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PS Tarate

M.V.Sc. Scholars, Department of
Veterinary Surgery and Radiology,
Maharashtra Animal and Fishery
Sciences University, Maharashtra, India

RV Raulkar

Associate Professor and Head,
Department of Veterinary Surgery and
Radiology, Maharashtra Animal and
Fishery Sciences University,
Maharashtra, India

Farheen Fani

Associate Professor, Department of
Veterinary Surgery and Radiology,
Maharashtra Animal and Fishery
Sciences University, Maharashtra, India

MG Thorat

Former Professor and Head, Department
of Veterinary Surgery and Radiology,
Maharashtra Animal and Fishery
Sciences University, Maharashtra, India

SR Chavan

M.V.Sc. Department of Veterinary
Surgery and Radiology, Maharashtra
Animal and Fishery Sciences University,
Maharashtra, India

Pooja Pharande

M.V.Sc. Scholars, Department of
Veterinary Surgery and Radiology,
Maharashtra Animal and Fishery
Sciences University, Maharashtra, India

AJ Choudhury

M.V.Sc. Scholars, Department of
Veterinary Surgery and Radiology,
Maharashtra Animal and Fishery
Sciences University, Maharashtra, India

Niharika Moon

M.V.Sc. Scholars, Department of
Veterinary Surgery and Radiology,
Maharashtra Animal and Fishery
Sciences University, Maharashtra, India

Corresponding Author:

RV Raulkar

Associate Professor and Head,
Department of Veterinary Surgery and
Radiology, Maharashtra Animal and
Fishery Sciences University,
Maharashtra, India

Clinico-therapeutic efficacy of Pentosan Polysulfate and Grapiprant for the management of osteoarthritis in dog

PS Tarate, RV Raulkar, Farheen Fani, MG Thorat, SR Chavan, Pooja Pharande, AJ Choudhury and Niharika Moon

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Abstract

The present clinical investigation entitled “Clinico-therapeutic efficacy of Pentosan Polysulfate and Grapiprant for the management of osteoarthritis in dog” was undertaken to evaluate and compare the therapeutic effectiveness of Pentosan Polysulfate Sodium (PPS) and Grapiprant, administered with nutraceutical supplementation, in the conservative management of canine hip osteoarthritis. A total of 25 dogs presented with hindlimb lameness or locomotor dysfunction were clinically and radiographically screened for osteoarthritis. Sixteen dogs diagnosed with hip osteoarthritis were selected, irrespective of age, breed, sex, or body weight, and randomly divided into two equal treatment groups. Group I received Pentosan Polysulfate Sodium at 3 mg/kg body weight subcutaneously once weekly for four weeks, along with oral supplementation of undenatured type-II collagen and omega-3 fatty acids. Group II was treated with Grapiprant orally at 2 mg/kg body weight once daily for seven days in combination with the same nutraceutical regimen. Physiological, clinical, haematological, biochemical, and radiographic parameters were evaluated on day 0, day 21, and day 45. Incidence analysis revealed the hip joint as the most commonly affected joint, with higher prevalence in Labrador Retrievers, middle-aged to older dogs, and males, indicating the influence of breed, age, and body conformation. Physiological parameters remained within normal limits throughout the study, suggesting the absence of systemic adverse effects. Haematological and biochemical parameters showed non-significant variations between groups and intervals. Clinical assessment demonstrated significant interval-wise improvement in pain, lameness, and weight-bearing ability in both groups; however, dogs treated with Pentosan Polysulfate Sodium showed comparatively superior and sustained improvement. Radiographic evaluation revealed progressive reduction in osteoarthritic changes, with greater improvement observed in Group I. In conclusion, both treatment protocols were effective; however, Pentosan Polysulfate Sodium (PPS) combined with nutraceutical supplementation produced superior and sustained clinico-radiographic improvement in canine hip osteoarthritis.

Keywords: Canine hip osteoarthritis, pentosan polysulfate sodium, grapiprant, lameness, radiographic evaluation, disease-modifying therapy

Introduction

The human-animal relationship has evolved since prehistoric times through domestication and co-evolution, significantly influencing human society and survival (Kacker and Srivastava, 2018). In India, rapid urbanization, increased disposable income, and the rise of nuclear families have contributed to a growing demand for companion animals, particularly dogs, which are now considered integral family members^[19].

Osteoarthritis (OA) is the most common joint disorder in dogs, characterized by progressive degeneration of articular cartilage, inflammation, pain, stiffness, and reduced mobility (Elders, 2000; Noth *et al.*, 2008). It affects approximately one in five dogs, imposing both clinical and economic burdens (Hielm-Bjorkman *et al.*, 2003; Aragon *et al.*, 2007; Anderson *et al.*, 2018). The condition is more prevalent in overweight, obese, and neutered animals, as well as in large breeds such as Labrador Retrievers, German Shepherds, and Rottweilers (Bland, 2015; Anderson *et al.*, 2020)^[1, 2, 3, 5, 12, 21].

Osteoarthritis may be primary (age-related) or secondary to conditions such as hip dysplasia, elbow dysplasia, patellar luxation, and cranial cruciate ligament rupture. Its pathogenesis involves degradation of cartilage matrix components, synovial inflammation, osteophyte formation, and subchondral bone remodeling (Huang *et al.*, 2010; Dubey *et al.*, 2018) ^[18]. Clinical signs include lameness, stiffness, reluctance to move, and pain on joint manipulation. Diagnosis is based on clinical evaluation and imaging modalities such as radiography, CT, and MRI (Braun and Gold, 2012) ^[6, 11].

Management of OA is primarily symptomatic and multimodal, involving NSAIDs, analgesics, nutraceuticals, physiotherapy, and surgical interventions in advanced cases (Cook and Payne, 1997). However, field conditions often limit effective diagnosis and treatment ^[10].

