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Study the effect of *Malva sylvestris* leaf extract (MSE) against CCl₄-induced nephrotoxicity in a model of male rats

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Abstract

Background: Carbon tetrachloride (CCl₄) is a well-known potent hepatonephrotoxic agent that causes oxidative stress and damage of tissues by producing reactive oxygen species (ROS). *Malva sylvestris* (MSE), the herbal plant of the Malvaceae family, is rich in phenolic and flavonoid compounds. MSE possesses strong antioxidant properties, which makes it effective against the abovementioned types of CCl₄-related nephrotoxicity. This research aimed to investigate the potential of *Malva sylvestris* leaf extract (MSE) against the kidney damage caused by CCl₄ in male rats.

Methods: Twenty-four adult male rats were divided into the following four groups: Control, CCl₄-treated, CCl₄+ MSE (100 mg/kg body weight), CCl₄+ MSE (200 mg/kg body weight). Two weeks of animal administrations were applied. Rats were intoxicated with CCl₄ to develop RF animal models through an intraperitoneal route while orally treated with MSE daily for two weeks. Kidney parameters such as BUN and Creatinine and oxidative stress and antioxidant parameters, such as MDA, SOD, CAT, and GSH, were evaluated in kidney tissue homogenates.

Results: CCl₄ significantly elevated MDA levels and suppressed SOD, CAT, and GSH, meaning severe oxidative stress and lack of antioxidant defense. MSE treatment at both doses strongly defended against these changes and showed a dose-dependent amelioration. It effectively reduced lipid peroxidation and enhanced SOD, CAT, and GSH activity close to the normal standard levels.

Conclusion: The results confirmed the strong nephroprotective effects and the potential of *Malva sylvestris* leaf extract, which coped with CCl₄-caused oxidative damage. MSE through its antioxidant mechanism reestablished the redox equilibrium against oxidative stress in renal tissues.

Keywords: *Malva sylvestris*, nephroprotective, CCl₄, oxidative stress, rats

Introduction

The kidneys, one of the most important organs in the body, are involved in various activities. Some of their activities include the production of urine that is removal of waste from the bloodstream is considered the primary role of the kidney most physicians refer to it as producing urine ^[1]. It aids in maintaining volume, pH, and ionic balance, among other homeostatic activities. In addition, other harmful metabolic byproducts are expelled ^[2]. Nephrotoxicity refers to the manifestation of kidney damage after exposure to drugs, chemicals, or other toxic agents. It is a severe field of concern since it is associated with acute renal failure, which has a significant impact on overall health ^[3]. Oxidative stress is in most cases implicated in the mechanisms of nephrotoxicity since it plays a vital role in the injury of renal cells caused by a range of nephrotoxic agents such as heavy metals and industrial chemicals and aminoglycoside antibiotics ^[4]. The first well-investigated nephrotoxin is CCl₄. CCl₄ acts with the first biochemical response which leads to the biochemical backlash of the cytochrome P450 in a hepatocyte. High reactivity causes injury post the development of acyl-CoA products. The injury developed through the down regulation of enzyme replication, and it initiates cellular apoptosis ^[5]. *Malva sylvestris*, commonly known as common mallow, is native to southern Europe and western Asia. *M sylvestris* is a biennial-to-perennial herbaceous plant from the Malvaceae family ^[6].

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Malva, is a tall herb with broad, heart-shaped, light green leaves that grows 2-3 feet in height. Beautiful purple blossoms that appear to be honeysuckle are produced by the plant. Malva flowers have been bioengineered with a thresher and are used for ME, which have been implicated in creating pharmaceutical agents authentic to microbial infections, colds, trachea, bronchi, beef cavities, salmonella, and general cardiac quarantine [7]. Several pharmacological activities have been conducted on *Malva sylvestris* L. because it possesses diuretic, laxative, expectorant and antitussive traits and is used to treat organ disorders such as diseases of the respiratory and digestive systems. The phytochemicals in *Malva sylvestris* cause it to act as an antioxidant because it counters oxidative stressors and prevents various illnesses, including CKD and diabetes [8]. Because of a wide range of nutrients such as calcium, potassium, magnesium, iron, and vitamins, Malva has been distinguished as a medication for a broad range of disorders [9]. Although traditionally the leaves, flowers, and seeds of the *Malva sylvestris* plant have been used as a healthy food in addition to a dietary problem, they are not as commonly consumed as before. The seeds taste like young hazelnut, while the leaves and young flowers were added to salads [10]. Due to the high quality of the mucilage stock, mallow is frequently used in folk medicine, and their use in other treatments is very common for a variety of reasons, such as for stomatitis and asthmatic bronchitis. Apart from that, *Malva sylvestris* is well-known for its anti-inflammatory, antibacterial, and astringent properties and can be used in the effective treatment of acne, carbuncles, furuncles, insect bites, and eczema, to name but a few [11, 12]. This study was conducted to examine the model of nephroprotection by *Malva sylvestris* leaves on CCl₄-induced renal damage in the rat.

