

Anti-Inflammatory and Anti-Arthritic Efficacy and Safety of Purified Shilajit in Moderately Arthritic Dogs

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Abstract

The objective of this investigation was to evaluate the efficacy and safety of purified Shilajit in moderately arthritic dogs. Ten client-owned dogs in a randomized double-blinded study received either a placebo or Shilajit (500 mg) twice daily for a period of five months. Dogs were evaluated each month for physical condition (body weight, body temperature, heart rate, and respiration rate) and pain associated with arthritis (overall pain, pain from limb manipulation, and pain after physical exertion). Serum samples collected from these dogs were examined each month for biomarkers of liver (bilirubin, ALT, and AST), kidney (BUN and creatinine) heart and muscle (creatine kinase) functions. The findings of this study revealed that dogs receiving Shilajit (Group-II) showed a significant ($P < 0.05$) reduction in pain from limb manipulation by day 60, and overall pain and pain after physical exertion by day 120. Maximum pain reduction, using all three criteria, was observed on day 150. Pain level remained significantly unchanged in dogs receiving the placebo. Dogs in either group showed no significant change ($P > 0.05$) in physical parameters or serum markers, suggesting that Shilajit was well tolerated by moderately arthritic dogs. It was concluded that Shilajit significantly ($P < 0.05$) reduced pain in osteoarthritic dogs and markedly improved their daily life without any side effects.

Keywords: Purified Shilajit; Osteoarthritis in canine; Shilajit safety; Anti-arthritic nutraceutical

Introduction

Currently, there are more than 78 million dogs in the US, and every fifth adult dog suffers from arthritis [1]. Dogs suffer more frequently from osteoarthritis (a chronic and progressive disease) than any other form of arthritis. Osteoarthritis, also known as degenerative joint disease, is a functional disorder of the joint, characterized by a change in joint shape secondary to a loss of articular cartilage, osteophyte formation, subchondral sclerosis, bone marrow lesions and synovial proliferation, with subsequent alteration of mechanical properties that result in decreased stability, movement and loading [2-9]. In the early stages of osteoarthritis, there is a progressive depletion of the cartilage proteoglycan leading to a net loss of matrix from the cartilage [10]. This leads to a cascade of negative events, including changes in enzymatic cleavage of proteoglycans and an increase in minor collagen types leading to structural damage and deterioration of the cartilage. The breakdown of cartilage can be increased with certain enzymes including the matrix metalloproteinase enzymes (MMPs). The severity of cartilage lesions in osteoarthritis can be cor-

related with the levels of collagenase (MMP-1) present [7-9]. The cascading events lead to increased friction and inflammation in the joints. Dogs suffering with osteoarthritis show stiffness of joints, crepitus, pain upon manipulation of the joint, periarticular swelling, palpable effusion, restriction in range of motion, lameness and pain and loss of function [7, 11-16]. The combination of history, physical exam, and radiograph can help diagnose osteoarthritis in a canine patient. Radiographs indicate osteophytosis and subchondral bone sclerosis that develops over time in osteoarthritic patients. MRI findings can reveal changes consistent with osteoarthritis in the cartilage [17,18].

There are multiple factors which influence dogs to develop arthritis, such as genetic predisposition, trauma or injury to the bones or joints, aging, poor nutrition, obesity and environmental factors [1,19]. Often, large breed dogs (e.g. German Shepherds, Labrador Retrievers, Siberian Huskies, Rottweilers and others) are more prone to develop osteoarthritis than are small breeds [20-22].

Arthritic dogs show a variety of signs and symptoms, from limping to an inability to walk due to joint stiffness. Pain is the number one complaint [11-14]. The objectives in treating arthritis are to minimize joint pain by reducing the inflammation and slowing the progression of the cartilage damage and to increase joint flexibility. These goals are achieved by employing a variety of pharmaceuticals, nutraceuticals, disease modifying agents and physical therapy along with acupuncture [14, 23-26]. Cyclooxygenase (COX) inhibiting non-steroidal anti-inflammatory drugs (NSAIDs, such as carprofen, deracoxib, etodolac, firocoxib, ketoprofen, meloxicam, robenacoxib, rofecoxib, tepoxalin, etc) are used with caution as they may cause some adverse effects, such as reduced appetite, vomiting, gastrointestinal bleeding and hepatic and renal damage and dysfunction [23, 27-32]. In a recent prospective (randomized, placebo-controlled, blinded) study, Monteiro-Steagall et al [33] found that the incidence of adverse effects was not statistically different between treated and control dogs.

