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Effect of oral supplementation with hydroxytyrosol in canines with osteoarthritis

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1. Abstract

Supplementation with hydroxytyrosol (HT) produced by Nova Mentis Ltd. in Ireland under commercial brand name 1-HT was evaluated in 10 canines diagnosed with osteoarthritis. The animals were between 8 and 12 years old, from different breeds and received a daily dose of 10 mg HT / kg BW for 120 days (Treated Group). A control group received only a placebo. Changes in tolerance to treatment were evaluated, including changes in body condition, stool consistency and complete blood analysis. Radiological and ultrasound analysis of the affected joint(s) was performed at baseline and at the end of the study. At days 0, 7, 14, 21, 28, 60 and 120 joint pain was assessed using the Melbourne scale. At the end of the study, C-reactive protein concentration was measured. Pain decrease in the treated group during the first 60 days post-treatment and remaining differentiated until the end of the study. The thickness of the articular cartilage was greater in dogs that received the treatment. The concentration of C-reactive protein did not differentiate the groups. Finally, the perception of the owners was positive, reporting a sensation of greater voluntary activity in their pets.

2. Introduction

Osteoarthritis (OA) and its progression to degenerative joint disease (DJD) are common presentations in canines. From a pathophysiological point of view, they are characterized by progressive loss of articular cartilage, subchondral bone remodeling, osteophyte formation and inflammation of the joint tissues (Bijlsma et al, 2011). Altered

joint loading due to instability from joint or ligament injury represents a significant risk factor for the onset and progression of DJD (Bijlsma et al, 2011; Guilak, 2011). From a molecular point of view, a vicious circle of inflammation and degradation of the articular cartilage is generated. Despite advances in the understanding of the disease and early diagnosis of DJD, curative treatments or treatments that slow the course of the disease are lacking. Pharmacological medications currently available to treat patients with OA focus on relieving inflammation and pain, but do not slow, stop or reverse the progression of joint cartilage degradation and other associated tissue damage (Clouet, 2009). In this context, there is growing interest in developing therapeutic strategies capable of mitigating the progressive degradation of joint tissues while relieving symptomatic pain associated with inflammation. Current epidemiological and experimental studies support a beneficial role of dietary polyphenols in several chronic diseases including OA (Shen et al, 2012; Annalisa et al, 2014).

Hydroxytyrosol, a plant polyphenol and a powerful antioxidant is mainly found in olive leaves and has various health benefits such as antioxidant, anti-bacterial, and anti-inflammatory properties. HT exerts its health benefits through the transfer of a hydrogen from its phenolic hydroxyl group to reactive oxygen species (ROS) which minimises damage by oxidative processes in mammalian cells. Oxidative stress can contribute to the development of inflammation and arthritis, neurodegenerative diseases, ageing, and DNA damage. HT has proven to be safe and non-toxic across a multitude of studies. Aunon-Calles et al. 2013a, have carried out Toxicological evaluation of pure hydroxytyrosol and, based on the results, a 'No Observed Adverse Effects Level (NOAEL)' of 500 mg/kg/ day was proposed, ensuring a safety profile for this compound. In a second study the same authors have reported no mutagenic or genotoxic effects of hydroxytyrosol in an invitro study (Aunon-Calles et al. 2013b).

In a human trial on 25 patients with knee degenerative joint disease (DJD) HT was shown to have the ability to control pain associated with the disease (Takeda et al, 2013). Other trials on primary human chondrocytes demonstrated that hydroxytyrosol (HT) is able to reduce the production of reactive oxygen species (ROS) and the associated DNA breakage, preventing chondrocyte apoptosis and suppressing the increase in caspase-3 (Facchini et al, 2014).

In rodents, the antioxidant effect of HT was found to increase with doses from 10 mg/kg/day to 50 mg/kg/day (Cao et al,2014) and doses up to 300 mg/kg/day of HT are safe (Heilman et al, 2015). However, under special conditions, polyphenols could have a

paradoxical effect and become pro-oxidants, generating oxidized metabolites (Boots et al, 2005). In another study, it was found that the consumption of a low dose of 20 mg/kg/day of HT during resistance exercise induces an antioxidant effect, while the high dose of 300 mg/kg/day reverses that effect by inducing systemic oxidative stress (Al Fazazi et al, 2018). These metabolites induce oxidative damage to key proteins such as glutathione (Boots et al, 2007). This paradoxical effect suggests that high doses may induce a pro-oxidant environment. Similarly, high doses of HT have been shown *in vitro* to increase ROS generation within tumor cells, leading to their apoptosis (Sun et al, 2014). No studies are known to have been performed in canines.

Numerous studies have recently highlighted the potential of natural compounds, including nutraceuticals, to slow down or treat DJD in humans, rats and rabbits (Chen, 2011; Chen 2012; Chen et al, 2012; Csakiet al, 2009; Bang, 2009; Haseeb et al, 2013; Largo, 2003; Wang et al, 2012; Phitak, 2012; Mevel, 2014). However, no similar reports are known in canines.

The aim of this work was to evaluate the clinical effect of HT supplementation (10 mg HT / kg BW) in canines with osteoarthritis.

3. Materials and Methods

3.1 Selection of animals

Ten dogs were included in the study: German Shepherd (n=1), Labrador (n=1), Rottweiler (n=1), Dachshund (n=1), Brittany (n=1) and mixed breeds (n=5), between 8 and 12 years old, diagnosed with osteoarthritis and/or DJD in one of the 4 limbs and/or lumbosacral spine. The animals belonged to private owners. The number of dogs in the study was limited due to strict inclusion criteria and availability of voluntary participants.