Materials and Methods

Plant Material and Extract: Preparation Leaves of *Malva sylvestris* L. were collected and authenticated from Babylon province, Iraq. The plant leaves were air-dried under shade in ambient temperature for two weeks. After drying, the plant material was grinded and sieved through a fine mesh sieve to obtain the fine powder. The hydro-alcoholic extract of MSE was prepared by macerating Eq. 400 gram powdered leaves in Eq. 800 mL of 70% ethanol for 72 hours. After 72 hours, the extract was filtered and the solvent was evaporated under reduced pressure in the rotary evaporator to get the methanolic extract. The crude methanolic extract was stored at 4 °C in the Refrigerator until further use.

Experimental Animals: Healthy adult male Wistar rats, weighing 180-220 g acclimatized for a period of 7 days before starting orally fed with minimum acclimatization period of 1 week. Animals were kept under controlled condition and maintained under 22±2 °C, 12 hour light/dark cycle at 50-60% humidity. The rats were allowed for food ad libitum and water ad libitum. The experiment was performed after getting approval from the Institutional Animal Ethics Committee in Al-Qasim green university and complied with the national laws related to animal care and use.

Experimental Design

Rats were randomly assigned to five groups, with six animals in each group.

- **Group I (Control):** Received distilled water orally and corn oil intraperitoneally (i.p.) for four weeks.
- **Group II (CCl₄):** Received distilled water orally and CCl₄ (1 ml/kg body weight, 20% CCl₄ in corn oil) i.p. twice a week for four weeks.
- **Group III (CCl₄ + MSE Low Dose):** Received MSE (100 mg/kg body weight) orally once daily and CCl₄ i.p. as in Group II.
- **Group IV (CCl₄ + MSE High Dose):** Received MSE (200 mg/kg body weight) orally once daily and CCl₄ i.p. as in Group II.

Oral treatments commenced one week prior to the first CCl₄ administration and continued throughout the four-week CCl₄ exposure period.

Results

As shown in Table 1, CCl₄ treatment caused a remarkable impairment of renal function as established by the increased levels of BUN and creatinine in serum on Group II when compared to the control treated animals at $p < 0.01$. The mean BUN concentration was 65.2±3.8 mg/dL in CCl₄-treated animals as opposed to 20.1±1.5 mg/dL in control. Also, the level of creatinine reached 1.8±0.1 mg/dL vs. 0.6±0.05 mg/dL in control. The co-treatment of MSE at 100 mg/kg and 200 mg/kg substantially alleviated the levels of group treated animals at $p < 0.05$ and $p < 0.01$, respectively; thus, MSE at 200 mg/kg resulted in 32.5±2.1 mg/dL and 0.9±0.08 mg/dL of BUN and creatinine, respectively.

Table 1: Renal Function Biomarkers (Mean ± SD)

Group	BUN (mg/dL)	Creatinine (mg/dL)
Control (N=6)	20.1±1.5	0.6±0.05
CCl ₄ (N=6)	65.2±3.8*	1.8±0.10*
CCl ₄ + MSE (100 mg/kg.bw), (N=6)	45.6±2.7#†	1.2±0.09#†
CCl ₄ + MSE (N=6) (200 mg/kg.bw)	32.5±2.1#†	0.9±0.08#†

* $p < 0.05$ vs. Control; # $p < 0.05$ vs. CCl₄; † $p < 0.05$ vs. CCl₄+MSE extract

