Case Report

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Peptide Therapy Improves Mobility in Older and Large Breed Canines: A Case Study

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ABSTRACT

Senescence can be defined as the normal, time-dependent changes that arise during the later stages of life in every animal. Aging in pets gives rise to a range of symptoms that generally involves a decline in overall mobility and a decrease in overall activity. The severity and onset of these aging symptoms depend on a variety of factors including breed size, genetics, weight, general joint health, nutrition, environmental factors and lifestyle as well as normal wear and tear on joints. A regenerative therapy that targets inflammatory pathways and regeneration is presently lacking in canine therapeutics. Due to their stem cell origin, Nano Organo Peptides (NOP) have anti-inflammatory effects, as well as regenerative and reparative properties. Due to these properties, NOPs offer the potential to target a vast array of pre-clinical models. In this case study, our data demonstrated that NOP therapy was tolerated by two canine subjects and a significant improvement in their mobility and activity was observed.

KEYWORDS: Peptide therapy; Mobility; Motor function; Nano organo peptides (NOP); Anti-inflammatory; Regenerative; Aging dog therapeutics

INTRODUCTION

The incidence and severity of osteoarthritis can negatively impact the quality of life of aged dogs [1]. Osteoarthritis is more prevalent in older and larger breed dogs and the incidence and severity depends on the canine joints involved. Peptide therapy is the use of targeted signaling amino acid chains to instruct cells on the functions they need to perform [2]. As the aging process continues there is a higher incidence of joint damage. Currently, treatment options are limited. Anti-inflammatory medications exist to treat the inflammation but not the destructive underlying process in the joints. Biological therapies exist but are not intended for long term use. There is an unmet need to safely and effectively treat or delay joint damage in dogs.

Amino acids play a role in almost every system of the body, including muscle, connective tissue and nervous system function. Accordingly, the use of peptides may be beneficial in improving overall mobility. Peptides are metabolized into individual amino acids and are recycled by the body, unlike many drug therapies which are eliminated or can accumulate, causing toxicity or side effects. Peptides are linear polymers formed by a series of amino acid residues that are linked together with peptide bonds [3]. Whereas proteins typically contain between 50 and 2000 amino acid residues and have a mean molecular weight between 5.5 and 22kDa, peptides are composed of less than 50 resides and have a lower molecular weight than proteins. Short peptides have been demonstrated to play an important role in the modulation

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of transcription, transmission of biological information, and in restoring genetic alterations that occur with aging. These peptides are signaling molecules that act as regulatory factors through their interaction with DNA and histone proteins. Moreover, the physiological process of senescence is highly influenced by peptide regulation of homeostasis and is related to the aging of cells, tissues, and organs [4].

Nano Organo Peptides (NOP) are tiny molecules that are 3nm in size and have a molecular weight of less than 10kDA [5]. NOPs are procured from mammalian stem cells and are processed through a proprietary parallel-extraction process but are unique in that they undergo multiple ultrafiltrate steps through specialized Millipore filters to receive the cellular material within the cell, known as the molecular-level ultrafiltrates. NOP contents are extracted from organ specific cells with an initially high molecular mass and separated through by ultrafiltration through micro-Millipore filters that selectively allow substances with a molecular mass of less than 10kDa to pass. The low molecular weight and high solubility of NOPs permit them to be delivered sublingually and or by injection (subcutaneous or intramuscular). As a result, NOPs have been investigated for variety of applications including cosmetics [6] and regenerative organ repair [7]. In this case report, we hypothesized that the NOP properties of the peptide acting signaling agent would agonistically interact with the NOP receptor. Our results indicate an improvement in the mobility and activity levels observed as the ability to get up from a down position, desire to play and go outside in the canines tested.

CASE REPORT

Subject A is a female Shiloh Shepherd dog aged 9 years and 10/12 months and weighing 98 lbs. She began to demonstrate motor function deficits, which qualified her to participate in this study. She began having difficulty standing from a down or sitting position and was hesitant when climbing stairs. Assistance was also needed getting in and out of the owner's vehicle, while in the past these activities were performed independently and with exuberance. Subject A also demonstrated lethargy and a canine ophthalmologist noted that her eyes did not look as bright as they had previously. Subject B is a female Shiloh Shepherd aged 9 years and 5 months and weighing approximately 100lbs. Similar to the reported behavioral changes observed in Subject A, Subject B also began having difficulties standing from a down position as well as climbing the stairs both ascending and descending. Her posterior legs began to cross over which would normally be indicative of degenerative myelopathy, a debilitating and slowly progressive spinal cord disease with a genetic basis. The dog had become lethargic and arthritic.

