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Research Article

Therapeutic Efficacy and Safety Evaluation of a Novel Chromium Supplement (Crominex®+3-) in Moderately Arthritic Horses

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Abstract

Objective: The objective of this investigation was to evaluate therapeutic efficacy and safety of Crominex®-3+ (a complex of trivalent chromium, *Phyllanthus emblica* (Amla) extract and purified Shilajit) in moderately arthritic horses.

Background: Currently, millions of horses suffer from osteoarthritis (OA) around the world. OA inflicts horses because of excessive running, intense exercise, injury and infection, immune disorder, aging, genetic predisposition, and poor nutrition. Due to multiple etiologies and complex pathophysiological pathways, management of OA in horses is a challenging task for today's veterinarians. Presently, among various options, the use of nutraceuticals appears to be a preferred choice because of their efficacy and safety.

Methods: Eleven client-owned arthritic horses in a randomized double-blinded study received placebo or 1000 mg of Crominex®-3+ (containing 20 mg of chromium, 300 mg of amla extract, and 300 mg of purified Shilajit) daily in two divided doses for a period of five months. On a monthly basis, each horse was evaluated for arthritis associated pain (overall pain, pain upon limb manipulation, and pain after physical exertion) and given a full physical examination. At the same time intervals, serum samples were examined for biomarkers of liver (total bilirubin, gamma-glutamyl transferase, and aspartate aminotransferase), kidney (blood urea nitrogen and creatinine), and heart and skeletal muscle (creatine kinase) functions; and blood samples were examined for complete blood count (CBC).

Results: Findings of this investigation revealed that horses receiving Crominex®-3+ exhibited a significant ($P< 0.05$) reduction in arthritic pain noted as early as within 30 days (31-33%), with a maximum reduction after five months (69-77%) of treatment. Pain level remained significantly unchanged ($P>0.05$) in the horses receiving placebo. No significant change occurred in physical parameters, serum biomarkers or CBC in horses on placebo or Crominex®-3+, which suggested that Crominex®-3+ was well tolerated by arthritic horses.

Conclusion: Crominex®-3+ significantly ($P< 0.05$) ameliorated arthritic pain and improved quality of life without causing any untoward effects in the arthritic horses. Crominex®-3+ was well tolerated by arthritic horses and safe for long-term use.

Keywords: Equine arthritis; Osteoarthritis; Arthritic pain; Lameness; Crominex® -3+; Trivalent chromium; Amla extract; Shilajit

Introduction

Among all animal species, equine and canine suffer from arthritis more than any other species. Currently, millions of horses around the world suffer from osteoarthritis (OA). OA can inflict horses due to a single or multiple factors, such as aging, intense exercise, injury, immune disorder, genetic predisposition, and poor nutrition [1-3]. OA, also known as chronic degenerative joint disease (DJD), is an inflammatory disease characterized by osteophyte formation, subchondral sclerosis and bone marrow lesions, and changes in the synovial membrane, progressive cartilage degeneration, and changes in the soft tissues of the joint. These morphological alterations eventually lead to decreased stability and loading, loss of joint mobility, lameness, pain and dysfunction of the affected joint [4-8]. The joints most frequently affected by OA include those of the knee, fetlock, coffin, pastern, and hock. Up to 60% of lameness in horses can be due to OA.