Exposure to CCl₄ results in a significant increase in renal tissue MDA content, a biomarker of lipid peroxidation, in Group II. It reached 15.3±1.1 nmol/mg protein compared to the control group. The activities of endogenous antioxidant enzymes, SOD, CAT, and the level of GSH were significantly reduced in the CCl₄ group compared to controls. The treatment with MSE resulted in a dose-dependent attenuation of the MDA increase and normalization of antioxidant enzymes activities and GSH levels. The 200 mg/kg MSE dose reduced MDA to 6.1±0.5 nmol/mg protein, increased SOD 39.5±2.8 U/mg protein, CAT 59.2±3.9 U/mg protein, and GS H 4.1±0.2 μmol/g tissue significant and demonstrated antioxidant action (Table 2).

Table 2: Oxidative stress and antioxidant parameters (Mean ± SD)

Group	MDA (nmol/mg protein)	SOD (U/mg protein)	CAT (U/mg protein)	GSH (μmol/g tissue)
Control (N=6)	4.2±0.3	45.1±3.5	68.9±4.3	4.8±0.3
CCl ₄ (N=6)	15.3±1.1 *	15.8±1.2*	28.5±2.1*	1.5±0.1*
CCl ₄ + MSE (100 mg/kg.bw) (N=6)	8.9±0.7 #†	32.4±2.6#†	48.1±3.5#†	3.2±0.2#†
CCl ₄ + MSE (100 mg/kg.bw) (N=6)	6.1±0.5 #†	39.5±2.8#†	59.2±3.9#†	4.1±0.2#†

* $p < 0.05$ vs. Control; # $p < 0.05$ vs. CCl₄; † $p < 0.05$ vs. CCl₄+MS extract

Figure 1 shows the impact of CCl₄ induced oxidative stress and MSE-mediated intervention, at two different doses MSE-100 mg/kg and MSE-200 mg/kg of body weight, on the various oxidative stress-related biochemical markers of antioxidative defense in tissue samples. The levels of MDA, a measure of lipid peroxidation, were significantly elevated in the CCl₄ treated group, implying elevated oxidative damage. MSE treatment significantly decreased MDA levels, suggesting reduced lipid peroxidation. The lowered SOD and CAT activities that are significantly lower in the CCl₄ group were an indication of oxidative stress-induced enzyme

inactivation. MSE treatment resulted in the resumption of enzyme activity at or near control levels, with this effect was greater at a dose of 200 mg/kg. A drastic reduction in GSH level was observed after CCl₄ exposure. MSE treatment demonstrated a marked increase in the GSH level as compared to the CCl₄ group. CCl₄ exposure resulted in substantial oxidative imbalance. Still, MSE treatment led to a dose-dependent mitigation as the enzymatic and non-enzymatic components of antioxidative defense system; SOD, CAT and GSH levels were restored, while lipid peroxidation was lowered.

