Randomised double-blind, positive-controlled trial to assess the efficacy of glucosamine/chondroitin sulfate for the treatment of dogs with osteoarthritis

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Abstract

Thirty-five dogs were included in a randomised, double-blind, positive controlled, multi-centre trial to assess the efficacy of an orally-administered glucosamine hydrochloride and chondroitin sulfate (Glu/CS) combination for the treatment of confirmed osteoarthritis of hips or elbows. Carprofen was used as a positive control. Dogs were re-examined on days 14, 42 and 70 after initiation of treatment. Medication was then withdrawn and dogs were re-assessed on day 98. Response to treatment was based on subjective evaluation by participating veterinarians who recorded their findings at each visit. Dogs treated with Glu/CS showed statistically significant improvements in scores for pain, weight-bearing and severity of the condition by day 70 ($P < 0.001$). Onset of significant response was slower for Glu/CS than for carprofen-treated dogs. The results show that Glu/CS has a positive clinical effect in dogs with osteoarthritis.
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1. Introduction

Osteoarthritis (OA) is characterised by low-grade inflammation that leads to progressive degenerative changes in the structure and function of a joint (Beale, 2004). In dogs, most OA occurs secondary to joint injury, joint instability or developmental abnormalities of the joint that result in accelerated turnover of the articular cartilage (McLaughlin and Roush, 2002).

Conventional therapy using corticosteroids or non-steroidal anti-inflammatory drugs (NSAIDs), is designed to reduce inflammation and relieve pain and stiffness. Use of NSAIDs has been limited by adverse effects which have been ascribed to the blockade of homeostatic mechanisms involving cyclooxygenase (Vane and Botting, 1996). The commonest adverse effect in dogs is gastrointestinal erosion and ulceration (Kore, 1990). A new generation of NSAIDS, including carprofen and meloxicam, has enhanced anti-inflammatory activity and reduced side-effects (Holtsinger et al., 1992; Forsyth et al., 1998).

Glucosamine (Glu) and chondroitin sulfate (CS) are components of many dietary supplements used for treatment of OA in several species. Glucosamine is an amino-monosaccharide precursor of the disaccharide unit of glycosaminoglycan, which is the building block of proteoglycans, the

ground substance of articular cartilage (Bassler et al., 1992). Chondroitin sulfate, a polymer of repeating disaccharide units (galactosamine sulfate and glucuronic acid) is the predominant component of articular cartilage and is a natural component of several other body tissues including tendons, bones and vertebral discs (Paroli et al., 1991).

The combination of Glu/CS has been shown to protect against chemically induced synovitis in dogs (Canapp et al., 1999), to stimulate cartilage metabolism and to inhibit its degradation (Lippiello et al., 1999; Johnson et al., 2001). The combination has also been reported to reduce symptoms of OA in humans (Leffler et al., 1999; Das and Hammad, 2000), and the clinical signs of OA in horses (Hanson et al., 1997) and dogs (Johnson et al., 2001). Beneficial structure-modifying effects have been demonstrated histologically in experimental models using rabbits (Lippiello et al., 1999), rats (Beren et al., 2001) and dogs (Johnson et al., 2001). In addition, Glu/CS is well tolerated when administered to dogs for prolonged periods (McNamara et al., 1996). However, one placebo-controlled trial evaluated meloxicam, carprofen and Glu/CS with manganese for the treatment of OA in dogs and reported no significant improvement in the dogs given the Glu/CS with manganese product (Moreau et al., 2003).

This prospective, randomised, double-blind, positive-controlled, multicentre clinical trial was conducted to assess the efficacy in dogs of orally administered Glu/CS for the treatment of clinical OA of elbows and/or hips.

2. Materials and methods

2.1. Animals

Forty-two client-owned dogs were recruited by eight participating veterinarians. Twenty-four dogs were entire males, ten entire females, six neutered females and two neutered males. Twenty-eight dogs were Labrador or Golden retrievers and their crosses. The remainder included ten other breeds. Informed owner consent was obtained and the trial protocol was approved by the University's Ethics Committee and licensed by the Department of Health and Children under the Cruelty to Animals Act (1876) and the Department of Agriculture and Food.