Recently, dog owners and veterinarians have considered managing osteoarthritis in dogs with herbs and nutraceuticals. Today, in humans and animals, glucosamine and chondroitin sulfate are the most common nutraceuticals to provide building blocks to repair the cartilage and to minimize and slow down the progression of osteoarthritis to ease inflammatory pain [24,25, 34-37].

Shilajit is a blackish brown exudate from the sedimentary rocks of the pristine himalayan mountains at about 10,000 ft altitude. Purified shilajit is prepared from this exudate by a proprietary extraction process. The main constituents of shilajit are dibenzo- α -pyrones (DBPs), DBP-chromoproteins and fulvic acids with DBP core. On the other hand, alluvial (plant based) fulvic acids do not have DBP core and do not have the same therapeutic efficacy as shilajit. In fact, alluvial fulvic acids are used as fertilizers. Shilajit exerts many important roles in biological systems: (1) improves bioavailability of minerals and nutrients, (2) provides electrolytes, (3) detoxifies toxic substances, including heavy metals, (4) improves immune system and (5) exhibits antioxidant properties. Shilajit has been used for more than 3000 years for both preventative health and for treating many diseases in humans, including diabetes, arthritis, hypertension, immune dysfunction and loss of memory [38-40]. The present study was undertaken to discover the therapeutic efficacy and safety of purified Shilajit in moderately arthritic dogs. The hypothesis of the present investigation was that purified Shilajit will provide anti-inflammatory and anti-arthritic effects in moderately arthritic dogs with minimal side effects. In this paper, we present the findings of Shilajit as an effective and safe supplement that exerts anti-inflammatory and anti-arthritic effects in osteoarthritis dogs. Shilajit appears very promising and offers an alternative to many other previously reported pharmaceuticals and nutraceuticals.

Materials and methods

Animals

Ten client-owned moderately arthritic dogs, weighing between

40-65 pounds, were used in this study. These dogs, based on signs of joint stiffness, lameness and radiographic evidence, had pain at the level of moderate arthritis. Our inclusion criteria of dogs for this study excluded those having liver, kidney or heart disease, neoplasia, cancer or any other major disease. Institutional Animal Care and Use Committee (IACUC) approval and owner consents were obtained prior to the initiation of this study.

Experimental design

In a randomized double-blinded study, ten client-owned dogs received a placebo (Group-I) or Shilajit (Group-II). The placebo group contained only two dogs because IACUC advised us to keep to the number of dogs to a minimum due to the fact that arthritic dogs suffer from pain for a period of five months. Moreover, findings from our previous studies revealed that dogs receiving placebo showed no improvement in arthritis pain [11-14]. Eight dogs in Group-II received purified Shilajit (500 mg) twice daily (one capsule before morning meal and one capsule before evening meal) for a period of five months. None of the dogs received any treatment or supplement for 3 to 4 weeks prior to the study or during the study period.

Pain measurement

At pre-determined intervals (i.e. 30 days), each dog was evaluated for overall pain, pain upon limb manipulation and pain after physical exertion, for a period of five months. Overall pain, on a scale of 1-10, was graded as: 0, no pain; 2.5, mild pain; 5, moderate pain; 7.5, severe pain; 10, severe and constant pain. Pain after limb manipulation, on a scale of 0-4, was evaluated as: no pain: 0, mild pain: 1, moderate pain: 2, severe pain: 3, severe and constant pain: 4. Pain after physical exertion, on a scale of 0-4, was evaluated as: no pain: 0, mild pain: 1, moderate pain: 2, severe pain: 3, and severe and constant pain: 4. The physical examination of each limb started with the forelimbs and ended with the rear limbs. The evaluation focused on manipulation of the limbs in a forward, backward and circular motion. Three main joints in each limb included for evaluation were the shoulder joint, knee joint and stifle joint. Popping and cracking of the joint as well as vocal pain were noted for each canine. Detailed criteria of the measurement of pain are provided in our earlier publications [11-14]. The present investigation was carried out on moderately arthritic dogs. A moderately arthritic dog exhibits overall pain of about 5 on a scale of 1-10; pain upon limb manipulation about 2 on a scale of 1-4; and pain after physical exertion about 2 on a scale of 1-4.