For an effective treatment of OA in equine, understanding of its pathophysiology is required. The pathophysiology is very complex because it involves multiple etiologies and molecular and cellular mechanistic pathways. In OA, cartilage degradation is due to an imbalance between synthesis and degradation of extracellular matrix components. Deterioration of cartilage and increased cartilage lesions have been correlated with increased activities of certain enzymes, including the matrix metalloproteinases (MMPs) and aggrecanases. Proteoglycans and their component glycosaminoglycans are degraded early in the OA process. Most of the collagen degradation is affected by MMP-1, MMP-3, and MMP-13. Recent evidence also suggests that aggrecanase causes proteoglycan degradation in OA. Proinflammatory cytokine IL-1β produced in OA triggers several biological effects by stimulating mitogen activated protein kinase (MAPK) phosphorylation, which results in activation of transcription factors. IL-1β also stimulates chondrocytes to produce inducible nitric oxide synthase (iNOS), cyclooxygenase-2 and phospholipase 2A, resulting in the production of nitric oxide (NO), prostaglandin E_2 (PGE_2) and platelet activating factor [9-11]. Enhanced release of NO and PGE_2 promotes degradation of proteoglycans and collagen, inhibits proteoglycan synthesis, causes inflammation, and increases pain sensitivity. These cascading events and many others lead to increased friction and inflammation in the joint, pain, and loss of cartilage [12-20]. It is noteworthy that free radicals are also excessively generated and present in inflamed equine joints and seem to be responsible for hyaluronic acid degradation in joint fluid. Inhibition of these pathways can be a key to successful management of OA in horses.

In field conditions, the diagnosis of OA is usually based upon physical examination and radiographic evidence. Of course, in an early stage, there appears to be some discordance between radiographic changes and OA associated pain [21]. CT scan and/or magnetic resonance imaging (MRI) findings reveal changes of joint and cartilage degeneration consistent with OA [22-27].

Because the pathophysiology is complex, management of OA in equine appears to be a challenging task for veterinarians. Currently, in the management of OA, multipronged strategies are applied, involving invasive as well as non-invasive measures. The objectives in treatment of OA are to minimize joint pain by reducing inflammation and slow the progression of cartilage damage, and thereby increase the joint's flexibility, thus improving quality of life. To achieve these goals, a variety of pharmaceuticals, nutraceuticals, disease-modifying agents, stem cell therapy, gene therapy, and physical therapy with acupuncture can been used [5, 28-37]. Goodrich and Nixon [38] suggested that a proper combination of systemic NSAIDs, intra-articular steroids, viscosupplementation and chondroprotectants can be used to effectively treat OA and inhibit further progression of degenerative changes to the cartilage surface. In the recent past, nonsteroidal anti-inflammatory drugs (NSAIDs) have been used most commonly to manage OA [39-41]. Polysulfated glycosaminoglycan, sodium hyaluronan, sodium pentosan polysulfated, and autologous conditioned serum and autologous protein have also been evaluated in horses and other species as OA modifying agents [42-48]. Chronic use of some NSAIDS has been linked to adverse events, such as reduced appetite, gastrointestinal upset and bleeding, and hepatic, renal and cardiovascular risks [38,49-52].

Presently, non-pharmacologic intervention (nutraceuticals) is preferred over pharmacologic intervention (therapeutic drugs) to ease OA associated symptoms and slow down the condition's progression, because they are considered effective with minimal or no side effects. Glucosamine, chondroitin, type-II collagen, and several other nutraceuticals have been found effective in ameliorating OA associated pain in dogs and horses [5,34,38,53-57]. Other supplements used in managing OA in horses include methylsulfonylmethane, cetyl myristaleate, omega-3 fatty acids, Devil's claw, Rosehip, and Stinging nettle. In recent studies, we evaluated efficacy and safety of Crominex®-3+ (trivalent chromium, *Phyllanthus emblica* extract, and Shilajit) and purified Shilajit in moderately arthritic dogs, and found marked reduction in OA pain as well as remarkable improvement in daily life activity [58,59]. In the present study, we report that daily administration of Crominex®-3+ for a period of five months significantly ameliorated arthritis associated pain, improved physical activity, and was well tolerated by moderately arthritic horses.

Materials and Methods

Animals

Eleven client-owned pleasure horses were used in this investigation. These horses were chosen based upon outward visual signs of moderate osteoarthritis, such as tenderness or effusion in one or more joints of the limbs, reduced joint flexibility, crepitation of the joint on limb manipulation, and an increase in lameness upon flexion of the affected joint, as described in our previous study [5]. Any horse having any other major illness related to vital organs or tumor/cancer was not included in this investigation.

The research protocol of the present investigation for using moderately arthritic horses and their treatment was

approved by Murray State University's Institutional Animal Care and Use Committee (IACUC).