2.2. Inclusion/exclusion criteria

Dogs of any breed or sex with clinical signs of chronic lameness (present for at least one month), stiffness and joint pain and radiological evidence of OA of hips and/or elbows were eligible for inclusion. Animals which were pregnant; were receiving any medication; or had hepatic, renal or cardiovascular disease, gastrointestinal ulceration or a bleeding disorder were excluded. Dogs with lameness due to infectious, immune-mediated, neurological or neoplastic disease and dogs which had received any previous drug or dietary supplement for the treatment for OA were also excluded.

2.3. Pre-treatment evaluation

Dogs were clinically examined and samples were collected for baseline haematology, clinical chemistry and faecal occult blood tests during the pre-treatment assessment. Radiographs of the affected joints were interpreted by the radiologists at the UCD Veterinary Hospital, University College Dublin.

2.4. Assessment protocol

Veterinarians recorded the severity of the clinical signs at each visit using an ordinal scoring system (Table 1). The scoring system was developed based on subjective scoring systems as reported in previous studies (Vasseur et al., 1995; Holtsinger et al., 1992). Before commencement, participants were thoroughly briefed on the assessment protocol to achieve standardisation of observation and analysis. This was done by providing each participant with a detailed dossier of the trial protocol followed by a comprehensive explanation of the assessment protocols by one of the authors (GMcC).

2.5. Treatment products

Dogs were given either Glu/CS (Synoquin SA, VetPlus Ltd.) or carprofen (Rimadyl, Pfizer). Each gram of the Glu/Cs formulation contained the following active ingredients; glucosamine hydrochloride 475 mg/g, chondroitin sulfate 350 mg/g, N-acetyl-D-glucosamine 50 mg/g, ascorbic acid 50 mg/g and 30 mg/g of Zn sulfate. Each product was dispensed in size 00 gelatin Capsugel capsules and the capsules were presented such that on dispensing, each treatment was indistinguishable from the other, thus enabling the double-blind study. For the trial the Glu/CS capsules contained 750, 666 or 500 mg of the Glu/Cs formulation made up to 1 g with mannitol BP[1] filler. Carprofen capsules contained 10, 20, 25, 30, 50 or 75 mg of active ingredient made up to 1 g with mannitol BP filler. Placebo capsules contained 1 g of mannitol BP alone. Encapsulation was carried out according to GMP.[2]

2.6. Treatment protocol

Dogs were assigned to treatment groups centrally, by the trial co-ordinator, who assigned dogs to alternate treatment groups strictly by order of recruitment. The trial co-ordinator was not involved in the assessment of participating dogs. Glu/CS was administered according to the manufacturer's datasheet recommendation at a rate of 1 g of active ingredient twice daily to dogs weighing 5–19.9 kg, 1.5 g twice daily to dogs weighing 20–40 kg and 2 g twice daily to dogs weighing >40 kg for 42 days. After 42 days,

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[1] British Pharmacopoeia.
[2] Good Manufacturing Practice.

Table 1
Clinical scoring system for assessing dogs with osteoarthritis

Criterion	Clinical evaluation
Lameness	1. Walks normally 2. Slightly lame when walking 3. Moderately lame when walking 4. Severely lame when walking 5. Reluctant to rise and will not walk more than five paces
Joint mobility	1. Full range of motion 2. Mild limitation (10–20%) in range of motion; no crepitus 3. Mild limitation (10–20%) in range of motion; with crepitus 4. Moderate limitation (20–50%) in range of motion; ±crepitus 5. Severe limitation (>50%) in range of motion; ±crepitus
Pain on palpation	1. None 2. Mild signs; dog turns head in recognition 3. Moderate signs; dog pulls limb away 4. Severe signs; dog vocalises or becomes aggressive 5. Dog will not allow palpation
Weight-bearing	1. Equal on all limbs standing and walking 2. Normal standing; favours affected limb when walking 3. Partial weight-bearing standing and walking 4. Partial weight-bearing standing; non-weight-bearing walking 5. Non-weight-bearing standing and walking
Overall score of clinical condition	1. Not affected 2. Mildly affected 3. Moderately affected 4. Severely affected 5. Very severely affected