Pentosan Polysulfate Sodium (PPS) is a disease-modifying osteoarthritis drug with chondroprotective and anti-inflammatory properties, promoting cartilage repair and inhibiting degradation (Ghosh, 1999; Wijekoon *et al.*, 2018) ^[15]. Grapiprant, a selective EP4 receptor antagonist, provides targeted pain relief by inhibiting prostaglandin-mediated inflammation with fewer side effects compared to conventional NSAIDs (Nagahisa *et al.*, 2016; Sartin *et al.*, 2021) ^[20, 25, 31]. Nutraceuticals such as undenatured type-II

collagen and omega-3 fatty acids further support joint health and improve clinical outcomes.

Considering the need for effective and standardized treatment protocols, the present study was undertaken with the following objectives:

Objectives of the study

1. To compare the efficacy of Pentosan Polysulfate Sodium (PPS) and Grapiprant in osteoarthritis in dogs.
2. To study haemato-biochemical alterations associated with Pentosan Polysulfate Sodium (PPS) and Grapiprant therapy

4. Materials and methods

4.1 Study Location and Design

The study was conducted at the Department of Veterinary Surgery and Radiology, Veterinary Clinical Complex, PGIVAS, Akola. A total of 25 dogs with hind limb lameness or locomotor disability were screened, and 16 dogs with confirmed hip osteoarthritis were selected and randomly divided into two groups (n=8 each).

4.2 Treatment Protocol

Groups (n= no. of dogs)	Therapeutic Drugs and Protocol
Group I (n=8)	Inj. Pentosan Polysulfate Sodium @ 3 mg/kg BW by subcutaneous route at weekly intervals for four weeks. Tab. Undenatured type-II Collagen and Omega 3 fatty acid according to body weight orally.
Group II (n=8)	Tab. Grapiprant @ 2mg/kg BW OD orally for 7 days Tab. Undenatured type-II Collagen and Omega 3 fatty acid according to body weight orally.

4.3 Incidence Study

Incidence of osteoarthritis was calculated based on joint involvement, breed, age, and sex, and expressed as percentages.

4.4 Physiological Parameters

Rectal temperature, heart rate, and respiratory rate were recorded on day 0, 21, and 45 post-treatment.

4.5 Clinical Evaluation

- 4.5.1 Pain Assessment: Graded on a 0-3 scale (no pain to severe pain).
- 4.5.2 Lameness Scoring: Graded on a 0-4 scale (clinically sound to severe lameness).
- 4.5.3 Weight-Bearing Assessment: Graded on a 1-5 scale (normal to non-weight bearing).

All clinical parameters were evaluated on day 0, 21, and 45.

4.6 Haematological Analysis

Blood samples collected in EDTA vials were analysed for haemoglobin (Hb), total erythrocyte count (TEC), total leucocyte count (TLC), and differential leucocyte count (DLC) using an automated haematology analyser.

4.7 Biochemical Analysis

Serum samples were analysed for calcium, phosphorus, alkaline phosphatase (ALP), and total protein using a semi-automatic analyser.

4.8 Radiographic Examination

Radiographs of the hip joint were taken under sedation and general anesthesia using ventrodorsal extended view.

Osteoarthritic changes such as osteophytes, joint space narrowing, and subchondral sclerosis were recorded.

4.9 Radiographic Scoring

Severity of osteoarthritis was graded on a scale of 1-4 (slight to severe) based on standard radiographic criteria.

4.10 Statistical Analysis

Data were analysed using ICAR-WASP version 2.0. A two-way factorial design and ANOVA were used to determine significant differences between groups and time intervals.

5. Results and Discussion

5.1 Study Overview: Out of 25 dogs presented with hind limb lameness, 16 dogs diagnosed with hip osteoarthritis were included in the study. These animals were randomly divided into two groups (n=8 each) and subjected to two different therapeutic protocols along with nutraceutical supplementation. Clinical, physiological, hematological, biochemical, and radiographic parameters were evaluated at different intervals to assess treatment efficacy.

5.2 Incidence of Osteoarthritis

5.2.1 Overall Incidence: The hip joint was the most commonly affected joint with 16 cases (64%), followed by stifle joint 4 cases (16%), elbow joint 3 cases (12%), and carpal joint 2 cases (8%). These findings are in accordance with Subin (2005), Singh (2019), Varghese (2019), and Bano *et al.* (2022), who also reported higher incidence of hip osteoarthritis in dogs ^[4, 26, 27, 30].

5.2.2 Breed-wise Incidence

Among the 16 dogs affected with hip osteoarthritis, Labrador Retrievers showed the highest incidence (7 cases; 43.75%),

followed by German Shepherds (4 cases; 25%), Golden Retrievers (2 cases; 12.50%), and other breeds including Rottweiler, Doberman, and Great Dane (1 case each; 6.25%). These findings are in accordance with Subin (2005), Singh (2019), and Anderson *et al.* (2020), who reported higher susceptibility in large breeds due to increased body weight and joint stress [2, 26, 27].

5.2.3 Age-wise Incidence

Higher incidence was observed in dogs aged 5-10 years (9 cases; 56.25%), followed by dogs above 10 years (5 cases; 31.25%) and 1-5 years age group (2 cases; 12.50%). These findings are in agreement with Todhunter *et al.* (2003), Singh (2019), and Varghese (2019), indicating that osteoarthritis is a progressive age-related disorder [26, 29, 30].

5.2.4 Gender-wise Incidence

Out of 16 cases, males (9 cases; 56.25%) were more commonly affected than females (7 cases; 43.75%). Similar observations have been reported by Subin (2005) and Suheb *et al.* (2021), possibly due to increased activity and body weight in male dogs [27, 28].

5.3 Physiological Parameters

Rectal temperature, heart rate, and respiration rate remained within normal physiological limits in all animals throughout the study period, with no significant variation between treatment groups or observation intervals.