Supplement

Crominex®- 3+ (trivalent chromium, *Phyllanthus emblica* (Amla) extract, and purified shilajit) capsules and matching placebo capsules were obtained from Natreon Inc (New Brunswick, NJ, USA). Each Crominex® 3+ capsule contained 10 mg trivalent chromium, 150 mg amla extract, and 150 mg purified shilajit. All capsules (placebo and Crominex®-3+) looked alike (white in color and without any labeling) to maintain the standard of double-blinded study.

Physical examination

All horses were evaluated for body weight, heart rate, respiration rate, and body temperature on a monthly basis for a period of five months.

Blood and serum analysis

Blood and serum samples were collected from all horses on a monthly basis for a period of five months. Serum samples were assayed for liver (total bilirubin, gamma-glutamyl transferase, and aspartate aminotransferase), kidney (blood urea nitrogen (BUN) and creatinine), and heart and skeletal muscle (creatine kinase) functions. Blood samples were assayed for complete blood count (CBC) including total red blood cells (RBCs), total white blood cells (WBCs) and white cell differentials.

Table 1. Effects of placebo or Crominex® 3+ on physical parameters in arthritic horses.

Parameter	Control/ Treated	Day 0	Day 30	Day 60	Day 90	Day 120	Day 150
Body Weight (lbs.)	Control	1020.00 ± 33.86	1016.66 ± 31.77	1008.30 ± 40.45	1000.00 ± 48.89	1009.00 ± 33.56	1062.00 ± 44.54
	Treated	1008.00 ± 54.07	995.00 ± 37.61	1036.00 ± 54.30	1023.00 ± 47.42	1076.00 ± 64.21	1048.00 ± 57.41
Heart Rate (Beats/min.)	Control	39.67 ± 2.80	40.00 ± 5.06	36.33 ± 4.39	43.20 ± 3.50	46.80 ± 6.34	40.80 ± 0.80
	Treated	38.40 ± 3.06	46.00 ± 7.54	35.60 ± 3.97	36.00 ± 1.90	48.00 ± 5.83	38.80 ± 2.33
Respiration Rate (Resp./min.)	Control	26.00 ± 1.99	23.67 ± 2.03	22.00 ± 1.26	19.20 ± 1.20	30.00 ± 5.93	20.00 ± 0.00
	Treated	20.40 ± 2.40	30.40 ± 7.44	22.80 ± 1.96	18.00 ± 0.00	31.60 ± 4.07	18.00 ± 0.89
Body Temperature (˚F)	Control	99.07 ± 0.24	98.52 ± 0.14	99.32 ± 0.06	98.48 ± 0.70	97.76 ± 0.54	99.28 ± 0.18
	Treated	99.04 ± 0.41	98.72 ± 0.29	99.36 ± 0.25	99.16 ± 0.44	98.30 ± 0.51	99.32 ± 0.42

Each value represents Mean ± SEM (n=5-6).
No significant difference at any time point compared to day 0 (P>0.05).

Animal treatment

In a randomized double-blinded study, eleven moderately arthritic horses weighing between 910-1190 pounds (414-541 Kg) received placebo (Group-I, n=6) or Crominex®-3+ (Group-II, n=5) twice daily (one capsule in the morning and one capsule in the evening) for a period of 150 days. None of the horses received any other treatment/supplement for a month before the study or during the study period.

Pain assessment

On a monthly basis, each horse was evaluated for overall pain, pain upon limb manipulation, and pain after physical exertion for a period of five months. Criteria for pain measurement and scales used were based upon those described by the American Association of Equine Practitioners, and have been described in our previous publication (5). A horse having overall pain about 5 on a scale of 0-10; pain upon limb manipulation about 2 on a scale of 0-4; and pain after physical exertion about 2 on a scale of 0-4 was considered moderately arthritic.

Statistical analysis

The data presented are means ± SEM (n=5-6). Statistical significance of difference was determined by ANOVA coupled with Tukey-Kramer test (P<0.05) using the NCSS[9] Statistical Analysis and Graphics Software for Windows.

