. Previous diagnostic evaluations indicated inflammatory bowel disease, but an intestinal biopsy was never performed. Each time the patient was given the feline intestinal study product she would vomit within 30 minutes. If the product was given with food, no vomiting occurred. Continued utilization of the study product has resulted in significant patient improvement. In a number of canine patients, transient loose stools were observed on occasion. These resolved with no further intervention. Relationship to study
products is unclear in these cases because these dogs were known to ingest carrion, were fed table scraps, or had pre-existing gastrointestinal problems. No abnormalities were noted on routine laboratory evaluation in patients enrolled in this study.

Utilization of these nutritional products in conjunction with pharmaceutical therapies was determined to be of value. No detrimental interactions were identified in this limited study. Examples include concurrent use of canine cardiac formula and enalapril or antibiotics, canine hepatic formula and chemotherapy or diazepam, canine dermal formula and diphenhydramine, canine immune formula and chemotherapy, canine musculoskeletal formula and carprofen, canine intestinal formula and antibiotics, and feline immune, renal, and whole body formulas and antibiotics.

During the course of this study, it was determined that whole food nutritional support can be beneficial for effective case management. Based on patient status and full case evaluation, these whole food nutritional products can be used as the sole patient therapies or can be used in conjunction with other therapies. It should be noted that many of the patients in this study had chronic problems that tended to be more challenging to effectively address. The results of this study demonstrate that all patients benefit from whole food nutritional support. Some patients had dramatic responses while others had responses that were subtle and required more time for full resolution. No significant detrimental effects were associated with these products at this level of assessment. Likewise, no detrimental drug or supplement interactions were noted. The majority of owners were satisfied with the results obtained through use of the study products when used alone or in combination with other products. This translates into better owner compliance and improved patient management.

Patients were monitored for one month to 23 months. This gave opportunity to observe both short-term and long-term effects and benefits. The current study was designed to address basic questions about the products and was not intended to be definitive. Obviously this study leaves many questions unanswered. Ongoing, multi-center studies are focused on more precise evaluation of each patient along with complete documentation of the important parameters of product use. Future studies will strive to delineate cellular and metabolic events that contribute to the development of disease and seek to identify whole food nutritional approaches that optimize cellular healing responses.

References