the daily dose of Glu/CS was reduced by one-third for the subsequent 28 days. Carprofen was given in accordance with the manufacturer's datasheet at a loading dose of 2 mg/kg bodyweight twice daily for seven days followed by a once daily maintenance dose of 2 mg/kg. Mannitol-filled placebo capsules were administered as a second capsule daily to ensure blinding-compliance. A dosing chart was supplied to aid owner compliance. All medication was given with food. Veterinarians and owners were unaware which treatment was being administered. Animals were re-assessed on days 14, 42, 70 and 98 after initiation of treatment. Treatment was stopped on day 70. The capsules remaining were counted at each visit as a compliance check. If there was deterioration in a dog's signs between days 70 and 98, any necessary treatment was implemented at the discretion of the supervising veterinarian.

2.7. Data handling and statistics

The Mann–Whitney two-tailed test was used to compare the baseline data prior to treatment. Spearman rank correlation (Rs) testing was used to look for relationships between disease scores and demographic characteristics (weight and age). The Friedman repeated measures test with post hoc analysis (Daniel, 1978), where necessary, was used to look for significant changes ($\alpha = 0.05$) in the disease scores within treatment groups over time. Dogs for which data for a given parameter were not available for every time point, were not included in the Friedman analysis of that parameter. The one-tailed Mann–Whitney test (MWT) was used to compare changes in score at day 70. Changes in score were calculated for the five parameters by subtracting the day 70 score from the pre-treatment score for each dog. The power of the one-tailed MWT to detect a difference in median of 1.0 with 15 subjects in each group is estimated at 0.78 ($\beta = 0.22$, $\alpha = 0.05$, s.d. $\leqslant 1.03$). Minitab v.13.2 software (Minitab Inc.) was used to perform statistical analyses.

3. Results

Forty-two dogs were enrolled in the trial but six were withdrawn prior to day 14 and one at day 42. Reasons for withdrawal were failure to attend assessment appointments (three dogs in the Glu/CS group; one dog in the carprofen group), two adverse drug reactions (both in Glu/CS group) and one dog had required surgery (Glu/CS group). One dog (Glu/CS group) was administered a NSAID between day 70 and day 98 and one dog in the carprofen group died (due to intestinal torsion) between day 70 and day 98. As a result data for these last two dogs were not included in the Friedman repeated measures analysis but were included in the comparison of groups at days 0 and 70. In addition, one dog in the carprofen treated group was missing data for the overall condition variable and therefore was not included in the analysis of that variable. Table 2 summarises the age, sex, bodyweight and joints affected data for the 35 dogs completing the trial to day 70.

All dogs enrolled in the trial had haemogram and biochemical profile results within reference range, negative faecal occult blood tests and confirmed radiological evidence of osteoarthritis.

Mann–Whitney two-tailed comparisons of pre-treatment disease scores found no significant difference between the treatment and control groups. The results, using data for the 35 dogs completing the trial, are presented in Table 3. Significant and strong positive correlations (Rs > 0.55) existed between the pre-treatment disease score and the day 70 change in score ($P < 0.02$) for all parameters. This correlation was independent of treatment group, indicating that dogs with higher pre-treatment disease scores tended to have higher, positive changes in score (i.e., improvement) by day 70 than dogs with lower pre-treatment scores. These correlations suggest that the subjective scoring system may have been insensitive to improvements in dogs with lower pre-treatment disease scores.