This suggests that osteoarthritis is primarily a localized musculoskeletal disorder without systemic physiological involvement. Similar findings were reported by Subin (2005), Singh (2019), Varghese (2019), and Patel *et al.* (2025) [22, 26, 27, 30].

5.4 Clinical Parameters

A progressive and significant improvement was observed in clinical parameters including pain, lameness, and weight-bearing ability in both groups during the study period.

Pain scores showed marked reduction over time in all 16 dogs, indicating effective control of inflammation and nociception. However, comparatively better and sustained improvement was observed in Group I animals treated with Pentosan Polysulfate Sodium. These findings are in accordance with Suheb *et al.* (2021), Chopade (2024), and Patel *et al.* (2025) [9, 22, 28].

Lameness scores also showed significant improvement in all treated dogs, reflecting enhanced mobility and joint function. Greater clinical improvement observed in Group I may be attributed to the chondroprotective and cartilage-regenerating effects of pentosan polysulfate, as reported by Budsberg *et al.* (2007) and Bwalya *et al.* (2017) [7, 8].

Weight-bearing ability improved in all animals, indicating restoration of functional limb use. Group I animals showed comparatively superior improvement, which may be due to improved joint lubrication and reduced cartilage degeneration. Similar findings were reported by Elmesiry *et al.* (2016) and Wijekoon *et al.* (2018) [13, 31].

The improvement observed in Group II animals treated with Grapiprant may be attributed to selective EP4 receptor antagonism leading to effective analgesia, as described by Rausch-Derra *et al.* (2016) and Enomoto *et al.* (2024).

Additionally, the administration of undenatured type-II collagen and omega-3 fatty acids in both groups may have contributed to reduction in inflammation and improvement in joint health, as reported by Roush *et al.* (2010) and Gupta *et al.* (2011) [14, 16, 23, 24].

5.5 Haematological Parameters

Haematological parameters including haemoglobin, total erythrocyte count, total leucocyte count, and differential leucocyte count remained within normal physiological limits in all 16 dogs and did not show significant variation throughout the study period.

This indicates absence of systemic inflammatory or hematological changes, as osteoarthritis primarily affects joint structures. These findings are in accordance with Subin (2005), Singh (2019), Suheb *et al.* (2021), Bano *et al.* (2022), and Patel *et al.* (2025) [4, 22, 26, 27, 28].

5.6 Biochemical Parameters

Serum biochemical parameters including calcium, phosphorus, alkaline phosphatase, and total protein remained within normal limits in all animals and did not show significant variation between groups or observation intervals.

This suggests that osteoarthritis does not significantly influence systemic metabolic functions. Similar findings have been reported by Subin (2005), Rausch-Derra *et al.* (2016), Singh (2019), and Varghese (2019) [23, 26, 27, 30].

5.7 Radiographic Findings

Radiographic evaluation of all 16 dogs revealed progressive improvement in joint condition over time in both treatment groups. Changes observed included reduction in osteophyte formation, improvement in joint space, and better joint congruency.

The improvement was more pronounced in Group I animals treated with Pentosan Polysulfate Sodium, indicating its disease-modifying effects on cartilage and joint structures. These findings are in accordance with Suheb *et al.* (2021), Bano *et al.* (2022), Chopade (2024), and Patel *et al.* (2025) [4, 9, 22, 28].

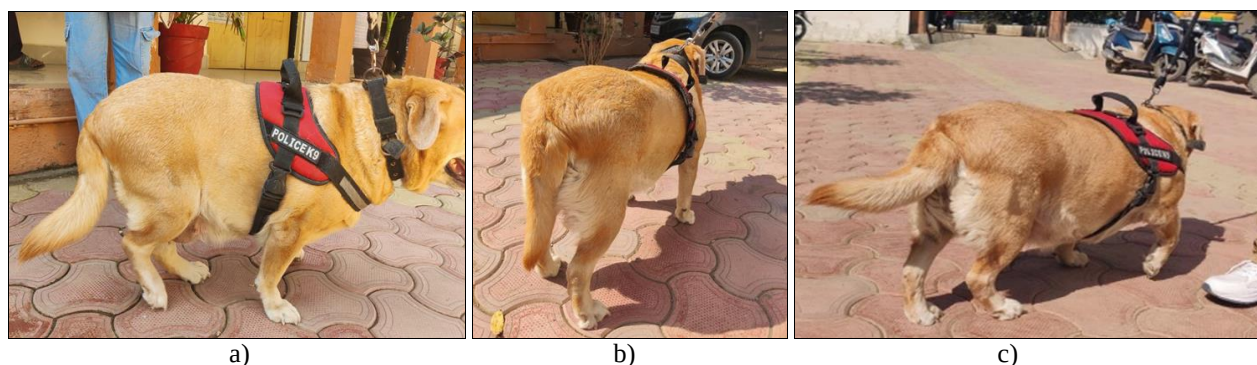


Fig 1: Dogs in Group I manifesting (a) Non-weight bearing while standing and walking (b) Partial weight bearing while standing and walking (c) Equal weight bearing on all limbs while standing and walking

