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A HERBAL REMEDY DERIVED FROM SUBSPECIES OF ROSA CANINA, IMPROVES THE IMMUNE RESPONSE, WORKING CAPACITY AND WELL-BEING OF DOGS? A PARALLEL, PLACEBO-CONTROLLED, DOUBLE-BLIND, RANDOMIZED STUDY

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Purpose: LitoVet a standardised powder made from subspecies of rose-hip (*rosa-canina*), produced by Hyben-Vital, Langeland, Denmark, has shown anti-inflammatory properties and improves the flexibility of joints and well-being in humans with osteoarthritis as well as in racing horse. It has also been demonstrated that the present powder improves the quality of human cartilage cells. The present study aimed to test whether the same powder might improve the immune response, working capacity and well-being of dogs.

Methods: Eighty six Greyhound dogs represented by both sexes mean age 4.25±1.75 years and weight 30.95±4.0 kg were randomly allocated to either LitoVet or placebo treatment for a three-month period. The animals were randomized in blocks of three with two dogs given LitoVet 10 gram daily as a dry powder added to the food and one dog given the same amount of placebo powder with a similar taste, odour and colour. Both groups were then treated for a three-month period.

The anti-inflammatory capacity was estimated as chemotaxis of peripheral blood neutrophil leucocytes using a Boyden chamber and opsonized zymosan as a trigger and by estimating the total leukocyte counts. Anti-oxidative capacity was estimated by using chemiluminescence. Working capacity, endurance, motivation for different activities including training, litheness, speed, mood and quality of the fur was evaluated by the staff training the dogs by using standardised questionnaires after 6 and 12 weeks, respectively. In addition speed was estimated as meter/second in hounds during competition. LitoVet and placebo treated dogs were compared using Mann-Whitney. A p value of 0.050 or less was regarded as statistically significant.

Results: In vitro studies on neutrophils indicated a dose-dependent anti-inflammatory and anti-oxidative capacity of LitoVet ($p < 0.048$). Anti-inflammatory and anti-oxidative properties were also detected in vivo when the dogs had been treated for twelve weeks with LitoVet ($p < 0.046$ and $p < 0.010$, respectively). The questionnaires developed a consistent pattern. After 6 weeks treatment only litheness showed significant improvement in favour of active treatment ($p < 0.017$). After 12 weeks of treatment a significant change in favour of LitoVet treatment as compared to placebo was seen in the following parameters: working capacity $p < 0.021$, endurance $p < 0.047$, motivation for different activities including training $p < 0.014$, litheness 0.002, speed $p < 0.027$, mood $p < 0.026$ and quality of the fur $p < 0.045$. The improvement observed in the questionnaires was supported by the estimation of speed in competing dogs. There was no significant change in appetite or weight.

Conclusions: The present data suggest that LitoVet exhibits anti-inflammatory properties in dogs and works as a strong antioxidant. This can explain why the actively treated group of dogs showed an improvement in so many different activities as working capacity, litheness, speed and quality of the fur.

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HEALTH STATUS OF PATIENTS WHO RECEIVED TAPENTADOL PROLONGED RELEASE DURING AN OPEN-LABEL EXTENSION STUDY

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Purpose: Health status was assessed using the EuroQol-5 Dimension (EQ-5D) questionnaire in a 1-year open-label extension study of tapentadol prolonged release for the management of moderate to severe chronic pain (ClinicalTrials.gov Identifier: NCT00487435).

Methods: Patients were eligible for enrollment in this study if they completed 1 of 4 phase 3 studies (2 studies that evaluated the efficacy of

tapentadol prolonged release and oxycodone controlled release compared with placebo in patients with osteoarthritis pain [NCT00421928] or low back pain [NCT00449176], a crossover study that evaluated dose conversion between tapentadol immediate release and tapentadol prolonged release in patients with low back pain [NCT00594516], or a 1-year study that evaluated the long-term safety of tapentadol prolonged release compared with oxycodone controlled release in patients with osteoarthritis or low back pain [NCT00361504]). Patients who completed either of the efficacy studies, the crossover study, or who received oxycodone controlled release in the 1-year safety study were titrated to their optimal therapeutic dose of tapentadol prolonged release (100-250 mg bid) during a titration period of up to 4 weeks, and all patients continued on their optimal dose during a maintenance period of up to 48 weeks. Patients who received tapentadol prolonged release in the 1-year safety study continued on their optimal dose determined during that study. Average pain intensity during the past 24 hours was recorded every 4 weeks during the maintenance phase; mean pain intensity at endpoint was calculated using the last observation carried forward for values missing after early discontinuation. The EQ-5D measures health status using 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression [3 possible levels: no problems, some problems, or extreme problems]), as well as a health status index; patients completed an EQ-5D questionnaire at the end of treatment as well as at Months 1, 2, 3, 6, 9, and 12. Treatment-emergent adverse events (TEAEs) were recorded throughout the study.

Results: Patients (N = 1154) reported mean pain intensity scores of 3.87 at baseline and 3.65 at endpoint. At endpoint, the percentages of patients (regardless of prior treatment) who reported the most positive response on each dimension were as follows: no problems with mobility, 43.9%; no problems in self-care, 82.9%; no problems with performing usual activities, 40.6%; no pain or discomfort, 17.2%; and no anxiety or depression, 71.7%. Mean (standard error) changes from baseline on each dimension were as follows: mobility, -0.0 (0.01); self-care, -0.0 (0.01); usual activities, -0.0 (0.02); pain or discomfort, -0.1 (0.02); and anxiety or depression, -0.0 (0.01). The mean (SE) change from baseline in health status index was 0.0 (0.01). The most common ($\geq 10\%$) TEAEs reported during the study were headache (13.1%), nausea (11.8%), and constipation (11.1%).

Conclusions: The efficacy of tapentadol prolonged release for the management of moderate to severe chronic pain and improvements in health status with tapentadol prolonged release treatment have been demonstrated and reported previously in phase 3 studies. Treatment with tapentadol prolonged release (100-250 mg bid) for up to 1 year in this open-label extension study maintained pain control and health status for patients with moderate to severe osteoarthritis or low back pain. These results support the long-term use of tapentadol prolonged release for the management of moderate to severe chronic pain.

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SCREENING, RECRUITMENT AND BASELINE CHARACTERISTICS OF THE LONG-TERM EVALUATION OF GLUCOSAMINE SULPHATE (LEGS) STUDY PARTICIPANTS

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Purpose: Clinical trials evaluating potential 'disease-modifying' agents for osteoarthritis are required to demonstrate both symptomatic and structural benefit. Ideally, to reduce ceiling or floor effects, study participants are required to have at least moderate pain, yet retain sufficient tibiofemoral joint space to allow the measurement of narrowing over time. To describe study recruitment procedures and baseline demographics of people with symptomatic knee osteoarthritis participating in the Long-term Evaluation of Glucosamine Sulphate (LEGS) study (NCT00513422).

Methods: The LEGS study is a 2x2 factorial design randomised placebo-controlled clinical trial allocating participants to glucosamine sulphate (1500mg) and chondroitin sulphate (800mg) or matching placebo for two years. Participants are required to attend annual clinic assessments (including radiographs, knee MRI) and complete a bimonthly 7-day Participant Diary collecting prospective data on pain, physical activity, analgesia and work disability. Participants were recruited by small advertisements in local and national newspapers or directly from general practice. The LEGS study utilized a three stage screening process:

1. Telephone screening,