Dogs in the Glu/CS treatment group showed significant improvements ($P < 0.001$) in disease scores at day 70 for pain, weight-bearing and overall condition compared to

Table 2
Sex, age, joint(s) affected and bodyweight distribution for all 35 dogs which completed the trial

| | Total | Gender | | Affected joint(s) | | | Age (yr) | Weight (kg) |
		Male	Female	Hip	Elbow	H&E[a]		
Carprofen	19	12	7	3	14	2	9.1 ± 2.0 [5.5–13]	30.5 ± 10.5 [10.5–45]
Glu/CS	16	10	6	5	9	2	6.8 ± 3.5 [0.9–13]	32.7 ± 12.3 [11–58.5]
Totals	35	22	13	8	23	4	–	–

Age and weight data are expressed as mean ± SD and [range]. Glu/CS, glucosamine/chondroitin sulfate treatment group. Carprofen, positive control treatment group. The "Gender" and "Affected Joint(s)" columns show the number of dogs in each sub-category by treatment group.

[a] H&E is the dogs with both hip and elbow joints affected.

Table 3
Comparison of pre-treatment clinical scores for treatment and control groups

Parameter (pretreatment)	P-value[*]	Carprofen (n)	Glu/CS (n)
Lameness	0.5686	19	16
Joint mobility	0.2069	19	16
Pain	0.2122	19	16
Weight bearing	0.2618	19	16
Overall condition	0.1685	18	16

Key: n, number of dogs per treatment group; Glu/CS, glucosamine/chondroitin sulfate treatment group; carprofen, positive control treatment group. The carprofen treated group has data for only 18 dogs in the Overall Condition category whereas 19 dogs contributed data for the other parameters. This is due to an omission to award a score for overall condition for one of the dogs.

[*] Mann–Whitney test, two tailed, $\alpha = 0.05$, $1 - \beta = 0.64$, adjusted for ties. The P values indicate that the differences in the pre-treatment scores between the two treatment groups are not significant.

pre-treatment scores (Table 4). However, lameness ($P = 0.192$) and joint mobility ($P = 0.248$) scores were not significantly better than pre-treatment scores (Table 4) in the Glu/CS treated group. The data for the three parameters for which the Glu/CS group showed significant improvements are plotted in Fig. 1.

The carprofen treated group improved in all five parameters, although the time-points that were significantly better than the pre-treatment scores varied. Joint mobility was significantly improved at days 14, 42 and 70

($P < 0.001$). Weight-bearing was significantly improved at days 14, 42, 70 and 98 ($P < 0.001$). Joint pain was significantly improved at day 42 ($P = 0.003$). The lameness score was significantly improved at day 70 ($P < 0.001$). Overall condition score was significantly improved on days 42 and 70 ($P < 0.001$). The proportions of dogs improving on the two treatments are presented in Table 5.

Table 6 presents summary data for changes in score for the treatment groups at day 70. Mean reduction in disease score in carprofen-treated dogs was greater than in Glu/CS-treated dogs at day 70 for lameness, joint mobility, weight-bearing and overall condition scores. The average improvement in pain scores at day 70 was comparable for both groups. The median improvement in score for the Glu/CS group was not significantly less ($P > 0.05$) than the carprofen group for any parameter although significance was approached for lameness ($P = 0.0775$) and overall condition ($P = 0.0587$). Therefore, as the estimated power of the test, at 0.78, was adequate by convention, the results support the conclusion of non-inferiority of Glu/CS therapy at day 70 to carprofen therapy at day 70 in the treatment of osteoarthritis of the hip and/or elbow joints in dogs.

4. Discussion

The results of this trial show that dogs with OA had significant ($P < 0.001$) improvements in scores for pain,

Table 4
Improvement in clinical scores over time

| Parameter | Carprofen | | | Glu/CS | | |
	P-value	**	n	P-value	**	n
Lameness	0.000	Day 70	18	0.192	NS	15
Joint mobility	0.000	Day 14, 42, 70	18	0.248	NS	15
Pain	0.003	Day 42	18	0.000	Day 70	15
Weight bearing	0.000	Day 14, 42, 70, 98	18	0.000	Day 70	15
Overall condition	0.000	Day 42, 70	17	0.000	Day 70	15

The above results were obtained from Friedman repeated measures analysis of the clinical score data, blocked by animal, for carprofen and glucosamine/chondroitin sulfate treatment, respectively. As tied data were present in all data sets, the reported P-values have been adjusted for ties. $\alpha = 0.05$.