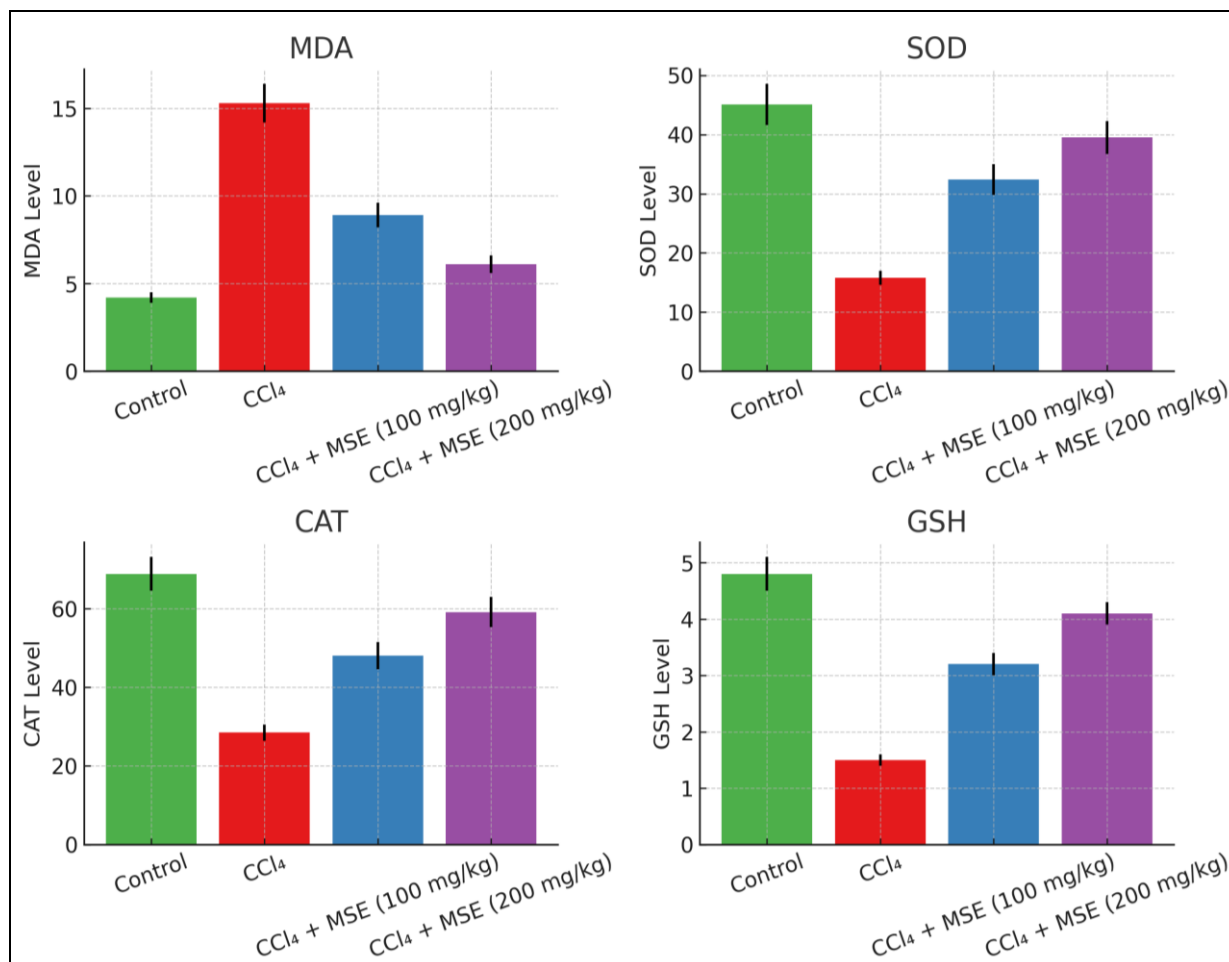


Fig 1: Oxidative Stress and Antioxidant Parameters (Mean $\pm$ SD) in different experimental groups

As shown in Figure 2, kidney sections from the CCl₄-treated group had significant histopathological disturbances in the cortex and medulla with tubular necrosis, vacuolar degeneration of epithelial cells, and an extremely dense inflammatory cell presence indicative of acute renal injury. In marked contrast, kidney sections from the MSE-treated group maintained the normal histology of renal tissue, and minimal inflammatory cellular background was seen which suggests that the MSE possessed a protective effect against CCl₄-induced nephrotoxicity. The MSE-treated and NC groups showed approximately normal histologic architecture with minor changes. The MSE possessed nephroprotective activity due to its anti-inflammatory and antioxidant efficacy, which is in accordance with the biochemical examinations.

Discussion

In this experiment, the protective impact of *Malva sylvestris* leaf extract on CCl₄-induced nephrotoxicity in male rats was

investigated. The results revealed that CCl₄-induced toxicity cause significant renal dysfunction, as exhibited by elevated BUN and serum creatinine, increased lipid peroxidation, and decreased activity of renal endogenous enzymatic and non-enzymatic antioxidant defense mechanisms like SOD, CAT, and GSH levels [13]. It is consistent with past findings that CCl₄-induced nephrotoxicity by the generation of ROS and trichloromethyl radicals and thus causing lipid peroxidation and oxidative damage. Overall, administration of MSE markedly reversed these derangements in a dose-dependent manner, indicating an antioxidant-mediated nephroprotective effect.

The extract particularly at 200 mg/kg produced a remarkable reduction in renal biomarkers, MDA concentration, and an increase in the levels SOD, CAT, and the GSH. It demonstrates that MSE could prevent oxidative stress and enhance the ability of the kidney antioxidant defense system to reduce cellular damages by free radicals [14].

