



**CANINE  
BIOLOGICS**

## **White Paper**

### **Formulation Methodology for Developing an Integrated Nutrition System to Support Dogs Fighting Cancer**

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## Introduction

Despite advances in canine cancer diagnosis and treatment in recent decades, the high prevalence of cancer in dogs has not declined. According to the American Veterinary Medical Association (AVMA), one in four dogs and more than half of all dogs over the age of 10 will develop cancer during their lifetime.

The world we live in today is riddled with environmental and man-made toxins. Canines, like their human counterparts, are bombarded daily by fertilizers, pesticides, pollution, heavy metals, formaldehyde, radon, BPA from plastics and numerous other sources.

Denver-based Canine Biologics has developed the world's first evidence-based integrated nutrition system formulated to support dogs fighting cancer. This system provides targeted nutrition to support the digestive, immune, integumentary and other physiologic systems in dogs. It can help reduce inflammation and assist with gaining or maintaining weight throughout the course of the disease and beyond. The nutrition system can also boost the immune response and support gastrointestinal and liver health in the face of damage from chemotherapy.

A significant challenge with some veterinary diets used for dogs with cancer is that while they may provide nutrition, they generally lack palatability making adequate ingestion of food a challenge. Canine Biologics considered that dogs with cachexia, as well as those undergoing chemotherapy or radiation therapy, may experience significant nausea and/or changes to their sense of smell that can lead to inappetence. Therefore, palatability was a critical component of the nutrition system it developed.

## New Methodology Needed

Manufacturing methods used by most commercial pet food companies leave much to be desired. The high heat and pressure used to process most commercial canned and kibble dog foods alters the ingredients in a variety of undesirable ways. Supplementing with synthetic vitamins and minerals or vitamin pre-mixes to overcompensate for the inevitable degradation of nutrients during transit and shelf life means that what starts out at the factory is quite different from what ends up in a dog's bowl.

Further degradation of nutrients occurs through repeated exposure to air, heat and light which oxidizes and chemically alters some ingredients, such as lipids. Large bags of commercial pet food tend to receive even more exposure to air as the bags are opened and closed repeatedly for feeding.

Canine Biologics supplements its integrated nutrition system with a blend of 26 natural plant extracts, amino acids, proteins, vitamins and minerals. Over-supplementation is unnecessary as all components are kept separate until the time of feeding to prevent oxidative damage and to preserve nutritional integrity.

The human-grade food and salmon oil are already highly palatable, but to ensure the nutrition system maintained its appeal once the supplement mix was added, the team added hydrolyzed pork liver to the supplement mix to enhance the flavor and increase the protein content.

## Research & Development

Canine Biologics was founded to create an entirely different way to feed and support dogs fighting cancer. Due to the high prevalence of canine cancer, the company's research team used scientific methods to formulate a nutrition system specifically to help with the symptoms and side effects of cancer and cancer treatments. Canine Biologics' sole mission is to create optimal nutritional support for canine cancer patients.

To achieve this, the company assembled a team including veterinarians with PhDs in tumor immunology and nutrition. They were tasked with developing the food and a proprietary supplement mix as two of the three components in the company's nutrition system. The third piece of the system is wild-caught salmon oil used to deliver therapeutic levels of omega-3 fatty acids, especially DHA. To ensure the omega-3s are provided in a beneficial way, Canine Biologics sourced wild-caught Alaskan salmon oil that has undergone molecular distillation resulting in a high-purity oil tested to be free from toxins and contaminants including heavy metals like mercury. Together, the three components of the integrated nutrition system formula provide the optimal nutrition dogs need in their battle against their disease.

## Novel Approach to Canine Nutrition

Starting with extensive review into oncology studies and clinical trials, the research team used scientific methods to develop an evidence-based integrated nutrition system. Ingredients such

as arginine, silybin, beta glucans, cordyceps mushrooms, genistein and others were studied and selected for inclusion in this targeted-nutrition program to provide a broad spectrum of benefits.

Canine Biologics chose to cook each individual food ingredient separately—each to its lowest safe temperature—and then combine the ingredients and freeze dry them. By shipping the three components in separate containers and mixing them at feeding time, the company was able to eliminate processes that lead to nutrient degradation and oxidation. It costs more to do it this way, but it ensures optimal nutrition for dogs who need it most.