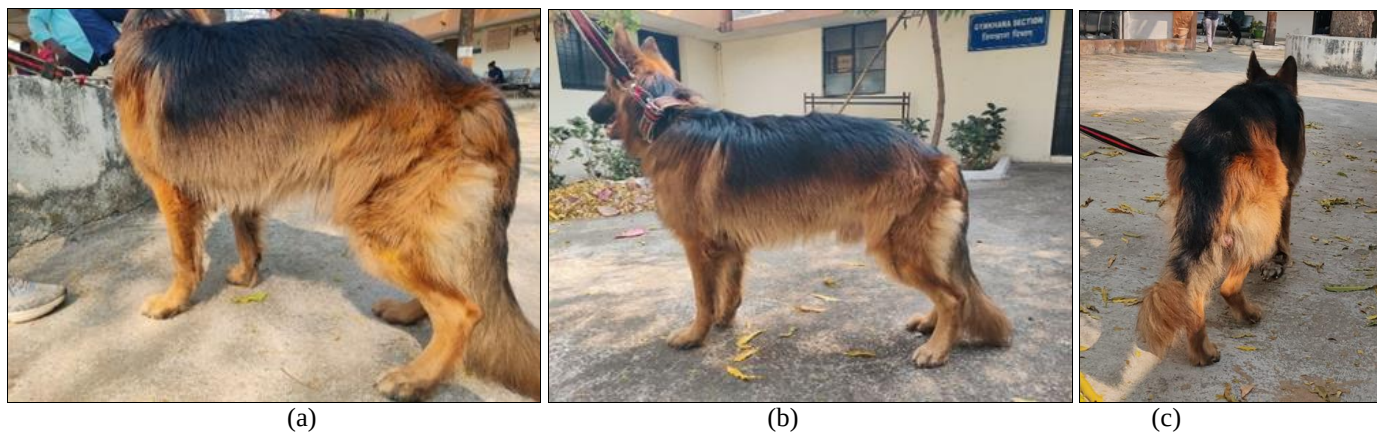
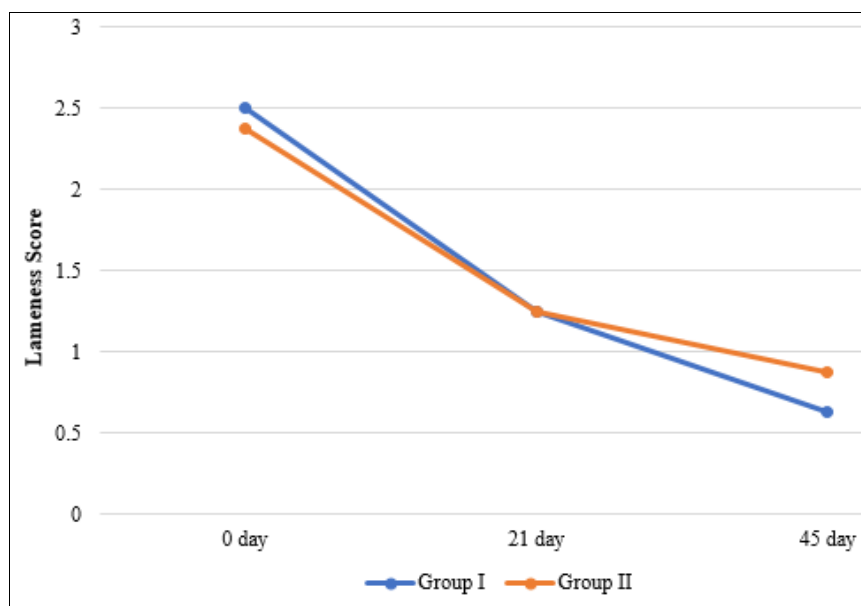
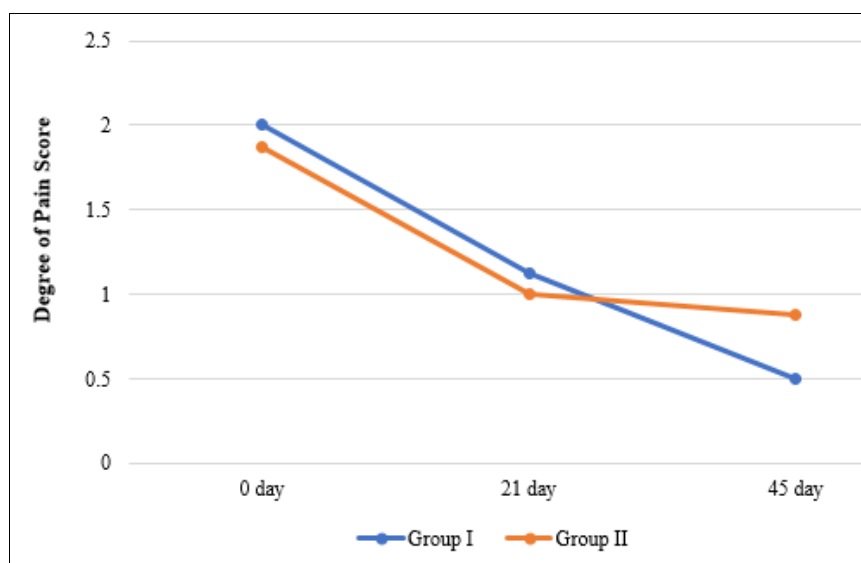


Fig 2: Dogs in Group II manifesting (a) Partial weight while bearing standing and non-weight bearing walking (b) Partial weight bearing standing and walking (c) Favours affected limb when walking