Results

Horses used in this study were diagnosed with OA and exhibited some of the common signs, such as swelling and tenderness in one or more joints, difficulty walking, stiffness after periods of inactivity, pain in joints, and lameness. Data presented in Table 1 show that physical examination of horses on a monthly basis for a period of five months revealed no significant change in body weight, heart rate, respiration rate, and body temperature when compared to baseline values of day 0 in either group (P>0.05).

Data of overall pain, pain upon limb manipulation, and pain after physical exertion in horses receiving placebo or Crominex®-3+ are shown in Figures 1-3. Significant reduction in overall pain (32%), pain after limb manipulation (31%), and pain after physical exertion (33%) was noted as early as 30 days in horses receiving Crominex®-3+. Using all three criteria of pain measurement, pain reduction was maximal after 150 days of treatment (77%, 69%, and 70%, respectively). At this time point, the horses became very active and performed normally in their daily activity, including walking and running.

At no time point, did horses in Group-I receiving placebo show significant reduction in pain using any criteria (Figures 1-3).

Horses receiving placebo or Crominex®-3+ showed no significant (>0.05) change in biomarkers of liver (total bilirubin, gamma-glutamyl transferase, and aspartate aminotransferase), kidney (BUN and creatinine), and heart and skeletal muscle (creatine kinase) functions (Table 2). Analysis of blood samples for CBC also did not reveal any significant change in any parameters (Table 3). Data of WBC differential are not presented.

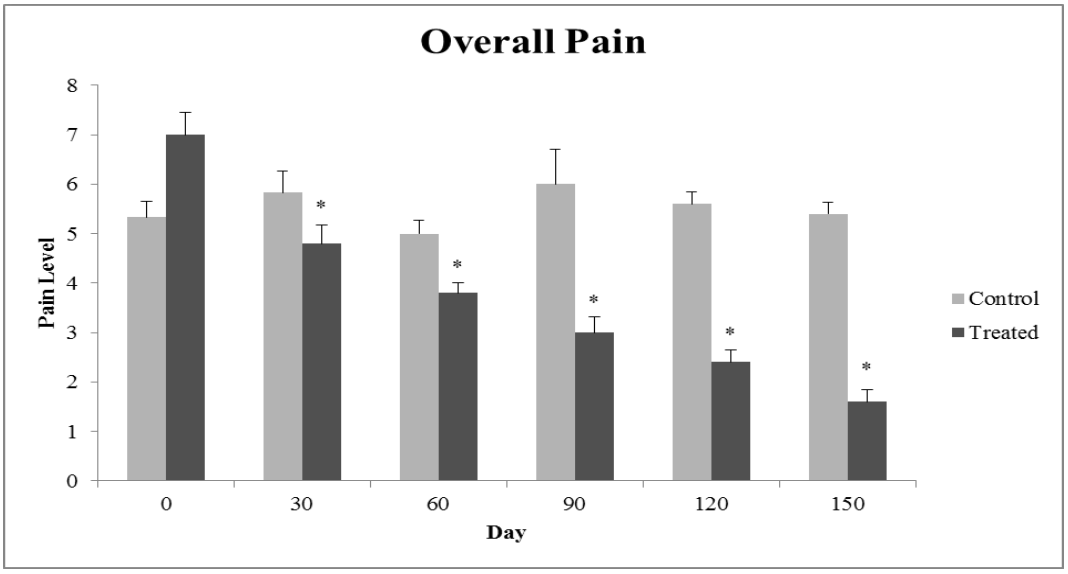

Figure 1. Effects of placebo or Crominex® 3+ on overall pain in arthritic horses. Overall pain was graded on the scale of 0 to 10 (0, no pain; 2.5, mild pain; 5, moderate pain; 7.5, severe pain; and 10, severe and constant pain).
For details of pain criteria, see Gupta et al [5].
Each value represents Mean ± SEM. *Denotes significant difference from day 0 (P<0.05).