3.2 Treatment

The clinical effect of supplementation of 1-HT® hydroxytyrosol powder (Nova Mentis Ltd., Ireland) in canines with osteoarthritis was evaluated in this study. 1-HT® hydroxytyrosol contains 25% hydroxytyrosol (active ingredient at ≥ 98% purity) and 75% chicory root inulin (excipient). The hydroxytyrosol in this mixture is biotechnologically manufactured. The dogs were administered at a daily dose of 40 mg of 1-HT® hydroxytyrosol / kg BW for 120 days to have the hydroxytyrosol (active ingredient) dose of 10 mg / kg BW.

Day 0 was taken as the start day of treatment. Animals were randomly assigned to one of the following groups:

- ✓ TREATED GROUP (n=5): oral hydroxytyrosol was administered in gastric digestion capsules
- ✓ CONTROL GROUP (n=5): placebo was administered in gastric digestion capsules.

No ethical document is required in support of this study, as no animal was at risk as 1-HT® hydroxytyrosol, was used at concentrations known to be safe and significantly below the NOAEL reported for HT by Auñon-Calles for pure hydroxytyrosol (500 mg/kg body weight).

3.3 Parameters evaluated

3.3.1 Parameters of tolerance and safety to treatment

Dogs underwent a complete clinical examination at the start of the study. Body condition score and fecal consistency were assessed on days 0, 7, 14, 21, 28, 60, and 120. A hematological examination was performed at the start of the study to recruit the animals to the study and was repeated at the end of the study (day 120) to assess changes. Body condition score was assessed on a scale of 1 to 5, where 3 is normal weight, 1 cachectic state, and 5 obese. Fecal consistency was assessed on a scale of 1 to 5, where 1 is liquid consistency (diarrhea) and 5 is hard and dry consistency. Hematological analysis included complete blood count (hematocrit percentage, red blood cell count, hemoglobin concentration, red blood cell indices (mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration(MCHC)) , leukocyte, neutrophil, eosinophil and monocyte count, as well as platelets) and blood biochemistry (plasma concentration of urea, glucose, creatinine, total proteins, albumin, globulins, and albumin:globulin ratio, glutamic-pyruvic acid transaminase (GPT), alkaline phosphatase (ALP), glutamic-oxaloacetic acid transaminase (GOT), tiroxine (T4) and thyroid-stimulating hormone (TSH) concentrations.

3.3.2 Parameters associated with the osteoarticular process

At the beginning and at the end of the study, radiological and ultrasound analysis of the affected joint(s) was performed. At days 0, 7, 14, 21, 28, 60 and 120, joint pain was assessed using the Melbourne scale (Hernandez-Avalos et al, 2020; Raušer et al, 2020). At the end of the study, the concentration of C-reactive protein was measured as an indicator of proinflammatory activity (Williams et al, 2020).

The radiographic images were obtained on 24x30cm radiographic film, KODAK®b brand. Simultaneously and at a distance of 3 cm from the x-rayed limb. An Omega®c X-ray machine, model 100/100 T, was used. The machine was positioned at a focus-film distance of 90 cm. The kilovoltage and milliamperage per second were determined according to the thickness of the region evaluated in each animal, with 0.02 seconds being the minimum exposure time and 0.05 the maximum. The radiographs were developed in an automatic processor. The radiographic images were digitized by means of a table scanner and were evaluated in an image analysis program, Image J, which allowed obtaining different grayscale values from each plate [minimum value 0 (black) vs maximum value 256 (white)]. From each radiographic incidence, 8 measurements were made (4 in the dorsal bone of the joint and 4 in the ventral bone), and an average grayscale value was calculated for each of the bones, to finally obtain a single average grayscale value. Ultrasound images were obtained using a Mindray DP-30 ultrasound scanner, using a 75L38EA linear transducer with a frequency of 7.5 MHz, which is ideal for obtaining good quality musculoskeletal tissues.

3.3.2 Observational parameters recorded by the pet owner

Two subjective parameters of the owners were incorporated into the study, but were considered relevant because it was a clinical study. On days 0, 7, 14, 21, 28, 60 and 120, the owners of the animals were asked about the level of activity of their pets, so that they could consider them “active” or “not active” (sedentary). Finally, at the end of the study, the owners were asked about their perception of the treatment, so that they could answer whether they considered the treatment to have been positive, neutral or negative. A positive response was considered when the owner expressed a total conviction that there was a positive effect of the treatment on their pet, making it more active and with a notable improvement in its mood. A neutral response was considered when the owner did not notice any good or bad changes as a result of the treatment in their pet. Finally, a negative response was considered when the owner attributed the treatment to negative effects on the health of their pet.