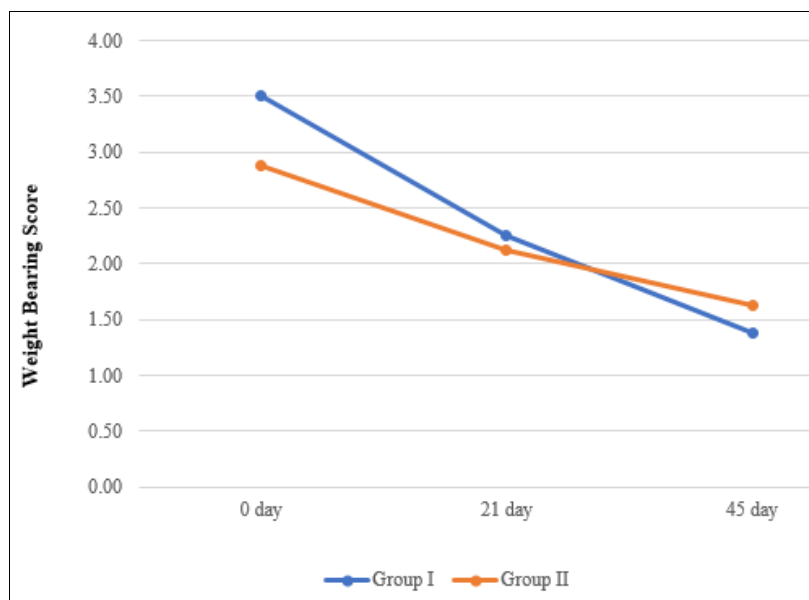
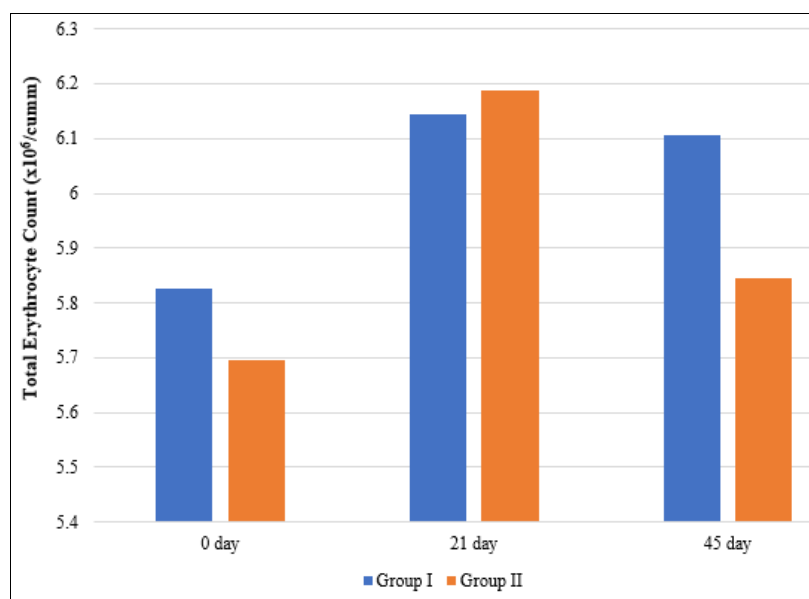
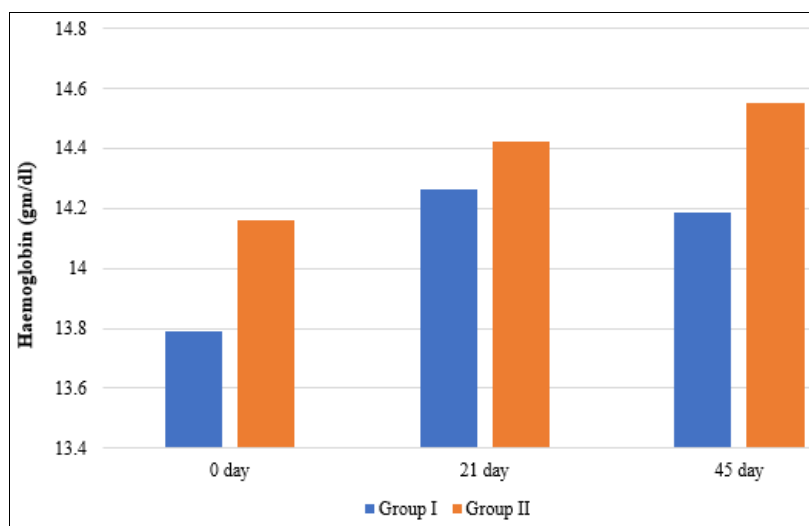
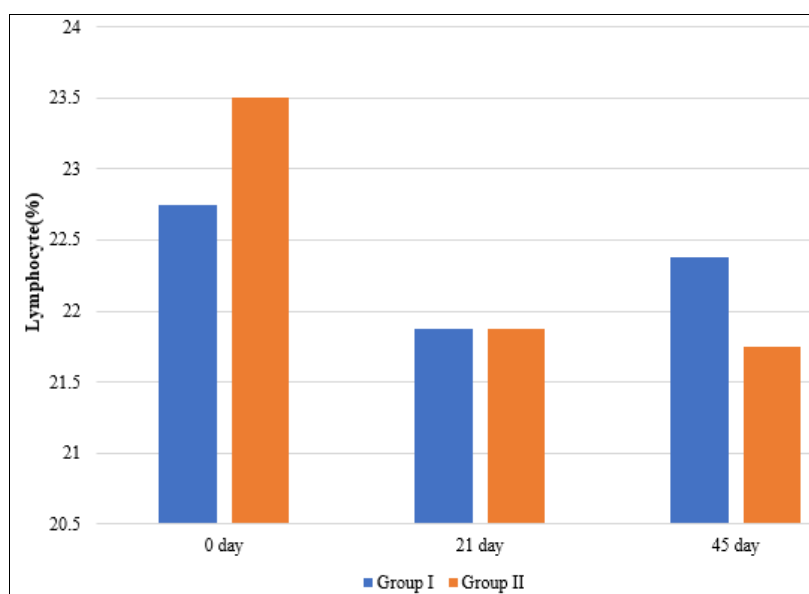
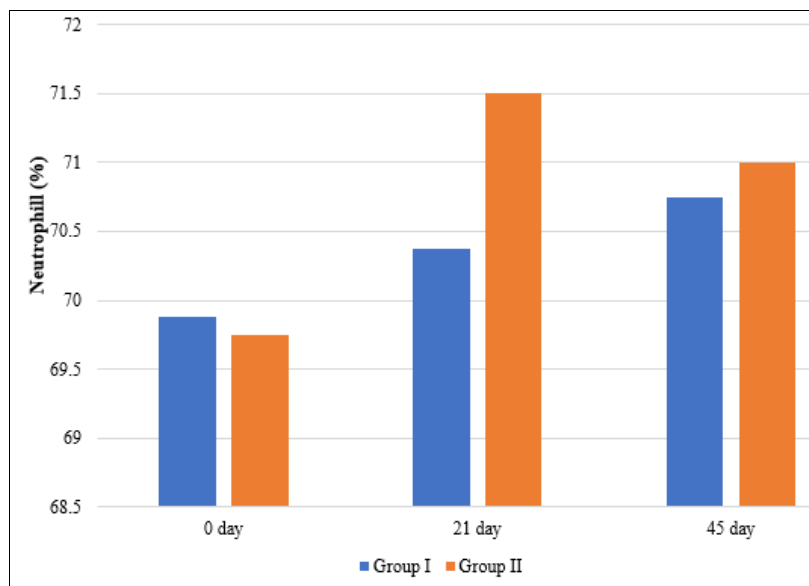
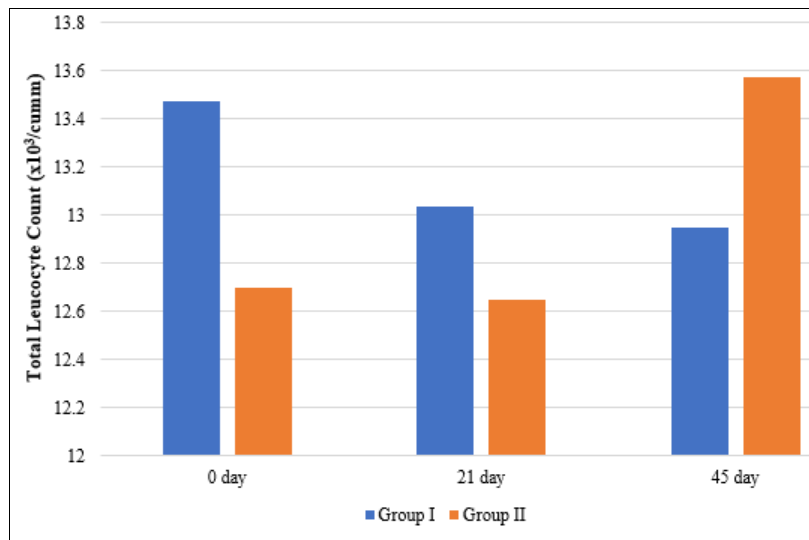