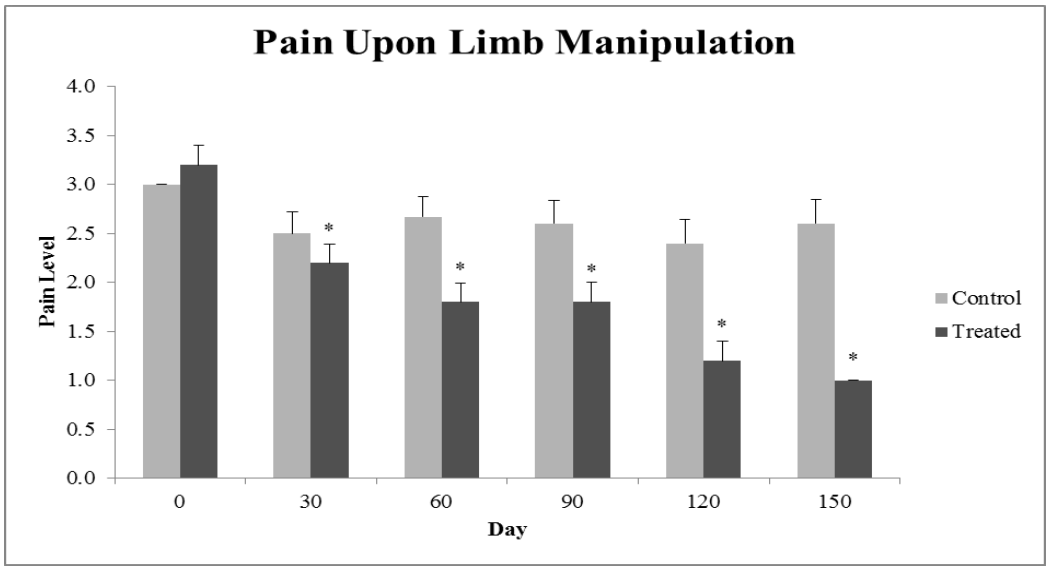

Figure 2. Effects of placebo or Crominex® 3+ on pain upon limb manipulation in arthritic horses. Pain upon limb manipulation was graded on the scale of 0 to 4 (0, no pain; 1, mild pain; 2, moderate pain; 3, severe pain; and 4, severe and constant pain). For other details of pain assessment criteria, see Gupta et al [5].
Each value represents Mean ± SEM. *Denotes significant difference from day 0 (P<0.05).