3.4 Statistical analysis

To analyze pain, a mixed linear regression model with repeated measures over time was fitted using the LMER function of the LME4 package of the RStudio programme (R Core Team, version 4.2.2) where the fixed explanatory variables were the Group, the second-degree polynomial of Time (days of treatment) and the interaction between the two. The random explanatory variable was the animal. The GGEFFECTS package was used to obtain the model's predictions and to graph them. To analyze the rest of the

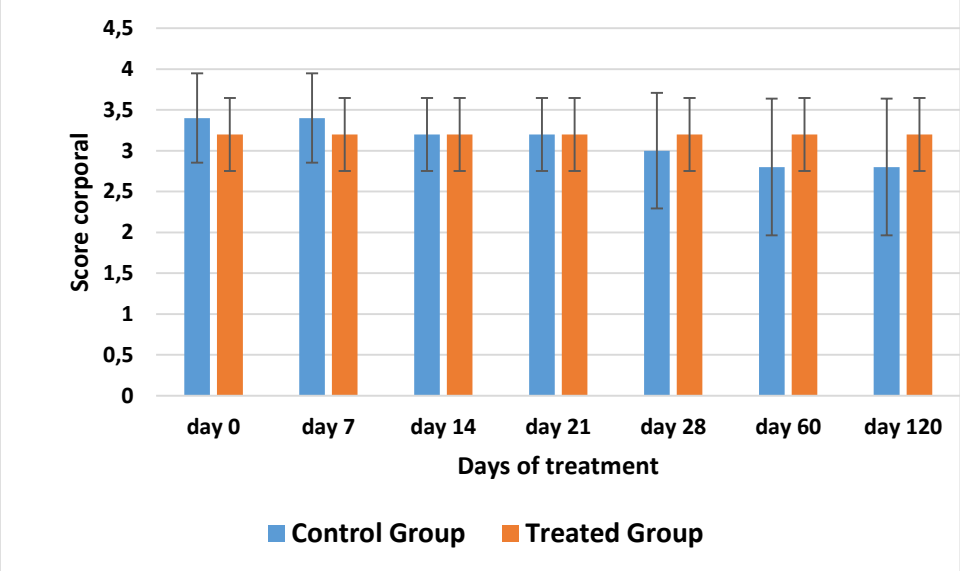
parameters, first the difference between the final evaluation (120 days) and the initial evaluation (Day 1) was calculated, and then an ANOVA analysis was performed on those variables with normal distribution and homoscedasticity, while the variables that did not meet these assumptions were analyzed using the non-parametric Kruskal-Wallis test. In all cases, a p-value ≤ 0.05 was considered significant and a p-value ≤ 0.10 was considered a trend.

4. Result

4.1 Parameters of tolerance and safety to treatment

No significant variations were recorded in the body score throughout the treatment in either group (Figure 1). There were no variations in the consistency of the fecal matter throughout the treatment, nor were there differences between the groups. Finally, the hematological parameters were within the normal limits and there was no significant difference between the treated and untreated groups.

Figure 1: Average corporal score of canines in the Treated Group and the Control Group throughout the HT supplementation study (10 mg / kg BW).



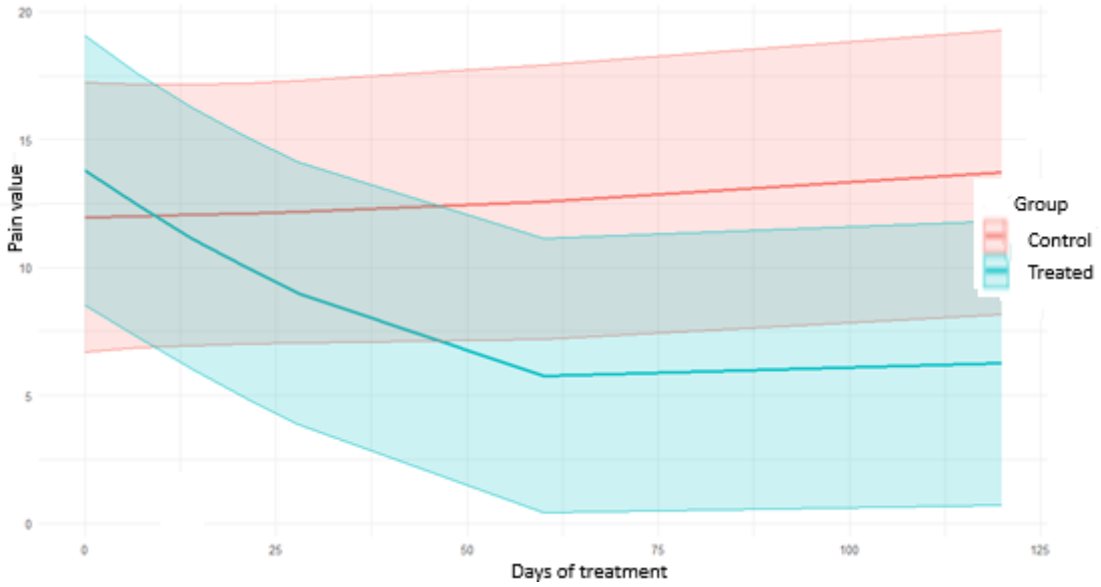
4.2 Parameters associated with the osteoarticular process

4.2.1 Parameters associated with the osteoarticular process Pain assessment

Pain was not affected by the Group (p=0.47), nor by the Time degree polynomial (p=0.46), but by the Time x Group interaction (p<0.01), since the Groups began the study

with a similar average pain index value, but during the first 60 days post-treatment there was a marked decrease in the pain index for the Treated Group, which then stabilized, while the pain index remained stable (with a slight upward trend) in the Control Group throughout the study (Figure 2).