Fig 3: Line graph for the degree of pain, lameness grading score weight-bearing on limbs score





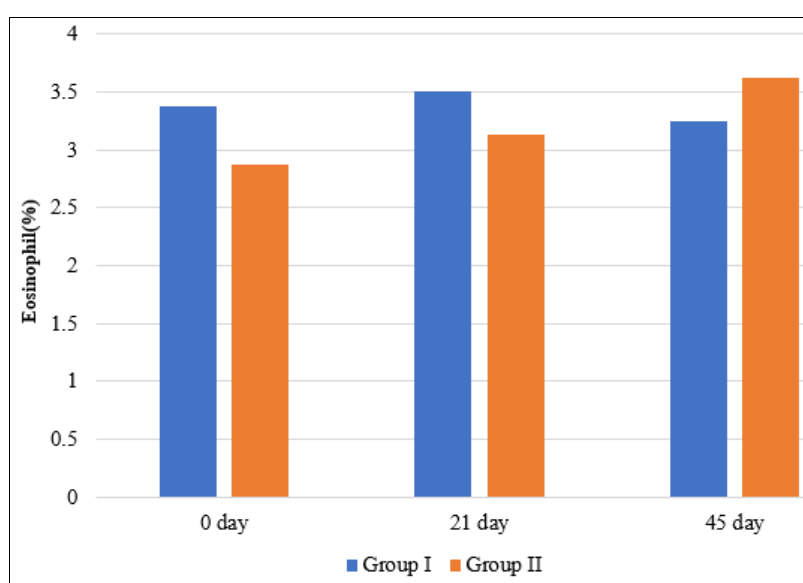
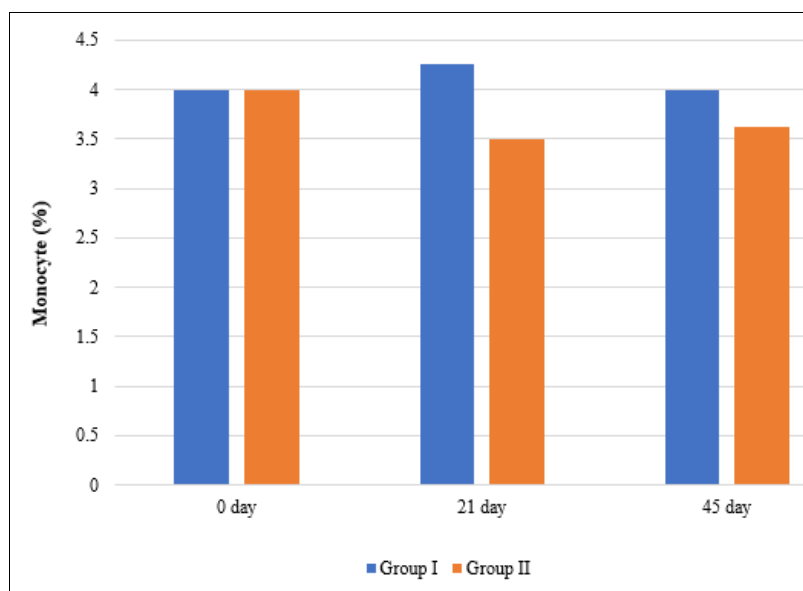
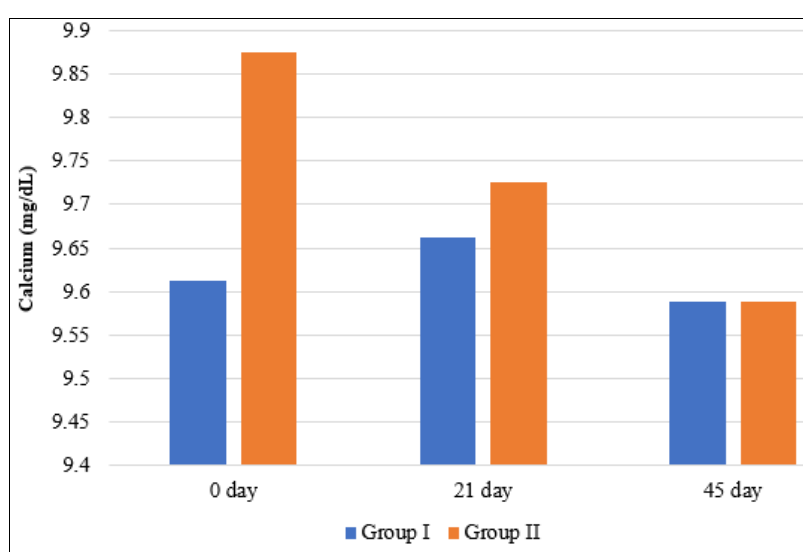