## Formulation Methodology

The base diet is comprised of high-quality, human-grade ingredients and is formulated to preferentially starve tumor cells by reducing the carbohydrate levels in the diet, decreasing insulin and lactate levels and thereby potentially reducing the cachexia process. Many cancer patients suffer from cachexia that results in muscle wasting and significant loss of body mass.

Reducing cachexia may lead to decreased weight loss and fewer treatment delays or complications. To effectively decrease carbohydrates, the development team increased the amount of fatty acids and amino acids. Omega-3 fatty acids have the additional benefit of providing immune system modulation, favoring an anti-cancer immune environment by changing the cytokine milieu and potentially decreasing levels of regulatory T cells.<sup>1</sup>

To potentially enhance the anti-cancer immune environment, additional supplements were added to aid in the treatment of lymphoma. Two important ingredients in the proprietary supplement blend are commonly used in Traditional Chinese Medicine: beta glucans and cordyceps mushrooms. These are now also backed by carefully constructed studies as noted below.

Beta glucans has been shown to have a synergistic effect when combined with chemotherapy drugs in the treatment of lymphoma.<sup>2</sup> Beta glucans has been shown to help stimulate the immune system and decrease the pro-tumor T regulatory cells found in increased numbers in lymphoma patients.

The cordyceps mushroom family has been shown to decrease bone marrow suppression induced by chemotherapy and enhance immune function in these immunosuppressed patients.<sup>3</sup> To help aid in protein supplementation and potentially aid in preventing chemotherapy side effects, a variety of amino acids were added to the formula. Glutamine supplementation has been shown to decrease chemotherapy side effects including esophagitis.<sup>4</sup> This leads to better gastrointestinal (GI) tract healing and tolerability of chemotherapy.

Arginine has been shown to be decreased in cancer patients, and a study of dogs with lymphoma showed an increased survival benefit by adding arginine to the diet.<sup>5</sup> This study also noted increased quality of life scores in dogs.

Milk thistle was chosen for inclusion in the supplement mix for its ability to decrease liver enzyme elevations in dogs receiving chemotherapy for treatment of lymphoma. By lowering liver enzyme levels, canine patients were better able to continue treatment and were more likely to be able to complete a full course of treatment.<sup>6</sup>

Genistein, a plant-derived isoflavone, was also selected for addition to the supplement mix. Genistein has shown to be an inhibitor of angiogenesis. It also sensitizes lymphoma to CHOP chemotherapy, enhancing the effect of this common chemotherapy protocol for the treatment of lymphoma.<sup>7</sup>

## Conclusion

The Canine Biologics integrated nutrition system uses a multi-faceted approach to fight cancer cachexia and provide optimal nutrition for critically ill dogs. The combination of a high-fat, low-carbohydrate, human-grade diet, along with a therapeutic dose of omega-3 fatty acids from salmon oil and a mix of evidence-based supplements may potentially stimulate the immune system and help alleviate the side effects of cancer and cancer treatments.

Canine Biologics is currently working to formulate additional diet options based on other proteins. The company is also working to formulate additional supplement blends designed to target some of the most common forms of canine cancer.

## Sources

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<sup>3</sup> The effect of Cordyceps Sinensis in the prognosis on patients receiving chemotherapy with malignant tumors: A systematic review and meta-analysis. Sun et. al. TMR Cancer 2020.

<sup>4</sup> Oral Glutamine Supplements Reduce Concurrent Chemoradiotherapy-Induced Esophagitis in Patients with Advanced Non-Small Cell Lung Cancer. Chang et. al. Medicine (2019) 98:8.

<sup>5</sup> Effect of Fish Oil, Arginine and Doxorubicin Chemotherapy on Remission Time and Survival for Canine Lymphoma. Ogilvie et. al. Cancer 88: 1916-1928.

<sup>6</sup> Prospective Randomized Clinical Trial Assessing the Efficacy of Denamarin for Prevention of CCNU-Induced Hepatopathy in Tumor-Bearing Dogs. Skorupski et. al. Journal of Veterinary Internal Medicine 011; 25:838–845.

<sup>7</sup> Genistein Sensitizes Diffuse Large Cell Lymphoma to CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) Chemotherapy. Mohammed et. al. Molecular Cancer Therapeutics 1361.