Physical examination

On a monthly basis, dogs were given a full physical examination for body weight, body temperature and heart rate. Normal values for these parameters are mentioned below Table 1.

| Parameter | Unit | Placebo/Treated | Day 0 | Day 30 | Day 60 | Day 90 | Day 120 | Day 150 |
|------------------|-----------|-----------------|------------|------------|-----------|------------|------------|------------|
| Body Weight | lb | Placebo | 54.1±11.05 | 54.0±10.8 | 53.4±9.85 | 54.6±8.95 | 53.6±9.95 | 53.7±9.5 |
| | | Treated | 54.5±3.37 | 54.9±3.53 | 54.4±3.26 | 54.9±3.16 | 54.5±3.22 | 54.9±3.27 |
| Heart Rate | Beats/min | Placebo | 135±15 | 120±0 | 115±5 | 90±10 | 98±2 | 99±1 |
| | | Treated | 106.8±4.96 | 117.6±5.89 | 96.5±6.47 | 102.4±3.40 | 102.8±4.60 | 108.9±2.81 |
| Body Temperature | °F | Placebo | 100.3±5.41 | 100.3±0.2 | 99.9±0.65 | 100.3±0.2 | 100.4±0.3 | 100.1±1.2 |
| | | Treated | 100.1±0.43 | 99.6±0.26 | 99.6±0.23 | 99.6±0.29 | 100.9±0.30 | 100.4±0.20 |

Values are means±SEM; Normal heart rate= 70-160 beats per minute; Normal body temperature= 101-102.5 °F.

Table 1: Effects of placebo or Shilajit (500 mg, bid) on physical parameters in moderately arthritic dogs

| Parameter | Unit | Placebo/Treated | Day 0 | Day 30 | Day 60 | Day 90 | Day 120 | Day 150 |
|-----------------|-------|-----------------|------------|-----------|------------|------------|-------------|------------|
| BUN | mg/dl | Placebo | 19.5±3.5 | 18±1 | 22±2 | 21±1 | 17±1 | 17±4 |
| | | Treated | 17.1±2.88 | 15.6±1.78 | 18.1±2.30 | 18.1±2.30 | 20.5±2.85 | 20.8±2.64 |
| Creatinine | mg/dl | Placebo | 0.92±0.16 | 0.75±0.02 | 0.72±0.02 | 0.76±0.09 | 0.81±0.02 | 0.82±0.03 |
| | | Treated | 1.00±0.09 | 0.79±0.03 | 0.79±0.04 | 0.79±0.09 | 0.92±0.05 | 0.94±0.04 |
| Total bilirubin | mg/dl | Placebo | 0.5±0.3 | 0.2±0 | 0.3±0.1 | 0.35±0.05 | 0.2±0 | 0.3±0.1 |
| | | Treated | 0.21±0.04 | 0.25±0.04 | 0.23±0.05 | 0.39±0.09 | 0.26±0.04 | 0.31±0.04 |
| ALT | IU/L | Placebo | 45.5±23.5 | 35.5±8.5 | 28±0 | 40±12 | 27±0 | 57.5±14.5 |
| | | Treated | 47.9±4.54 | 59.9±8.41 | 75.1±20.4 | 57.6±4.59 | 60.8±7.36 | 58.6±4.95 |
| AST | IU/L | Placebo | 127.5±39.5 | 123±33 | 84±4 | 104±15 | 779.5±629.5 | 166.4±25.7 |
| | | Treated | 198.4±44.7 | 349±80.9 | 224.6±66.2 | 132.0±28.2 | 246.0±84.8 | 166.4±25.7 |
| CK | IU/L | Placebo | 28.5±3.5 | 22±7 | 19.5±5.5 | 23.5±5.5 | 45.5±26.5 | 92.5±3.5 |
| | | Treated | 27.1±3.26 | 31.5±3.13 | 28.4±3.57 | 28.5±2.35 | 30.5±3.59 | 29.1±3.60 |

Values are means±SEM; Normal reference values: BUN (7-26 mg/dl); Creatinine (0.0-1.35 mg/dl); Total bilirubin (0.1-0.6 mg/dl); ALT (10-120 IU/L); AST (15-65 IU/L); CK (60-450 IU/L).

Table 2: Effects of placebo or Shilajit (500 mg, bid) on serum biomarkers of liver (bilirubin, ALT, and AST), kidney (BUN and creatinine), heart and skeletal muscle (CK) functions in moderately arthritic dogs

Serum biomarkers assays

Blood samples were collected from the cephalic vein using a 3 mL syringe with a 22 gauge needle and were stored in a marble top tube. Samples were then spun to collect serum and transferred to a red top tube for evaluation. Serum samples were collected each month and analyzed for liver (bilirubin, ALT, AST), kidney (BUN and creatinine), heart and muscle (CK) functions, using a Beckman AU 480 serum analyzer. The serum sample assay indicated that neither placebo nor Shilajit produced adverse effects in vital organs of arthritic dogs. Normal reference values of all serum parameters are provided below Table 2.