Fig 4: Bar Graphs for the Mean values of Haemoglobin (g/dl), Total Erythrocytic Count (x106/cumm), Total Leucocyte Count (x103/cumm), Neutrophils (%), Lymphocyte (%), Monocyte (%), Eosinophils (%)



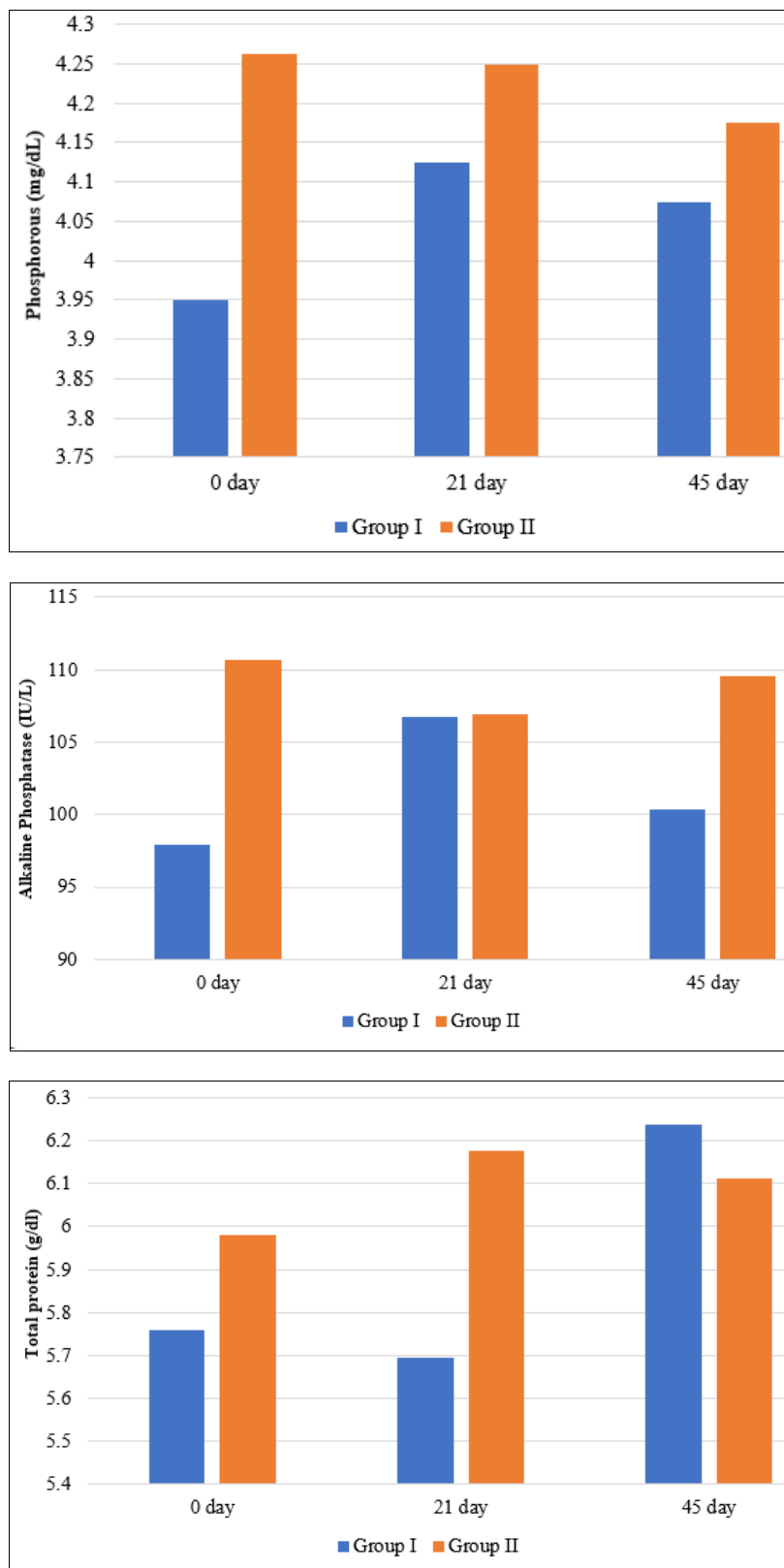


Fig 5: Bar Graphs for the Mean values of Calcium (mg/dl), Phosphorous (mg/dl), Alkaline Phosphatase (IU/L), Total Protein (g/dl)