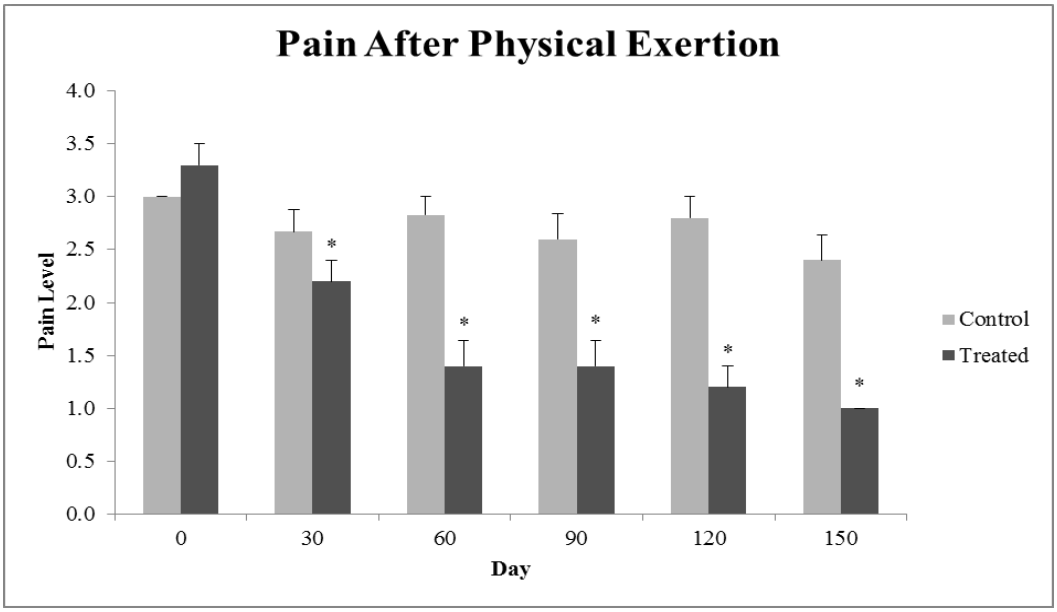

Figure 3. Effects of placebo or Crominex® 3+ on pain after physical exertion in arthritic horses.
Pain after physical exertion was graded on the scale of 0 to 4 (0, no pain; 1, mild pain; 2, moderate pain; 3, severe pain; and 4, severe and constant pain). For other details of pain assessment criteria, see Gupta et al [5].
Each value represents Mean ± SEM. *Denotes significant difference from day 0 (P<0.05).

Table 2. Effects of placebo or Crominex® 3+ on serum chemistry parameters in arthritic horses.

Parameter	Control/ Treated	Day 0	Day 30	Day 60	Day 90	Day 120	Day 150
Total Bilirubin (mg/dl)	Control	1.05 ± 0.08	1.22 ± 0.07	1.15 ± 0.07	0.90 ± 0.06	1.08 ± 0.10	1.04 ± 0.20
	Treated	1.30 ± 0.30	1.18 ± 0.12	0.98 ± 0.11	0.78 ± 0.07	0.92 ± 0.16	0.90 ± 0.20
GGT (IU/L)	Control	15.67 ± 1.54	19.33 ± 3.16	23.50 ± 5.45	16.60 ± 2.04	15.20 ± 1.65	14.60 ± 1.86
	Treated	14.40 ± 1.69	17.40 ± 3.17	19.00 ± 3.05	22.40 ± 7.37	19.50 ± 5.04	17.20 ± 2.48
AST (IU/L)	Control	251.17 ± 12.87	269.67 ± 16.87	261.17 ± 15.08	256.00 ± 29.85	243.60 ± 21.77	253.40 ± 28.13
	Treated	263.80 ± 17.38	277.60 ± 21.72	271.00 ± 14.00	286.60 ± 15.60	275.20 ± 7.95	267.40 ± 15.15
BUN (mg/dl)	Control	18.50 ± 1.73	18.67 ± 1.87	17.00 ± 1.69	19.60 ± 2.18	16.60 ± 1.43	15.80 ± 2.26
	Treated	17.40 ± 0.98	16.20 ± 0.86	14.60 ± 0.75	16.00 ± 1.22	16.20 ± 1.16	13.00 ± 1.92
Creatinine (mg/dl)	Control	1.30 ± 0.08	1.32 ± 0.13	1.28 ± 0.10	1.14 ± 0.07	1.21 ± 0.09	1.32 ± 0.07
	Treated	1.42 ± 0.07	1.46 ± 0.09	1.30 ± 0.08	1.14 ± 0.08	1.30 ± 0.08	1.25 ± 0.08
CK (IU/L)	Control	293.17 ± 57.43	326.50 ± 39.81	301.17 ± 54.14	368.20 ± 83.96	317.60 ± 62.99	322.20 ± 68.71
	Treated	392.20 ± 121.30	417.40 ± 63.23	397.00 ± 40.69	412.00 ± 63.37	303.00 ± 44.34	336.60 ± 28.74

Each value represents Mean ± SEM (n=5-6).
No significant difference at any time point compared to day 0 (P>0.05).

Table 3. Effects of placebo or Crominex® 3+ on complete blood count (CBC) in arthritic horses.