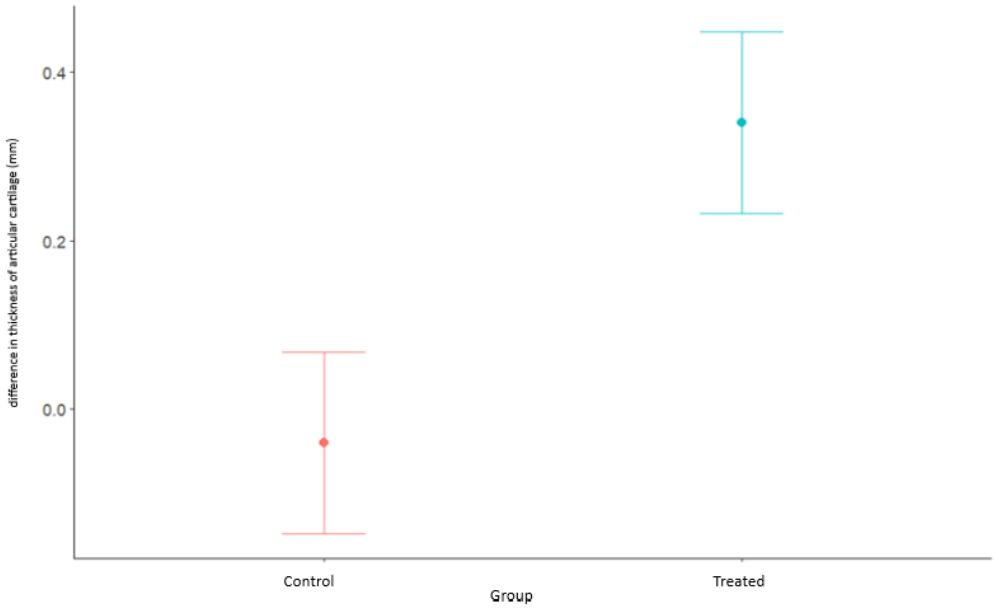
Figure 2. Smoothed plot of the predictions from the fitted model, showing the effect of Treatment and Time on the pain index. The shaded area corresponds to the 95% confidence interval.



4.2.2 Articular cartilage thickness

The articular cartilage in dogs receiving treatment had a difference from the control group between the thickness at the beginning and at the end of the study of 0.38 mm (95% CI: 0.03 – 0.73 mm; p=0.04), meaning that dogs receiving HT increased their articular cartilage thickness, compared to dogs without HT (Figure 3). The reports of each ultrasound are presented in appendices 1 to 10, at the end of the text.

Figure 3. Articular cartilage thickness after 120 days of treatment with HT (10 mg HT (purity ≥ 98%) / kg BW) /day-Treated Group) compared to placebo (Control Group)



4.2.3 Plasma C-reactive protein concentration

C-reactive protein showed no differences between groups at day 120, mean values of 4.6 (±0.6) and 4.9 (±0.6) mg/L (p=0.60) for the Treated and Control groups, respectively.

4.3 Observational parameters recorded by the pet owner

4.3.1 Activity level

The activity level was considered a subjective parameter, so it was not evaluated statistically nor proposed as a therapeutic indicator, but it is important because it is an important indicator when we depend on the owner's effort to maintain the treatment. Table 1 presents the activity level data of the 5 animals in each group throughout the study. As can be seen, between the first 2 to 3 weeks the owners perceived a positive effect, but this was only sustained in the Treated Group.

Table 1. Activity level of dogs treated with placebo (Control Group) or with HT (10 mg/kg/day – Treated Group) for 120 days.

Group	Animal	Treatment days						
		Day 0	Day 7	Day 14	Day 21	Day 28	Day 60	Day 120
Control	Brissa	Active	Active	Active	Active	Active	Not active	Not active
	Bruna	Active	Active	Active	Active	Not active	Not active	Not active
	Jackson	Active	Active	Active	Active	Active	Active	Active
	Lucky	Not active	Not active	Active	Active	Active	Active	Not active
	Nieves	Active	Active	Active	Active	Active	Active	Active
Total not actives		1/5	1/5	0/5	0/5	1/5	2/5	3/5
Treated	Coco	Not active	Not active	Active	Active	Active	Active	Active
	Delia Toto	Not active	Not active	Active	Active	Active	Active	Active
	Papo	Active	Active	Active	Active	Active	Active	Active
	Pipa	Not active	Not active	Not active	Active	Active	Active	Active
	Toto	Not active	Not active	Active	Active	Active	Active	Active
Total not actives		4/5	4/5	1/5	0/5	0/5	0/5	0/5

4.3.2 Owners' perception of the impact of treatment on their pets

After treatment (day 120), the owners of the animals in the Treated Group perceived an improvement with the treatment in three animals and no changes in two others, while those who gave placebo to the animals in the Control Group perceived no improvements in four animals and one of them had a positive perception.

5. Discussion

The decrease in objective pain and articular cartilage thickness observed in the present study suggest that HT treatment had a beneficial effect on chronic joint processes. The pain generated in these processes represents a key factor in restricting the patient's quality of life (Malfait and Schnitzer, 2013). However, in the pathogenesis of osteoarthritis, articular cartilage is the central structure on which damage develops

and there is agreement that a greater proinflammatory state, greater oxidative damage mediated by ROS (Lepetsos and Papavassiliou, 2016; Bolduc et al, 2019; Zahan et al, 2020) and a lower autophagy capacity (Chin and Pang, 2017) are responsible for the damage, and therefore the pain. Numerous studies have demonstrated the anti-inflammatory and antioxidant capacity of HT (Hu et al, 2014; Achmon and Fishman, 2015; Velotti et al, 2023). Its anti-inflammatory capacity has already been demonstrated in models of intervertebral disc degeneration in rats, with a decrease in inflammatory mediators and ROS production (Yu et al, 2022). HT also reduced inflammation and pain in models of endometriosis (Cordaro et al, 2021) and fibromyalgia in rats (D'Amico et al, 2021), in the latter case at oral doses of 10 mg/kg, identical to the present study. In models of osteoarthritis induced by injections of monoiodoacetate in rats, HT reduced mechanical hyperalgesia and spontaneous pain, even a repeated daily treatment completely counteracted osteoarticular pain without developing tolerance to the antinociceptive effect (Recinella et al, 2022). Unfortunately, these authors used a mixture of olive polyphenols and not pure HT, as in the present work. Currently having synthetic HT, free of all contaminants, opens the possibility of evaluating its effects and therapeutic potential in greater detail (Britton et al, 2019).