**Where $P < 0.05$, post hoc testing identified the time-points the group had significantly improved scores compared to the pre-treatment assessment. Neither treatment had any time points that were significantly worse than the pre-treatment assessment. The numbers of dogs included in the Friedman analysis are less than the number completing the trial due to the requirement to have data for every timepoint, therefore dogs that were missing data were omitted. Key: NS, not significant; n, number of dogs included in analysis; Glu/CS, glucosamine/chondroitin sulfate treatment group; carprofen, positive control treatment group.
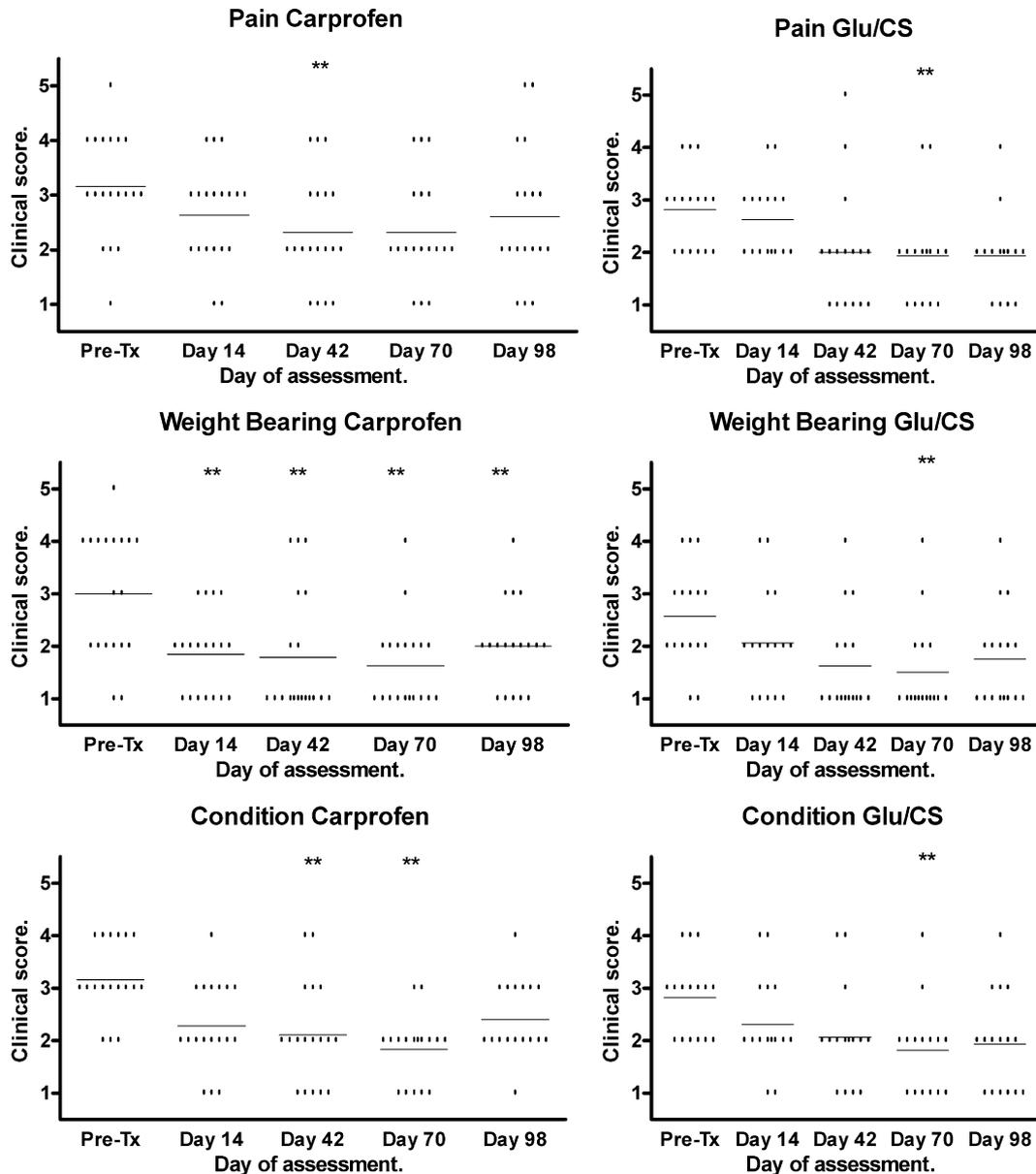
Fig. 1. Plots of pain, weight-bearing and overall condition scores for carprofen and glucosamine/chondroitin sulfate treated dogs. Each point represents the score recorded for an individual dog. The dogs were assessed pre-treatment and then received either carprofen or glucosamine with chondroitin sulfate for 70 days with assessment on days 14, 42 and 70. On day 98 the dogs had received no treatment for 28 days and were assessed for the final time. Higher scores correspond to more severe clinical signs. The mean score for each assessment day is shown with a solid horizontal line. Key; Pre-Tx, pre-treatment assessment; Glu/CS, glucosamine/chondroitin sulfate treated group, ** indicates assessment days when scores were significantly different from pre-treatment scores ($P \leqslant 0.003$). Data are graphed on an intention-to-treat basis for the 35 dogs completing the trial to day 70.