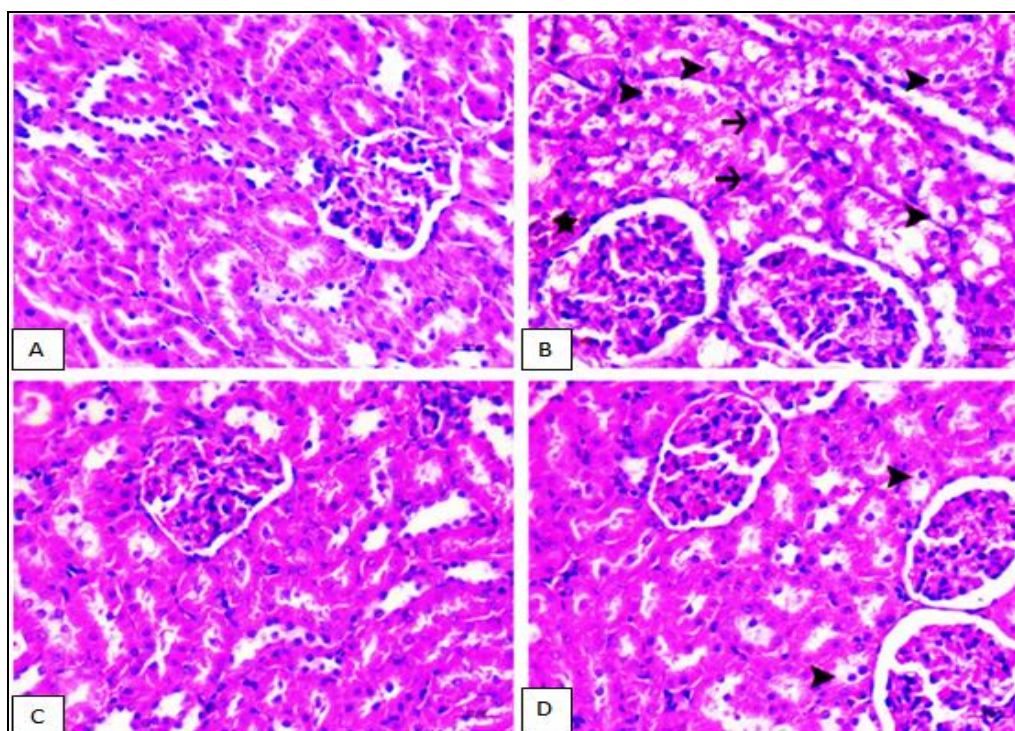


Fig 2: Histopathological analysis of kidney tissues of rats (H&E staining) MSE ameliorated *Malva sylvestris* extract (MSE) renal effect, Representative photomicrographs of kidney sections. Group A, control group, presents normal glomerular and tubular sensitivity. Group B, treated with CCl₄, diagnosis is confirmed by marked tubular necrosis, epithelial cell degeneration and dense inflammatory infiltration, and all signs of acute sensitization appearance. Group E, treated with the MSE "Dose 100 mg/kg", the impact shows a slight reduction in structural incontinence and inflammation. Group H, treated with MSE "Dose 200 mg/kg" and diagnosis are confirmed by normal structural sensitivity, leader-responsive glomeruli and tubules, minimal expression of inflammatory cells. These morphological aggregates are supportive of MSE nephroprotective action, in support of antioxidant and anti-inflammatory activity

The antiradical activity of *M. sylvestris* can be justified by its remarkable amounts of flavonoids and phenolic acids and polysaccharides, which demonstrate radical scavenging in addition to metal binding activities. Similar antioxidant and somatoprotective effects of *M. sylvestris* have been confirmed in hepatic and renal toxicity models [15]. MSE bioactive components like quercetin, kaempferol, and gallic acid might have contributed to the stabilization of cellular membrane integrity and thus the conservation of enzymatic tissues antioxidant defense systems. Furthermore, it was found to cause a significant decrease in lipid peroxidation, representing an inhibition of the peroxy radical chain during reduction within the renal tissues [16]. The increased level of SOD and CAT shows the activation and protection of the two critical antioxidant enzymes against inactivation by oxidation by MSE administrations. Moreover, the raised content in GSH revealed a reinvigorated redox balance because it detoxifies hydrogen peroxide and lipid hydroperoxides [17]. Therefore, all parameters suggest that the extract could reinstate the oxidative balance in the treated kidney. These results supported the previous reports that natural antioxidants may provide substantial nephroprotection from chemically induced oxidative damage. CCl₄-mediated nephrotoxicity has been studied as a model of oxidative stress-mediated nephropathy [18, 19]. This structural confirmation of MSE's protective effect was extended by histopathological analysis. In the CCl₄ group, the kidneys presented severe architectural damage, marked by tubular and outer medulla necrosis, and inflammatory cell infiltration, indicative of acute renal injury. It is clear that administration of MSE before CCl₄ exposure significantly reduced the severity of lesions observed in the CCl₄ groups. Renal tubular and glomerular architecture was relatively well preserved and differences were observed. These structural improvements reinforced the biochemical