Although we are not aware of any clinical trials with canines with osteoarthritis, there is evidence of the use of polyphenols such as HT in humans. In this regard, Chin and Pang (2017) compiled 4 clinical trials in humans with osteoarthritis where treatment with olive-derived polyphenols was effective in reducing pain. Three of them used several components of the olive tree, making it difficult to evaluate the therapeutic agent. In one of them, Takeda et al (2013) supplemented 10 mg of HT daily orally for four weeks and managed to reduce the pain generated by knee osteoarthritis.

Considering that the evaluation of blood profiles, as well as body score and fecal matter data did not vary between groups, they confirm the safety of the evaluated treatment. This coincides with the fact that HT is considered an extremely safe supplement with no risk of toxicity at therapeutic doses (Mével et al, 2016).

Despite the positive clinical results of the treatment, such as pain reduction, and the bibliographic background on the anti-inflammatory capacity of HT, the concentration of C-reactive protein was not different between the groups at the end of the treatment. Indeed, in a docking experiment, a computational method that predicts the binding mode of a ligand to a macromolecular target, HT showed the ability to bind by hydrogen bond to the ProA12 residue of the C-reactive protein, thus reducing its proinflammatory and pain-stimulating effect (Rahman et al, 2022). However, CRP

increases considerably in acute inflammatory processes, where it behaves as a good indicator of the evaluation of the inflammatory process, and not so much in chronic processes, typical of osteoarthritis (Jin et al, 2015).

Voluntary activity, despite being a subjective assessment, takes on importance in clinical studies with guardians who must maintain prolonged treatments. In the present work, voluntary activity at the end of the study was adequate in all animals treated with HT, and only in 2 of the 5 animals in the Control Group. After three weeks of treatment, all animals in the HT Treated Group were considered active by their owners. This highlights the need to maintain sustained treatments for weeks before expecting effects on pain in osteoarthritis processes (Chin and Pang, 2017; Frumuzachi et al, 2024).

Articular cartilage loss is considered irreversible in osteoarthritis, with a tendency to progressive degradation (Roos et al, 2016). For this reason, the increase in articular cartilage thickness in the present work represents a significant finding. This positive effect could be due to different properties of HT. Zhi et al (2018) suggest that TH inhibits the inflammatory response of chondrocytes through the enhancement of SIRT6-mediated autophagy. SIRT6 prevents the development of osteoarthritis by reducing the inflammatory response and chondrocyte senescence (Nagai et al, 2015). On the other hand, chondrocytes largely depend on autophagy as a repair mechanism during cell damage, due to their limited mitotic capacity (Aigner et al, 2001). This effect adds to the already demonstrated antioxidant capacity of HT on chondrocytes (Cetrullo et al, 2016). The evaluation of antioxidant or anti-inflammatory parameters is added to the expected changes at the structural level in the different layers of cartilage (McCoy, 2015). Many mechanisms of action have been demonstrated with invasive methods and in experimental animals, so it is still necessary to develop indicators for noninvasive clinical studies.

6. Conclusions

In agreement with the literature, oral treatment with 10 mg HT/kg BW for 120 days did not negatively affect the treated dogs, which maintained their body condition, hematological parameters and stool consistency, indicating absolute tolerance to the treatment.

The treatment reduced pain compared to the control, requiring four weeks to demonstrate the interaction time by treatment and with a sustained effect until the end

of the study. This coincided with the fact that the treated animals presented a greater thickness of the articular cartilage at the end of the treatment, demonstrating the chondroprotective and anti-inflammatory effect of HT.

Being a clinical study, the perception of the owners was positive, reporting a sensation of greater voluntary activity in their pets.

Taken together, these results encourage the use of HT as a natural therapeutic tool to improve the quality of life of canines with osteoarthritis.

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12th of December 2024

Dr. Guillermo Mattioli

Laboratorio de Nutrición Mineral
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Appendix 1

Dog 1 (Nieves) – Control group – pretreatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr./Dra.: Corrada
Especie: Canino — Raza: Mestizo
Sexo: Hembra — Edad: — Pelaje:
Propietario: Grattoni — Paciente: Nieves
Región de estudio: Abdominal

CONTROL FECHA: 17/07/2023

OBSERVACIONES

Articulacion coxofemoral derecha: Cartilago articular hipoecoico con un espesor de 2 mm (vista medial) y 3 mm (vista lateral) superficie osea subcondral ecogenica lisa
Articulacion coxofemoral izquierda: Espesor del cartilago articular de 1,8 mm (vista medial) y 3,2 mm (vista lateral) con superficie osea subcondral ecogenica y lisa
Liquido articular escaso conservado en ambas articulaciones
Articulacion intervertebral lumbar cinco y seis con areas hiperecoicas irregluares y aumento de tamaño del borde ventral del cuerpo vertebral (carilla articular) sugerente de mineralizacion