Parameter	Control/ Treated	Day 0	Day 30	Day 60	Day 90	Day 120	Day 150
RBC (10^6/µL)	Control	7.29 ± 0.38	7.21 ± 0.29	7.63 ± 0.31	6.91 ± 0.64	7.05 ± 0.19	7.83 ± 0.54
	Treated	7.26 ± 0.57	8.04 ± 0.56	7.72 ± 0.35	6.79 ± 0.26	7.63 ± 0.42	8.16 ± 0.48
WBC (K/µL)	Control	8.85 ± 0.48	8.21 ± 0.39	8.64 ± 0.69	8.08 ± 0.56	7.73 ± 0.20	9.12 ± 0.82
	Treated	10.27 ± 1.44	9.82 ± 0.90	9.15 ± 1.08	9.13 ± 1.58	8.96 ± 1.55	9.54 ± 1.12
HGB (g/dL)	Control	12.65 ± 0.68	12.35 ± 0.56	13.06 ± 0.54	11.84 ± 1.01	11.96 ± 0.32	13.34 ± 0.94
	Treated	12.32 ± 1.22	13.26 ± 1.04	12.78 ± 0.66	11.30 ± 0.58	12.32 ± 0.65	13.30 ± 0.93
HCT (%)	Control	34.60 ± 1.69	35.05 ± 1.44	36.05 ±1.12	34.04 ± 3.50	33.12 ± 0.90	36.96 ± 2.07
	Treated	33.86 ± 3.10	37.70 ± 2.95	36.16 ± 2.46	32.96 ± 2.24	35.98 ± 2.20	37.80 ± 2.50
MCV (fL)	Control	47.50 ± 0.68	48.65 ± 0.71	47.37 ± 1.14	49.26 ± 1.75	47.02 ± 0.68	47.36 ± 1.08
	Treated	46.42 ± 1.60	46.84 ± 1.21	46.76 ± 2.03	48.44 ± 1.90	47.20 ± 1.78	46.26 ± 1.01
MCH (pg)	Control	17.33 ± 0.14	17.13 ± 0.13	17.12 ± 0.13	17.22 ± 1.86	16.98 ± 0.17	17.04 ± 0.29
	Treated	16.90 ± 0.52	16.46 ± 0.23	16.54 ± 0.25	16.62 ± 2.24	16.14 ± 0.30	16.26 ± 0.31
MCHC (g/dL)	Control	36.53 ± 0.35	35.22 ± 0.47	36.22 ± 0.75	35.06 ± 0.91	36.12 ± 0.29	35.98 ± 0.56
	Treated	36.38 ± 0.28	35.16 ± 0.55	35.52 ± 0.94	34.44 ± 0.71	34.34 ± 0.65	35.14 ± 0.35

Each value represents Mean ± SEM (n=5-6).
No significant difference at any time point compared to day 0 ($P>0.05$).

Discussion

Presently, the equine industry suffers from the crippling disease osteoarthritis (OA) more than any other chronic disease. Horses become non-productive and quality of life diminishes as the disease progresses. As a result, the economic loss to horse owners amounts to billions of dollars annually. In spite of intense efforts in the quest for a better treatment of OA in horses, there is no magic cure because of the disease's multiple etiologies and complex pathophysiological pathways. The present study was therefore undertaken to evaluate therapeutic efficacy and safety of a novel formula Crominex®-3+ in moderately arthritic horses.

Horses receiving Crominex®-3+ (500 mg) twice daily exhibited significant reductions in pain associated with arthritis (overall pain, 32%; pain upon limb manipulation, 31%; and pain after physical exertion, 33%) as early as one month after treatment. Maximum pain reductions (77, 69, and 70%, correspondingly) occurred after five months of treatment (Figures 1-3). These data suggest that like other supplements, Crominex®-3+ provided anti-inflammatory and anti-arthritic effects in moderately arthritic horses [5,34,55,58,59]. In a recent study, Fleck et al. (58) found Crominex®-3+ as a unique formula that provided significant antioxidant, anti-inflammatory and anti-arthritic effects without eliciting any untoward events in moderately arthritic dogs within 90 days, with maximal pain reductions by 150 days. Horses responded to Crominex®-3+ treatment much earlier than dogs (30 days vs. 90 days), in terms of significant ($P<0.01$) pain reduction, which might be due to greater bioavailability of active ingredients in horses compared to dogs (Figures 1-3) [58]. Of course, at this time, we have no bioavailability data to substantiate this fact.