weight-bearing and overall clinical condition when treated with oral Glu/CS or carprofen for 70 days, as subjectively assessed by veterinarians. Compared to the dogs given carprofen, significant improvement occurred later in the course of treatment for the Glu/CS-treated group; day 70 versus day 42 for carprofen for most parameters assessed.

As osteoarthritis is a painful condition and in order to address ethical responsibilities and the welfare of the participant dogs, a positive control was used instead of a placebo. Carprofen was chosen as it has been extensively tested for efficacy and safety (Holtsinger et al., 1992) and was a suitable product for encapsulation. It is not possible

to establish whether encapsulation altered the pharmacokinetics of carprofen. However, the positive clinical response observed is comparable to the results of the subjective orthopaedic assessments of carprofen-treated dogs in the trials of Moreau et al. (2003), Vasseur et al. (1995) and Holtsinger et al. (1992) who reported significant improvements in clinical signs after 30, 14 and 14 days, respectively.

A recognised limitation of this trial is the lack of an objective assessment of the joints (Budsberg, 1997). It was not possible to perform ground force reaction measurements as was done in the trials of Moreau et al. (2003) and Vasseur et al. (1995) as this was a multicentre

Table 5
Dogs in carprofen and glucosamine/chondroitin sulfate treatment groups with improved scores at days 14, 42, 70 and 98

	Lame. carprofen	Lame. Glu/CS	Joint mobility carprofen	Joint mobility Glu/CS	Pain carprofen	Pain Glu/CS	WB carprofen	WB Glu/CS	Cond carprofen	Cond. Glu/CS
Day 14	**58%**	**50%**	**68%**	**38%**	**42%**	**31%**	**79%**	**44%**	**61%**	**44%**
	[11/19]	**[8/16]**	**[13/19}**	**[6/16]**	**[8/19]**	**[5/16]**	**[15/19]**	**[7/16]**	**[11/18]**	**[7/16]**
	21%	19%	26%	6%	21%	0%	32%	6%	27%	6%
	(4/19)	(3/16)	(5/19)	(1/16)	(4/19)	(0/16)	(6/19)	(1/16)	(5/18)	(1/16)
Day 42	**52%**	**44%**	**68%**	**50%**	**58%**	**56%**	**68%**	**75%**	**66%**	**62.5%**
	[10/19]	**[7/16]**	**[13/19]**	**[8/16]**	**[11/19]**	**[9/16]**	**[13/19]**	**[12/16]**	**[12/18]**	**[10/16]**
	32%	19%	21%	25%	16%	31%	26%	25%	28%	19%
	(6/19)	(3/16)	(4/19)	(4/16)	(3/19)	(5/16)	(5/19)	(4/16)	(5/18)	(3/16)
Day70	**68%**	**50%**	**68%**	**50%**	**58%**	**68%**	**79%**	**69%**	**94%**	**81%**
	[13/19]	**[8/16]**	**[13/9]**	**[8/16]**	**[11/19]**	**[13/16]**	**[15/19]**	**[11/16]**	**[17/18]**	**[13/16]**
	32%	19%	26%	19%	26%	25%	37%	25%	39%	19%
	(6/19)	(3/16)	(5/19)	(3/16)	(5/19)	(4/16)	(7/19)	(4/16)	(7/18)	(3/16)
Day 98	**61%**	**40%**	**50%**	**46%**	**56%**	**73%**	**78%**	**67%**	**65%**	**67%**
	[11/18]	**[6/15]**	**[9/18]**	**[7/15]**	**[10/18]**	**[11/15]**	**[14/18]**	**[10/15]**	**[11/17]**	**10/15**
	6%	20%	17%	13%	22%	13%	28%	27%	18%	20%
	(1/18)	(3/15)	(3/18)	(2/15)	(4/18)	(2/15)	(5/18)	(4/15)	(3/17)	(3/15)