Dog 1 (Nieves) – Control group – post-treatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr./Dra.: Corrada
Especie: Canino — Raza: Mestizo
Sexo: Macho — Edad: 14 años — Pelaje: Negro
Propietario: Grattoni — Paciente: Delia Toto
Región de estudio: Articular

CONTROL FECHA: 25/01/2024

OBSERVACIONES

Articulacion coxofemoral derecha: Cartilago articular hipoecoico con un espesor de 2,3 mm (vista medial) y 3 mm (vista lateral) superficie osea ecogenica lisa
Articulacion coxofemoral izquierda: Espesor del cartilago articular de 2,3 mm (vista medial) y 3 mm (vista lateral) con superficie osea ecogenica y lisa
No se evaluaron otras articulaciones

Appendix 2

Dog 2 (Pipa) – Treated group – pretreatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr.|Dra.: Corrada
Especie: Canino — Raza: Mestizo
Sexo: Hembra — Edad: — Pelaje:
Propietario: Grattoni — Paciente: Pipa
Región de estudio: Abdominal

CONTROL FECHA: 15/07/2023

OBSERVACIONES
Articulacion coxofemoral derecha: Cartilago articular con un espesor de 2,4 mm hipoecoico (vista medial) y 1,6mm (vista lateral) con superficie subcondral ecogenica lisa
Articulacion coxofemoral izquierda: Espesor del cartilago articular de 2,7 mm (vista medial) y 1,8 mm (vista lateral) consuperficie subcondral ecogenica y lisa
Ambas con escaso liquido articular

Dog 2 (Pipa) – Treated group – post-treatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr.|Dra.: Corrada
Especie: Canino — Raza: Mestizo
Sexo: Hembra — Edad: 14 años — Pelaje: Marron
Propietario: Grattoni — Paciente: Pipa
Región de estudio: Articular

CONTROL FECHA: 25/01/2024

OBSERVACIONES
Articulacion coxofemoral derecha: Cartilago articular con un espesor de 2,3 mm hipoecoico (vista medial), con superficie osea lisa hiperecoica
Articulacion coxofemoral izquierda: Espesor del cartilago articular de 2,3 mm (ventana medial) y superficie osea hiperecoica y lisa
Ambas con escaso liquido articular

Appendix 3

Dog 3 (Bruna) – Control group – pretreatment - ultrasound

diagnóstico ecográfico

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr./Dra.: Corrada
Especie: Canino
Raza: Mestizo
Sexo: Hembra
Edad:
Pelaje:
Propietario: Grattoni
Paciente: Bruna
Región de estudio: Abdominal

CONTROL

FECHA: 15/07/2023

OBSERVACIONES

Articulacion intervertebral lumbar cinco y seis: No se observa el espacio articular, en su lugar se halla una linea hiperecoica con sombra posterior sugerente de calcificacion
Articulacion coxofemoral derecha: Cartilago articular con un espesor de 2,1 mm hipoecoico y superficie osea ecogenica lisa, espacio articular de 3,3 mm
Articulacion coxofemoral izquierda: Espesor del cartilago articular de 1,9 mm y superficie osea ecogenica y lisa, espacio articular de 2,9 mm
Ambas con escaso liquido articular, no se observa aumento en zonas declive

Dog 3 (Bruna) – Control group – post-treatment - ultrasound

diagnóstico ecográfico

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr./Dra.: Corrada
Especie: Canino
Raza: Mestizo
Sexo: Hembra
Edad:
Pelaje: Negro y blanco
Propietario: Grattoni
Paciente: Bruna
Región de estudio: Abdominal

CONTROL

FECHA: 25/01/2024

OBSERVACIONES

Articulacion coxofemoral derecha: Cartílago articular con un espesor de 2,4 mm hipoecoico y superficie osea ecogenica lisa, espacio articular de 3,4 mm
Articulacion coxofemoral izquierda: Espesor del cartilago articular de 1,8 mm y superficie osea ecogenica y lisa, espacio articular de 2,5 mm
Liquido articular sin particularidades
Articulacion intervertebral lumbar cinco y seis: En su lugar se halla una linea hiperecoica con sombra posterior sugerente de calcificacion, sin visualizarse el espacio intervertebral

Appendix 4

Dog 4 (Brissa) – Control group – pretreatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr.|Dra.: Corrada
Especie: Canino — Raza: Rottweiler
Sexo: Hembra — Edad: — Pelaje: Negro y fuego
Propietario: Corrada — Paciente: Brisa
Región de estudio: Abdominal

CONTROL FECHA: 17/07/2023

OBSERVACIONES

Articulacion femorotibiorrotuliana izquierda (vista craneal) con superficie osea ligeramente irregular con puntillado ecogenico y espacio articular de 8 mm
Articulacion femorotibiorrotuliana derecha (vista craneal) con espacio articular de 6 mm y superficie osea lisa con menor puntillado ecogenico que la rodilla izquierda
Ambas articulaciones con contenido liquido anecoico en regular cantidad
Articulacion intervertebral lumbar cinco y seis con areas hiperecoicas irregluares entre ambos cuerpos vertebrales sugerente de mineralizacion (espondilosis?)