findings and suggested that MSE protect cellular and tissue integrity when imitating toxic attack. The reduction in the entrance of inflammatory cells into the kidney may be due to the anti-inflammatory impact of MSE, whether direct or indirect. MSE may also reduce inflammatory cell filtration by reducing the expression of cytokines due to its anti-inflammatory effect. The fact that MSE protects the nephron from oxidative attack means that it can be used as a supplement or prophylactic measure for the treatment of kidney oxidative pathologies.

Conclusion

To conclude, it can be inferred that *Malva sylvestris* leaf extract reversed CCl₄-induced oxidative renal damage, and it exerted a marked nephroprotective and antioxidant effect against rats. It substantially restored the most quantitatively important renal function and levels of activity of antioxidant enzymes and diminished the levels of lipid peroxidation in a dose-dependent effect of CCl₄. The results further imply that *M. sylvestris* has an ability to attenuate oxidative stress via the enhancement of endogenous antioxidants generated by antioxidants and preserving renal cellular integrity. This conclusion suggests that it can be used in future studies to isolate active ingredients, or even complete analysis of the molecular pathway as a nephroprotective remedy.

Conflict of Interest

Not available

Financial Support

Not available

Reference

1. Aiello SE, Mays A. The Merck Veterinary Manual.

- Whitehouse Station, NJ: Merck & Co. Inc.; 1998, p. 2032-2033.
2. Ajadi RA, Adebisi AA, Otesile EB, Kasali OB. Erythrocyte sedimentation rates and leukogram changes in canine model of osteoarthritis. *Niger J Physiol Sci.* 2018;33(1):105-108.
 3. Allen MJ, Hoffmann WE, Richardson DC, Breur GJ. Serum markers of bone metabolism in dogs. *Am J Vet Res.* 1998;59:250-254.
 4. Arens S, Schlegel U, Printzen G, Ziegler WJ, Perren SM, Hansis M. Influence of materials for fixation implants on local infection: an experimental study of steel versus titanium DCP in rabbits. *J Bone Joint Surg.* 1996;78(4):647-651.
 5. Beale B. Orthopedic clinical techniques: femur fracture repair. *Clin Tech Small Anim Pract.* 2004;19:134-50.
 6. Bhavani DS, Krishna NH, Sreenu M, Venkata G. Evaluation of biochemical parameters for assessment of long bone fracture healing in young dogs subjected to bone plating. *Pharma Innov J.* 2022;11(7S):642-644.
 7. Breur GJ, Allen MJ, Carlson SJ, Richardson DC. Markers of bone metabolism in dog breeds of different size. *Res Vet Sci.* 2004;76(1):53-5.
 8. Chaurasia A, Jawre S, Singh R, Shahi A, Pathak R, Das B, *et al.* Evaluation of haemato-biochemical parameters using different biomaterials in fracture healing of dogs. *Int J Curr Microbiol Appl Sci.* 2019;8(5):2265-71.
 9. Chhatrola M, Marvania N, Fefar D. Evaluation of minimally invasive plate osteosynthesis for long bone fractures in dogs. *Pharma Innov J.* 2022;11(11):938-41.
 10. Gadallah S, Marzok M, El-Husseiny I. Studies on some complications of long bone fracture repairs in dogs. *Kafrelsheikh Vet Med J.* 2009;7(1):314-36.
 11. Golish SR, Mihalko WM. Principles of biomechanics and biomaterials in orthopaedic surgery. *J Bone Joint Surg.* 2011;93(2):207-12.
 12. Hayashi K, Schulz KS, Fossum TW. Principles of fracture diagnosis and management. In: Fossum TW, editor. *Textbook of Small Animal Surgery.* 5th Ed. Missouri: Elsevier Health Sciences; 2019, p. 976-1025.