Statistical analysis

The data presented are means ± SEM. Statistical significance of difference was determined by analysis of variance (ANOVA) coupled with Tukey-Kramer test ($P < 0.05$) using the NCSS2000 Statistical Analysis and Graphics Software for Windows®.

Results

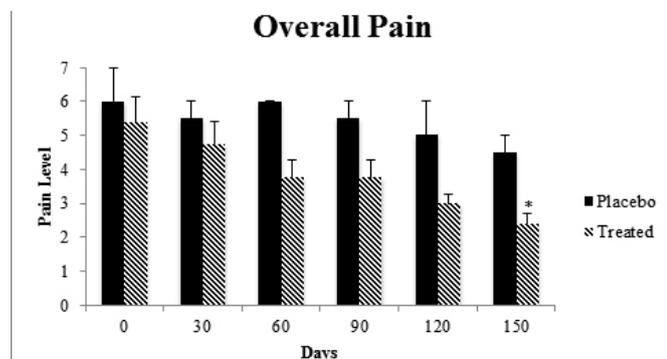
In this double-blinded clinical trial, moderately arthritic dogs receiving placebo (Group-I) or purified Shilajit (500 mg) twice

daily for a period of five months, were evaluated for physical parameters, pain level and serum biomarkers of liver, kidney, heart and muscle functions.

On a monthly basis, each dog was examined for pain level (overall pain, pain after limb manipulation and pain after physical exertion) and the data are shown in Figures 1-3. While evaluating overall pain, the key points were to observe the dog's gait, range of motion, ability to sit or lie down, ability to rise from a sitting position, ability to rise from a lying position, and posture while standing. Group-II dogs receiving Shilajit showed significant ($P < 0.05$) reduction in overall pain by day 120 (3.00 ± 0.27) compared to day 0 (5.38 ± 0.75). The maximum reduction in overall pain was noted on day 150 (2.38 ± 0.32). Dogs receiving placebo showed no significant change in overall pain.

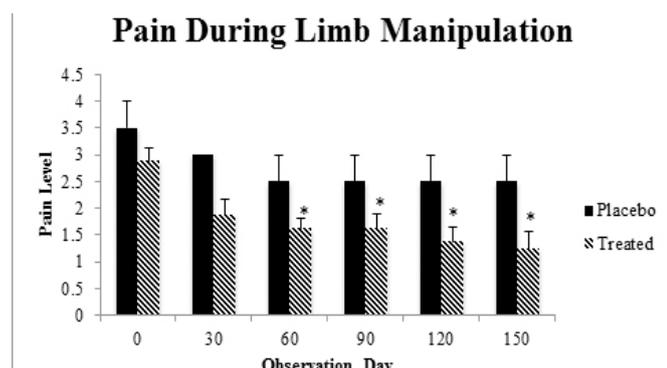
Pain after limb manipulation was measured in each limb of the dog (placed in lateral recumbency) for flexibility, joint integrity, crepitation and vocalization. The pain level was significantly reduced by day 60 (1.63 ± 0.18) and the trend continued until day 150 when the pain level was maximally reduced (1.25 ± 0.31) (Figure 2). Pain after limb manipulation remained significantly unchanged in Group-1 (placebo) dogs. Figure 3 shows the data of pain after physical exertion in dogs receiving placebo or Shilajit. The canines were evaluated for pain after three minutes of jogging. After jogging, pain level was assessed

based on the dog's unwillingness to move, body position, limping, flexibility, joint integrity, crepitation and vocalization. Significant reduction in pain after physical exertion was noted on day 120 (1.37 ± 0.26) compared to day 0 (2.63 ± 0.26) in dogs receiving Shilajit. The maximum reduction in pain was observed on day 150 (1.25 ± 0.28). Dogs on placebo showed no significant change in pain level.



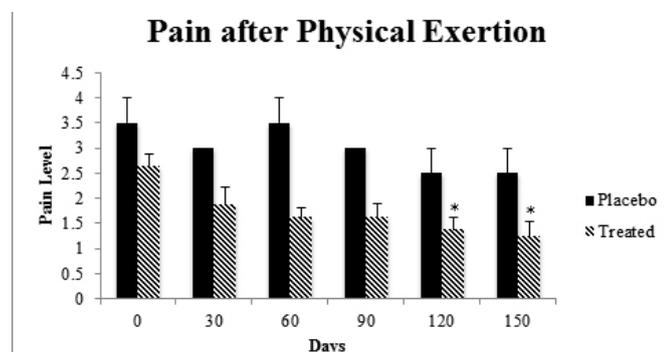
*Significantly different compared to pre-treated values ($P < 0.05$).