Percentages and numbers in bold print indicate dogs improved by one score or more compared to pre-treatment score. Non-bold percentages and numbers are dogs improved by two scores or more. For numbers within parentheses the numerators are the numbers of dogs improved while the denominators are the number of dogs with scores for that parameter at that time point. Administration of therapy began on day 1 and was stopped on day 70. The dogs were assessed again 28 days later, on day 98. Lame., lameness score; WB, weight bearing score; Cond., overall condition score.

Table 6
Comparison of improvement in clinical parameters at day 70

Parameter	Carprofen median (mean)	Glu/CS median (mean)	95% CI of difference in medians	P-value
Lameness	1.0 (1.1)	0.5 (0.6)	0, 1	0.0775
Joint mobility	1.0 (1.0)	0.5 (0.5)	0, 1	0.0907
Pain	1.0 (0.8)	1.0 (0.9)	−1, 1	>0.5
Weight bearing	1.0 (1.4)	1.0 (1.1)	0, 1	0.2380
Overall condition	1.0 (1.4)	1.0 (1.0)	0, 1	0.0587

Day 70 was the last day of treatment. Changes in score were calculated by subtracting the scores for each dog on day 70 from the dogs' pre-treatment score. The median and mean change in score and the 95% confidence interval (CI) for difference in medians are given. The P-value was obtained from a one tailed Mann–Whitney test comparing treatment groups at day 70 for each parameter. ($\alpha = 0.05$, $1 - \beta = 0.78$). Glu/CS, glucosamine/chondroitin sulfate treatment group. Carprofen, positive control treatment group.

trial. Subjective assessment of weight bearing was used instead.

The assignment-to-treatment-group process was based on alternating test product strictly by the order of recruitment and could be criticised as less than optimal randomisation. However, the person who assigned treatment group was not involved in the assessment of dogs or the analysis of the data. In addition, comparison of pre-treatment disease scores for all recruited dogs ($n = 42$) and for dogs completing the trial ($n = 35$) found no significant difference between the treatment groups for any of the parameters evaluated.