TREATMENT

NOP treatments were done in two phases over a course of 534 days with Certificates of Analysis outlining concentration, pH and sterility in Appendix 1.

Phase 1 ran from Day 1 to Day 15 and Phase 2 from Day 18 to 534. To understand the importance of phase-based treatment, we chose to treat Subject A in both phases, and Subject B in a single phase. Comparing the results from these two subjects will allow a phase comparison to gain a better understanding on the efficacy of the treatment in large breed senior dogs. The treatments used were based on observations of the canines' behaviors and symptoms. In Phase 1, Subject A was given subcutaneous injections of NOPs derived from bone and placenta on Days 1, 3, 6, 9, 12 and 15 (Table 1).

Table 1: Phase 1 study design for subject A.

Subject A - Phase 1	2.5 ml NOP per Subcutaneous Injection					
	Day 1	Day 3	Day 6	Day 9	Day 12	Day 15
Bone	X	X	X	X	X	X
Placenta	X	X	X	X	X	X

In Phase 2, Subject A was given injections NOPs derived from bone, placenta, central nervous system (CNS), cartilage, liver, pancreas, muscle, synovial fluid and spinal cord given by intramuscular injection on Days 18, 24, 30, 33, 37, 77, 125, 133, 177, 290, 360, 386, 402, 443, 460, 502 and 534 (Table 2).

Table 2: Phase 2 study design for subject A.

Subject A - Phase 2	2.5ml NOP per Subcutaneous Injection															
	Day 18	Day 24	Day 30	Day 33	Day 77	Day 125	Day 133	Day 199	Day 290	Day 360	Day 386	Day 402	Day 443	Day 460	Day 502	Day 534
Bone			X		X	X	X	X	X	X						
Placenta		X		X		X	X	X	X	X						
CNS			X		X											
Cartilage		X			X	X	X	X	X	X						
Liver			X		X											
Pancreas		X		X												
Peripheral Muscle		X		X						X						
Synovial Fluid						X	X	X	X	X						
Spinal Cord											X	X	X		X	X

In Phase 1, Subject B was given injections of bone and placenta peptides subcutaneously (Table 3). In Phase 2, Subject B was given injections of bone, placenta, CNS, cartilage, liver, pancreas, muscle, synovial fluid and spinal cord peptides given intramuscularly (Table 4).

Table 3: Phase 1 study design for subject B.

Subject B- Phase 1	2.5 ml NOP each Injections Given Subcutaneous of Each					
	Day 1	Day 3	Day 6	Day 9	Day 12	Day 15
Bone	X	X	X	X	X	X
Placenta	X	X	X	X	X	X

Table 4: Phase 2 study design for subject B.

Subject B - Phase 2	2.5ml NOP per Intramuscular Injection											
	Day 18	Day 24	Day 30	Day 33	Day 77	Day 125	Day 133	Day 199	Day 241	Day 290	Day 299	Day 303
Bone	X		X	X	X	X	X	X			X	X
Placenta	X			X		X	X	X			X	X
CNS			X		X					X		
Cartilage	X					X	X	X			X	X
Liver			X		X							
Pancreas	X			X								
Peripheral Muscle	X			X					X	X		
Synovial Fluid						X	X	X			X	X
Spinal Cord									X	X		

RESULTS

A Canine Mobility Assessment form was scored to assess the canines' pain, discomfort and mobility in managing daily activity (Table 5). We assigned these values as an assessment point to quantify the baseline mobility and improvements if any.

Table 5: Canine Mobility assessment form.

1	Slowing down on walks
2	Playing less than usual
3	Difficult jumping or climbing the stairs
4	Stiff when rising
5	Changes in sleeping position
6	Total value (sum of 1-5)

Table 6: Canine Mobility Assessment scores for Canines A and B through treatment period. Score 0 indicates no activity and scores 5 indicates full activity.