Crominex®-3+ is comprised of three active ingredients (trivalent chromium, *Phyllanthus emblica* (Amla) extract, and purified shilajit), and each ingredient is known to exert multiple physiological and pharmacological actions. Currently, Crominex®-3+ is indicated as an analgesic, but it also exerts other beneficial effects by maintaining normal cellular functions, such as glucose transport, lipid and triglyceride levels and enhanced cellular energy production [60-65]. Based on experimental research and clinical trials, the use of trivalent chromium for its anti-hyperglycemic action in type 2 diabetic patients (especially insulin resistance) is well established [64-67]. Chromium has been reported to alleviate insulin

resistance by antioxidant and anti-inflammatory effects [61,67-69]. Thus, chromium in Crominex® 3+ might have exerted anti-arthritic effects in horses by attenuating oxidative stress and inflammation, as described in arthritic dogs [58].

The amla extract from *Phyllanthus emblica*, by having very high $ORAC_{FN}$ value of 47,000 μmoles TE/g, exerts antioxidant and anti-inflammatory effects. It has been found that the antioxidant properties are due to the presence of low molecular weight hydrolysable tannoids (Emblicanin A, Emblicanin B, Pedunculagin, and Punigluconin), which produce stable vitamin C like effects without the pro-oxidant effects found in ascorbic acid, as discussed by Fleck et al [58].

Purified shilajit (a proprietary extract from blackish brown exudate obtained from Himalayan Mountains at an altitude of about 10,000 feet) is known to contain dibenzo-α-pyrones (DBPs), DBP-chromoproteins and fulvic acids with DBP core. By having multiple herbo-mineral and bioactive principles, shilajit exerts several physiological and pharmacological actions, such as cholinomimetic, antioxidant, antilipid peroxidase, anti-arthritic, anti-hyperglycemic, anti-inflammatory, antibacterial, antiulcerogenic, anti-aging, cognition enhancement, immunomodulatory, ovogenic and spermatogenic, cardioprotective, and energetic properties [70-82]. For more than 3000 years, Shilajit has been used for prevention and treatment of various human ailments, such as arthritis, diabetes, hypertension, loss of cognition, immune dysfunction, allergies, loss of libido, and found to be safe for long-term use.

Recently, we reported that twice daily administration of purified Shilajit alone (500 mg), or Shilajit (7.5 mg) in combination with trivalent chromium (500 μg) and amla extract (7.5 mg), for a period of five months significantly ($P<0.05$) ameliorated arthritic-pain and improved quality of life of moderately arthritic dogs without causing any untoward effects [58-59]. In horses, Crominex®-3+ was not only found to be equally effective in reducing arthritis pain, but the onset of action was also rapid compared to that in dogs. All three active ingredients (trivalent chromium, amla extract, and purified Shilajit) in Crominex® -3+ have strong antioxidant and anti-inflammatory properties [66,67,69,71-73]. Since OA pain is associated with oxidative stress and inflammation, it is highly possible that Crominex®-3+ attenuated arthritic pain by antioxidant and anti-inflammatory mechanisms. Additional properties of Shilajit, such as to boost the immune system, promote healing of bone fractures, increase muscle mass, enhance endurance, and anti-aging activity, might have also played roles in improvement of OA horses by Crominex®-3+ treatment.

At no time during this investigation, did horses receiving Crominex®-3+ show any significant (>0.05) change in physical parameters (Table 1), and in biomarkers of liver, kidney, or heart and skeletal muscle functions (Table 2). Analysis of blood samples for CBC also did not reveal any significant change in any parameters (Table 3). These findings suggested that Crominex®-3+ was well tolerated by arthritic horses and it is safe to use for long-term.

Conclusions

In a randomized double-blinded study, twice daily administration of Crominex®-3+ (1000 mg total) significantly ($P<0.05$) ameliorated inflammation and pain associated with arthritis in horses. There was no significant ($P>0.05$) change in physical parameters, complete blood count (CBC) or serum biomarkers of liver, kidney, heart and skeletal muscle functions, suggesting that Crominex®-3+ was well tolerated by arthritic horses and safe to administer long-term. Thus, Crominex®-3+ appears to be a unique formula that provides remarkable antioxidant, anti-inflammatory, and anti-arthritic effects in arthritic horses.

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