 13. Hegde Y, Dilipkumar D, Usturge S. Comparative evaluation of biochemical parameters during fracture healing in dogs. *Karnataka J Agric Sci.* 2007;20(3):694-695.
 14. Komnenou A, Karayannopoulou M, Polizopoulou ZS, Constantinidis TC, Dessiris A. Correlation of serum alkaline phosphatase activity with the healing process of long bone fractures in dogs. *Vet Clin Pathol.* 2005;34(1):35-38.
 15. Kumar V, Varshney AC, Singh M, Sharma SK, Nigam JM. Haemato-biochemical changes during fracture repair with hydroxyapatite-fibrillar collagen implants in calves. *Indian J Vet Surg.* 1999;20(2):92-93.
 16. Mahendra AM, Ranganath L, Vasanth MS. Effects of polymethacrylate in femoral fracture repair on haemato-biochemical parameters in dogs. *Indian Vet J.* 2007;84:587-589.
 17. Maiti BK, Sen TB, Singh B, Sanki S. Haemato-biochemical changes following application of Ilizarov technique in treatment of femur fracture in dogs. *Indian J Anim Health.* 1999;38:133-134.
 18. Niinomi M. Titanium-based biomaterials, the ultimate choice for orthopaedic implants-a review. *Metall Mater Trans.* 2002;32:477-486.
 19. Patil M, Dilipkumar D, Shivaprakash BV, Kasaralikal VR, Tikare VP, Ramesh BK. Physiological and haemato-biochemical changes during repair of femur fracture in dogs. *Pharma Innov J.* 2017;6(8):381.
 20. Phaneendra MSSV, Lakshmi ND, Raghunath M, Raju NKB, Adilaxmamma K. Evaluation of biochemical and haematological parameters for assessment of compound fracture healing in dogs with local antibiotic treatment. *Int J Livest Res.* 2018;8(4):138-143.
 21. Rani RU, Ganesh TN. Study of serum calcium, phosphorus and alkaline phosphatase during fracture healing of femur in goats. *Indian Vet J.* 2003;80(4):377-378.
 22. Reddy KJM, Dilipkumar D, Sekhar CEL, Srikanth Kulkarni, Kumar VM, Dhoolappa M. Clinical study on the use of titanium dynamic compression plate (Ti-DCP) for repair of femur fractures in dogs. *Pharma Innov J.* 2020;9(12S):8-18.
 23. Reddy KJM, Dilipkumar D, Sekhar CEL, Srikanth Kulkarni, Kumar VM, Dhoolappa M. Evaluation of haemato-biochemical parameters in repair of femoral fractures using titanium implants of intramedullary interlocking nail, dynamic compression plate and locking compression plate in dogs. *J Exp Zool.* 2021;24(1):223-6.
 24. Rudd RG, Whitehair JG. Fractures of the radius and ulna. *Vet Clin North Am Small Anim Pract.* 1992;22(1):135-48.
 25. Sastry GA. *Veterinary Clinical Pathology.* Delhi: CBS Publishers and Distributors; 1989, p. 1-25.
 26. Schalm OW, Jain NC, Carrol EJ. *Veterinary Haematology.* 3rd Ed. Philadelphia: Lea and Febiger; 1975, p. 807.
 27. Tembhurne RD, Gahlod BM, Dhakate MS, Akhare SB, Upadhye SV, Bawaskar SS. Management of femoral fracture with the use of horn peg in canine. *Vet World.* 2010;3(1):37-41.
 28. Toth C, Klarik Z, Kiss F, Toth E, Hargitai Z, Nemeth N. Early postoperative changes in hematological, erythrocyte aggregation and blood coagulation parameters after unilateral implantation of polytetrafluoroethylene vascular graft in the femoral artery of beagle dogs. *Acta Cir Bras.* 2014;29:320-327.
 29. Uhthoff HK, Bardos DI, Kiar LM. The advantages of titanium alloy over stainless steel plates for the internal fixation of fractures: An experimental study in dogs. *J Bone Joint Surg.* 1981;63(3):427-484.

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