Figure 1: Effects of placebo or Shilajit (500 mg, bid) on overall pain in moderately arthritic dogs. Overall pain was graded on a scale of 0-10 (0, no pain; 2.5, mild pain; 5, moderate pain; 7.5, severe pain; and 10, severe and constant pain). Details of overall pain measurement criteria are described in the text and our previous publications [11-14].



*Significantly different compared to pretreated values ($P < 0.05$).

Figure 2: Effects of placebo or Shilajit (500 mg, bid) on pain from limb manipulation in moderately arthritic dogs. Pain from limb manipulation was graded on a scale of 0-4 (0, no pain; 1, mild pain; 2, moderate pain; 3, severe pain; and 4, severe and constant pain). Details of pain measurement after limb manipulation criteria are described in the text and our previous publications [11-14].



*Significantly different compared to pretreated values ($P < 0.05$).

Figure 3: Effects of placebo or Shilajit (500 mg, bid) on pain after physical exertion in moderately arthritic dogs. Pain after physical exertion was graded on a scale of 0-4 (0, no pain; 1, mild pain; 2, moderate pain; 3, severe pain; and 4, severe and constant pain). Details of pain measurement after physical exertion criteria are described in the text and our previous publications [11-14].

Data of physical parameters (body weight, body temperature, and heart rate are shown in Table 1. Dogs receiving placebo or Shilajit showed no significant change in any physical parameters during the course of this investigation. Table 2 presents serum chemistry data for biomarkers of liver (bilirubin, ALT, and AST), kidney (BUN and creatinine), heart and muscle (CK) functions. Dogs receiving placebo or Shilajit showed no significant change in serum biomarkers during the study period of 150 days.

Discussion

Osteoarthritis is prevalent in dogs primarily due to aging, but it can also be due to obesity, poor nutrition, injury, genetic predisposition and other environmental factors [1, 19-22]. Dogs are also affected by osteoarthritis, a progressive degenerative disease characterized by loss of cartilage. Eventually, dogs suffer from pain and poor quality of life due to immobility.

Veterinarians have a wide range of options to treat and manage osteoarthritis, including surgery, NSAIDs, physical therapy with acupuncture, nutraceuticals and other disease modifying agents [13, 14, 23-26, 41].

Currently, glucosamine and chondroitin are the two most commonly used nutraceuticals to manage osteoarthritis in dogs, but their efficacy is limited [24, 35]. In the last ten years, we have evaluated the therapeutic efficacy and safety of many nutraceuticals in arthritic dogs [11-14]. In a most recent chronic study, we found that Crominex 3+ (a mixture of trivalent chromium, *Phyllanthus emblica* extract and purified Shilajit) was very effective in ameliorating arthritic pain in dogs without causing any untoward events [42].

In the present paper, we report that Shilajit alone at a higher dose (500 mg, bid) compared to that present in Crominex 3+ (7.5 mg, bid), is equally effective in reducing arthritic pain and enhancing the daily activity of dogs without exerting any side effects. Shilajit administration ameliorated arthritic pain in all three categories (overall pain, pain after limb manipulation, and pain after physical exertion) with maximum effect noted on day 150. Shilajit is a pale-brown to blackish-brown resinous substance and is a herbo-mineral complex compound that consists of humus and organic plant (*Styrax officinalis*, *Trifolium repens* and others) materials. By having many bioactive minerals and plant active principles, such as fulvic acid (low molecular weight substances like uronic acids, phenolic glycosides and amino acids), humic acid (low molecular weight substances like phenolic acids, anti-oxidants and free radical scavengers) and free and conjugated dibenzo- α -pyrones, Shilajit is known to exert multiple pharmacological actions. Some of these actions include antibacterial, anti-arthritic, anti-ulcerogenic, anti-hyperglycemic, immunomodulatory, anti-inflammatory, anti-radical, spermatogenic and ovogenic, anti-aging and energetic properties [28, 38, 40, 43-47]. Shilajit has been used for both preventative health and for treating many diseases (such as allergies, diabetes, hypertension, loss of memory, immune dysfunction, arthritis, loss of libido, etc) for more than 3000 years.

Since Shilajit has multiple bioactive principles, it is highly likely that it reduced the arthritic pain due to a variety of biochemical and pharmacological mechanisms, including anti-inflammatory, anti-oxidant, immune-modulatory and energetic properties.

Conclusions

In conclusion, Shilajit is an all-natural supplement which offers significant anti-arthritic properties including reduction of pain and inflammation. All dogs responded well to Shilajit administration without exhibiting any untoward effects, thereby giving this supplement an edge over many other nutraceuticals and pharmaceuticals.

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