	Day				
	0	28 (1 month)	56 (2 months)	112 (4 months)	224 (8 months)
Slowing Down on Walks	1	3	3	4	5
Playing Less Than Usual	1	2	3	4	5
Difficult Jumping or Climbing Stairs	1	3	3	4	5
Stiff When Rising	1	3	3	4	5
Total Score	4	11	12	16	20

Our results (Table 6) showed that the initial mobility score of the canines at baseline (Day 0) was 4 and after peptide treatment increased to 11 at Day 28 and then to 12 at Day 56. After 112 days (4 months), the mobility score further increased to 16, indicating improvements in the measures of mobility. We observed further improvements in mobility parameters with total mobility score of 20 by Day 224 (8 months), which represents a return to full mobility.

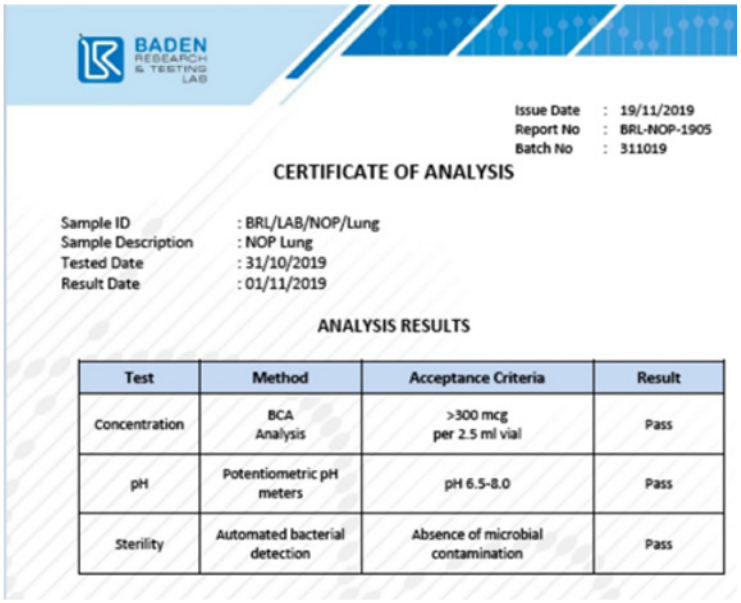
DISCUSSION

In this case study, we report the results of NOP injections into two canines, Subject A and Subject B to ascertain whether NOPs injections would be tolerated and cause an improvement in their mobility and activity. Both subjects appeared to be more energetic and able to get up from a sitting or down position, though there are no definitive markers available to quantify the results. Incidentally, we also observed that both subjects were also brought down to an optimal weight, which is better for joint and bone health, with no change in diet.

CONCLUSION

NOPs have been investigated for variety of applications including regenerative organ repair. In this case study, we report the results of NOP injections into two canines, Subject A and Subject B. Our results showed that the general activity of the dogs was significantly improved following peptide treatment within 1-2 months following peptide administration and return to normal level of mobility at 8 months. Though this case report cannot conclusively form conclusions due to only two canines used, it suggests that our therapy did not negatively impact the metabolic state and immune profile of the subjects, and hints at a level of safety with NOP therapy. Both subjects appeared to gain mobility and functionality, though there are no definitive markers available to quantify these results. Future studies are needed to assess functional outcomes of NOP therapy and increase the number of test subjects used.

Appendix 1: Canine Mobility Assessment scores for Canines A and B through treatment period. Score 0 indicates no activity and scores 5 indicates full activity.



BADEN RESEARCH & TESTING LAB

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Report No : BRL-NOP-1905
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CERTIFICATE OF ANALYSIS

Sample ID : BRL/LAB/NOP/Lung
Sample Description : NOP Lung
Tested Date : 31/10/2019
Result Date : 01/11/2019

ANALYSIS RESULTS

Test	Method	Acceptance Criteria	Result
Concentration	BCA Analysis	>300 mcg per 2.5 ml vial	Pass
pH	Potentiometric pH meters	pH 6.5-8.0	Pass
Sterility	Automated bacterial detection	Absence of microbial contamination	Pass

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