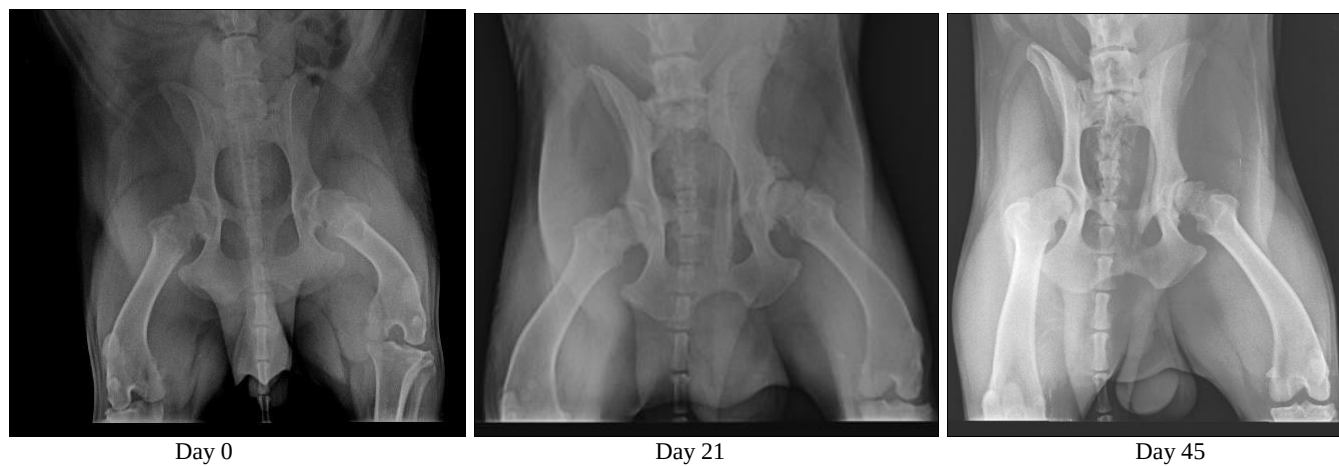


Fig 6: Group I Ventrodorsal view radiograph manifesting changes in radiographic scoring on day 0, day 21 and day 45

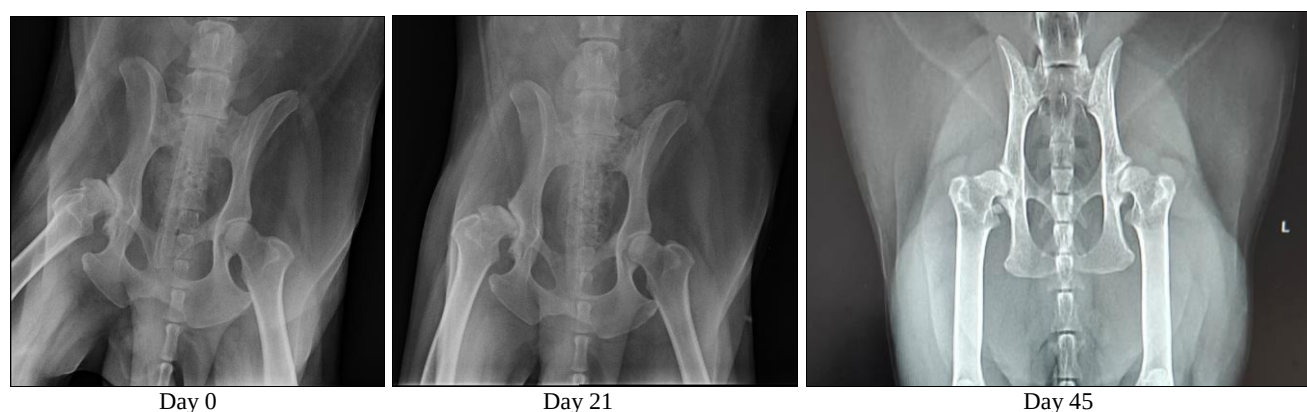


Fig 7: Group II Ventrodorsal view radiograph manifesting changes in radiographic scoring on day 0, day 21 and day 45

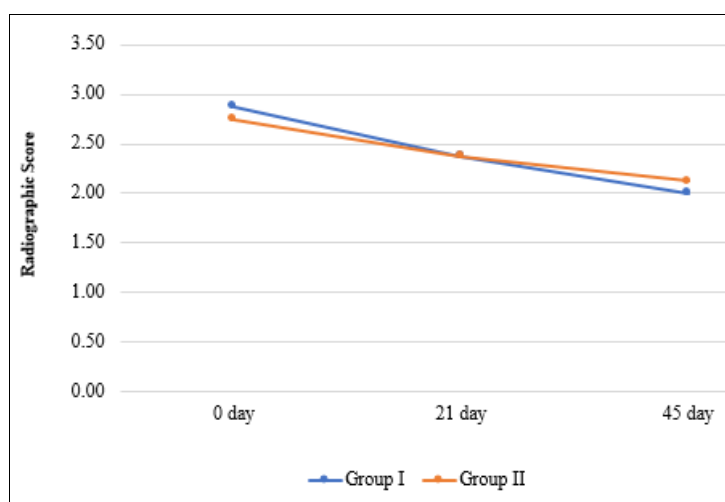


Fig 8: Line graph for Radiographic score

6. Conclusion: The present study establishes that both Pentosan Polysulfate Sodium (PPS) and Grapiprant, administered alongside nutraceutical supplementation (undenatured type-II collagen and omega-3 fatty acids), are clinically effective and safe in the management of canine hip osteoarthritis, as evidenced by significant improvement in pain, lameness, and weight-bearing ability without alterations in physiological, haematological, or biochemical parameters. Comparatively, PPS demonstrated superior and sustained therapeutic efficacy, reflected in greater clinical improvement and more marked radiographic restoration of joint architecture, attributable to its disease-modifying, chondroprotective, and cartilage-regenerative properties. In contrast, Grapiprant primarily provided symptomatic relief via selective EP4 receptor antagonism.

Thus, PPS in combination with nutraceutical support considered a more efficacious therapeutic modality for long-term management of canine hip osteoarthritis.

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8. Conflict of interest

The authors do not have any conflict of interest.

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