Dog 4 (Brissa) – Control group – post-treatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr.|Dra.: Corrada
Especie: Canino — Raza: Rottweiler
Sexo: Hembra — Edad: 11 años — Pelaje: Negro y fuego
Propietario: Corrada — Paciente: Brisa
Región de estudio: Abdominal

CONTROL FECHA: 25/01/2024

OBSERVACIONES

Articulacion femorotibiorrotuliana derecha (ventana craneal) con espacio articular de 5,7 mm y superficie osea lisa y escaso puntillado ecogenico, espesor del cartilago articular a nivel del femur de 2,3 mm
Articulacion femorotibiorrotuliana izquierda (ventana craneal), superficie osea ligeramente irregular con puntillado ecogenico y espacio articular de 6,8 mm, cartílago articular de 2,2 mm
Ambas articulaciones con contenido liquido anecoico en regular cantidad

Appendix 5

Dog 5 (Toto) – Treated group – pretreatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr.|Dra.: Corrada
Especie: Canino — Raza: Golden Retriever
Sexo: Macho — Edad: — Pelaje: Dorado
Propietario: Iribarne — Paciente: Toto
Región de estudio: Abdominal

CONTROL FECHA: 18/07/2023

OBSERVACIONES

Articulacion coxofemoral derecha: Cartilago articular con un espesor de 1,9 mm hipoecoico y superficie sobcondral ecogenica lisa
Articulacion coxofemoral izquierda: Espesor del cartilago articular de 2 mm y superficie subcondral ecogenica y lisa
Articulacion del codo izquierdo con cartilago articular hipoecoico con un espesor de 1,8 mm, con superficie ligeramente irregular, en las areas declives de la articulacion (union de la capsula articular con el hueso) se observa la superficie irregular con puntillado ecogenico compatible con enfermedad articular degenerativa / osteofitos

Dog 5 (Toto) – Treated group – post-treatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr.|Dra.: Corrada
Especie: Canino — Raza: Labrador
Sexo: Macho — Edad: — Pelaje: Dorado
Propietario: Iribarne — Paciente: Toto
Región de estudio: Abdominal

CONTROL FECHA: 06/02/2024

OBSERVACIONES

Articulacion del codo izquierdo con cartilago articular hipoecoico vista lateral de 3,4 mm y medial de 4,0 mm espesor y de 1,8 mm en su parte media, con superficie irregular, en las zonas de la articulacion entre la capsula articular y el hueso se observa la superficie irregular con puntillado ecogenico compatible con enfermedad articular cronica - degenerativa (no descartar osteofitos)
Articulacion coxofemoral izquierda: Espesor del cartilago articular de 2,2 mm en la vista medial y 2,4 mm en la vista lateral y superficie subcondral lisa
Articulacion coxofemoral derecha: Cartilago articular con un espesor de 2 mm en la vista medial y de 2,2 en la vista lateral, de aspecto hipoecoico y superficie sobcondral ecogenica lisa

Appendix 6

Dog 6 (Coco) – Treated group – pretreatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr.|Dra.: Corrada
Especie: Canino — Raza: Ovejero Aleman
Sexo: Macho — Edad: 11 años — Pelaje: Negro y fuego
Propietario: Cañete — Paciente: Coco
Región de estudio: Articular

CONTROL FECHA: 18/09/2023

OBSERVACIONES

Superficie articular del codo izquierdo (humero) con cartilago hipoecoico con un espesor de 1,4 mm, con superficie osea subcondral irregular, compatible con enfermedad articular degenerativa
Articulacion del codo derecho con cartilago articular del humero con un espesor de 2 mm y superficie osea hiperecoica lisa y regular.
Ambas articulaciones con periostio irregular a nivel de la union de la capsula articular
Articulacion coxofemoral derecha, espesor del cartilago de la cabeza femoral de 1 mm, izquierda 1,3 mm, superficie lisa y hueso subcondral hiperecoico

Dog 6 (Coco) – Treated group – post-treatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr.|Dra.: Corrada
Especie: Canino — Raza: Ovejero Aleman
Sexo: Macho — Edad: 11 años — Pelaje: Negro y fuego
Propietario: Cañete — Paciente: Coco
Región de estudio: Abdominal

CONTROL FECHA: 21/03/2024

OBSERVACIONES

Articulacion humero radio cubital derecha con cartilago articular del humero con un espesor de 1,8 mm y superficie osea hiperecoica lisa y regular.
Articulacion coxofemoral derecha, espesor del cartilago de la cabeza femoral de 1,1 mm de aspecto hipoecoico, superficie lisa y hueso subcondral hiperecoico
Superficie articular humero radio cubital izquierda (humero) con cartilago hipoecoico con un espesor de 1,6 mm, con superficie osea hiperecoica e irregular

Appendix 7

Dog 7 (Delia Toto) – Treated group – pretreatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr.|Dra.: Corrada
Especie: Canino — Raza: Mestizo
Sexo: Hembra — Edad: — Pelaje:
Propietario: Grattoni — Paciente: Delia Toto
Región de estudio: Articular

CONTROL FECHA: 15/07/2023

OBSERVACIONES

Articulacion coxofemoral derecha: Cartilago articular con un espesor de 2,3 mm hipoecoico y superficie sobcondral ecogenica lisa
Articulacion coxofemoral izquierda: Espesor del cartilago articular de 2,8 mm y superficie subcondral ecogenica y lisa
Ambas con escaso liquido articular, no se observa aumento en zonas declive
Articulacion del hombro derecho: Cartilago articular hipoecoico conservado con 1,8 mm de espesor, superficie osea lisa conservada
Articulacion intervertebral lumbar cinco y seis con areas hiperecoicas irregluares entre ambas carillas articulares sugerente de calcificacion (espondilosis?)