The benefits of the use of Glu and CS for OA have long been greeted with scepticism due to the lack of reliable information regarding their absorption, pharmacokinetics and mechanisms of action. Pharmacokinetic studies on glucosamine and chondroitin sulfate in dogs using ^{14}C-glucosamine and ^{35}S-labelled CS found that 87% of an orally administered dose of radiolabelled Glu and 70% of the labelled CS were absorbed (Conte et al., 1995; Setnikar et al., 1986). Some of the other issues have been addressed in species such as the horse (Du et al., 2004) and the dog (Adebowale et al., 2002). Adebowale and coworkers (2002) showed that both Glu and CS are bioavailable after oral dosing and that low molecular weight CS displays significant accumulation upon multiple dosing. In addition both Glu and CS are reported to have a tropism for articular cartilage (Setnikar and Rovati, 2001). The safety profiles of glucosamine and chondroitin sulfate have been evaluated in human (Rovetta et al., 2002; Towheed and Anastassiades, 1999) and veterinary (McNamara et al., 1996, 2000) trials and have been deemed excellent and the popularity of these products as alternatives to NSAIDS has been enhanced because they have fewer side-effects (Muller-Fassbender et al., 1994; Hanson et al., 1997). McNamara et al. (1996, 2000) monitored healthy dogs and cats given Glu/CS and manganese over 30 days, at twice the manufacturers recommended dosage and reported only minor, non-clinically significant changes in haematological and haemostatic values. The safety of Glu/CS for long term use in dogs has not been evaluated. Adverse reactions reported in both human and veterinary

literature predominantly affected the gastrointestinal tract and resolved spontaneously on withdrawal of the medication. In the present study, the two cases of adverse reactions in the Glu/CS group presented as gastrointestinal upsets on days four and nine respectively. One case resolved spontaneously and the second resolved after ranitidine therapy. In the latter case the owner was unwilling to persevere with the trial and in the former the gastrointestinal signs returned when treatment was resumed and so the dog was withdrawn.

Several clinical trials in humans support the use of Glu/CS administered as individual components or in combination in treatment of OA (Towheed et al., 2001; Busci and Poor, 1998; Muller-Fassbender et al., 1994). The action of Glu and CS has been shown to be synergistic in vitro (Lippiello et al., 2000). There are few reports of clinical studies in dogs despite widespread use of Glu/CS in this species. In a survey of 2524 veterinarians evaluating the perceived clinical efficacy of an oral Glu/CS compound in dogs, 89% and 83% of respondents rated it as "good/excellent" in regards to improved mobility and alleviating pain, respectively (Anderson and Slater, 1997). In experimental studies, positive responses were obtained in dogs given Glu/CS for 21 days prior to induction of acute synovitis (Canapp et al., 1999) and in dogs given Glu/CS with manganese with cranial cruciate ligament injury (Johnson et al., 2001).

There are several dietary supplements containing Glu/CS available in the veterinary market. These preparations differ in composition, purity and source of glucosamine and chondroitin sulfate. They also contain varying amounts of additional compounds such as manganese, omega-3 fatty acids, antioxidants, minerals and herbal agents. There are no published studies comparing similar individual or combination dietary supplements for the treatment of OA in dogs.

Moreau et al. (2003) in a randomised, double-blind placebo-controlled trial assessed the efficacy of 60 days treatment with Glu/CS with manganese, carprofen or meloxicam for the treatment of OA in dogs. The results were evaluated by measuring ground reaction forces, by subjective clinical assessment by a veterinarian and by owners' observations. Significant improvement, using gait analysis, was recorded for all dogs receiving carprofen or meloxicam. The Glu/CS and manganese group showed no significant response as determined by the objective gait analysis or by either of the subjective assessments. Possible explanations for the non-performance of the Glu/CS and manganese may be that the product was indeed ineffective, or, that the dose administered to some dogs and the duration of the initial loading-dose period were less than the manufacturer recommended or, that the timescale (60 days) of the trial did not allow the Glu/CS and manganese to reach its full therapeutic potential. In the present study, improvements in pain, weight-bearing and overall condition scores in the Glu/CS group were not significant until day 70 ($P < 0.001$). The slow onset of action of Glu/CS

has been reported in human trials (Vaz, 1982) and anecdotally in dogs (Budsberg et al., 2000).

The significance of the maintenance of improvement in disease scores when compared to pre-treatment scores, for both groups, one month after cessation of treatment is uncertain but is an aspect worthy of further investigation.

5. Conclusion

This is the first report demonstrating that the clinical signs of OA in dogs improved significantly after 70 days of treatment with oral glucosamine hydrochloride and chondroitin sulfate. Future clinical trials of Glu/CS should monitor dogs for a minimum period of 70 days and incorporate an objective measurement such as force plate gait analysis.

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