Dog 7 (Delia Toto) – Treated group – post-treatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr.|Dra.: Corrada
Especie: Canino — Raza: Mestizo
Sexo: Macho — Edad: 14 años — Pelaje: Negro
Propietario: Grattoni — Paciente: Delia Toto
Región de estudio: Articular

CONTROL FECHA: 25/01/2024

OBSERVACIONES

Articulacion coxofemoral derecha: Cartilago articular con un espesor de 2,9 mm hipoecoico y superficie osea ecogenica lisa
Articulacion coxofemoral izquierda: Espesor del cartilago articular de 2,7 mm y superficie osea ecogenica y lisa
Ambas con escaso liquido articular, no se observa aumento en zonas declive
Articulacion del codo izquierdo: Cartilago articular hipoecoico conservado con 2,1 mm de espesor y superficie osea lisa conservada

Appendix 8

Dog 8 (Pappo) – Treated group – pretreatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr.|Dra.: Corrada
Especie: Canino — Raza: Mestizo
Sexo: Macho — Edad: — Pelaje: Negro
Propietario: Gamarra — Paciente: Pappo
Región de estudio: Abdominal

CONTROL FECHA: 25/10/2023

OBSERVACIONES

Articulacion femorotibiorrotuliana izquierda (vista craneal) con superficie osea lisa y espesor de la tibia de 12 mm , ligamento cruzado anterior hipoecoico con un espesor de 14 mm (no se logra visualizar la ruptura)
Articulacion con contenido liquido anecoico y escaso puntillado ecogenico en suspension, considerar proceso inflamatorio cronico

Dog 8 (Pappo) – Treated group – post-treatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr.|Dra.: Corrada
Especie: Canino — Raza: Mestizo breton
Sexo: Macho — Edad: — Pelaje: Blanco y marron
Propietario: Gamarra — Paciente: Pappo
Región de estudio: Abdominal

CONTROL FECHA: 26/03/2024

OBSERVACIONES

Articulacion femorotibiorrotuliana izquierda (vista craneal) con superficie osea lisa y espesor del cartiago articular de 11 mm a nivel de la tibia y 25 mm a nivel del femur, ligamento cruzado anterior hipoecoico con un espesor de 14 mm. Articulacion con contenido liquido anecoico y escaso puntillado ecogenico en suspension
Articulacion femorotibiorotuliana derecha con espesor del cartilago articular de 13 mm en la tibia y 3,2 mm en el fémur, con escaso puntillado ecogenico en cavidad articular

Appendix 9

Dog 9 (Lucky) – Control group – pretreatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr./Dra.: Corrada
Especie: Canino — Raza: Mestizo
Sexo: Macho — Edad: — Pelaje:
Propietario: Bertea — Paciente: Locky
Región de estudio: Abdominal

CONTROL FECHA: 06/11/2023

OBSERVACIONES

Articulacion humero radio cubital izquierda vista craneal, con superficie osea irregular con puntillado hiperecoico y vista lateral con similar caracteristica, espesor del cartilago articular de 1,5 mm
Articulacion femoro tibio rotuliana izquierda con espacio articular hipoecoico con puntillado ecogenico en suspension y superficie osea irregular con puntillado hiperecoico, espesor del cartilago articular de 1,7 mm

Dog 9 (Lucky) – Control group – post-treatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr./Dra.: Corrada
Especie: Canino — Raza: Mestizo
Sexo: Macho — Edad: — Pelaje: Negro y marron
Propietario: Bertea — Paciente: Lucky
Región de estudio: Articular

CONTROL FECHA: 29/02/2024

OBSERVACIONES

Articulacion humero radio cubital izquierda vista craneal con espesor del cartilago articular de 1,6 mm y superficie osea irregular con puntillado hiperecoico y superficie articular lateral con ecoestructura de iguales caracteristicas
Articulacion femoro tibio rotuliana izquierda con espesor del cartilago articular de 1,5 mm, espacio articular hipoecoico ligeramente heterogeneo y superficie irregular con puntillado hiperecoico

Appendix 10

Dog 10 (Jackson) – Control group – pretreatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr.|Dra.:
Especie: Canino — Raza: Daschund
Sexo: Macho — Edad: 8 años — Pelaje: Negro y fuego
Propietario: Corrada — Paciente: Jackson
Región de estudio: Abdominal

CONTROL FECHA: 17/11/2023

OBSERVACIONES

Se visualizan las articulaciones intervertebrales lumbares L3-L4, L4-L5, L5-L6 y L6-L7 con espacio intervertebral menos definido, en su lugar se halla una linea ligeramente ecogenica sugerente de ligamento longitudinal ventral ligeramente fibrosado / mineralizacion incipiente, solo se observa el espacio en articulacion L3-L4 de 1,8 mm

Dog 10 (Jackson) – Control group – post-treatment - ultrasound

diagnóstico **ecográfico**

Sebastián Pascale
Médico Veterinario M.P. 9312

HISTORIA CLÍNICA

Dr.|Dra.: Corrada
Especie: Canino — Raza: Daschund
Sexo: Macho — Edad: — Pelaje: Negro y fuego
Propietario: Corrada — Paciente: Jackson
Región de estudio: Articular

CONTROL FECHA: 25/01/2024

OBSERVACIONES

En una exploracion de las articulaciones intervertebrales lumbares L3-L4, L4-L5, L5-L6 y L6-L7 se observa el espacio intervertebral menos definido, reemplazado por una linea ecogenica compatible con ligamento longitudinal ventral fibrosado + mineralizacion, solo se observa el espacio en articulacion L3-L4 de 1,8 a 2 mm