P-ISSN: 2410-8863
E-ISSN:2958-6178
https://djvs.uodiyala.edu.iq
Pages: 1-10

Diyala Journal for Veterinary Sciences
Vol. 3 No.2 June (2025)

https://doi.org/10.71375/djvs.2025.03201

Amelioration of anti-inflammatory properties of Acetaminophen by Agmatine sulphate

Mahaba S. M. Zwelef [1], Nibras N. A. Alabbas [2]
ORCID [1]: 0009-0007-1278-1528, **ORCID [2]:** 0000-0002-5541-9277
Department of Physiology, Biochemistry and Pharmacology, College of Veterinary Medicine, University of Baghdad, Iraq
Corresponding Email: mahaba.salah1400a@covm.uobaghdad.edu.iq

Important dates: **Received:** April 03, 2025; **Accepted:** May 28, 2025; **Published**: June 01, 2025

Abstract:

Background: The management of inflammatory conditions like gout arthritis often involves acetaminophen for pain relief, though its anti-inflammatory efficacy is limited. Agmatine sulfate has been shown to potentially enhance the anti-inflammatory properties of acetaminophen, offering a promising approach to improving treatment outcomes for gout patients. Forty male wister albino rats, were used in this study and divided into five groups (n= 8 rats/group) and orally administered with the followings: Group 1 received 1000mg/kg of agmatine sulphate; Group 2 received 1000mg/kg of acetaminophen; Group 3 animals were co-administered with 900mg/kg of acetaminophen and 100mg/kg of agmatine sulphate, respectively; Group 4 rats were co-administered with 700mg/kg of acetaminophen and 300mg/kg of agmatine sulphate, respectively. Group 5 is co-administered with acetaminophen (500mg/kg) and agmatine sulphate (500mg/kg), respectively.

Aims: The present study was conducted to investigate the anti-inflammatory effect of acetaminophen (using various doses of acetaminophen-agmatine sulphate combination) against gouty arthritis induced by monosodium urate crystals in male rats.

Results: This study found that all gouty arthritis treated groups had significantly low levels ($P<0.05$) of white blood cells and visual weight-bearing test. Haemoglobin and red blood cell counts in groups 4 and group 5 demonstrated high significant values ($P<0.05$). Joint stiffness in groups 1 and group 5 were significantly decreased ($P<0.05$). Conversely, mobility test exhibited the high significant score ($P<0.05$) in all groups. Erythrocyte sedimentation rate exhibited a substantial decrease ($P<0.05$) in groups 4 and group 5.

Conclusions:Overall, this study indicated that agmatine enhances the therapeutic profile of acetaminophen as mild anti-inflammatory agent when given as combination

P-ISSN: 2410-8863
E-ISSN:2958-6178
https://djvs.uodiyala.edu.iq
Pages: 1-10

Diyala Journal for Veterinary Sciences
Vol. 3 No.2 June (2025)

https://doi.org/10.71375/djvs.2025.03201

Keywords: Agmatine sulphate, gout arthritis, anti-inflammatory

Introduction:

Gouty arthritis (GA), caused by disorder resulting from disturbance in urine metabolism (Chi *et al*., 2020), It was regarded as one of the most wide spreading chronic health issues (Hasan, 2014). It is primarily driven by increased uric acid production (QassimHosein *et al*., 2016), often exacerbated by acute and chronic inflammation and tissue injury (Zhao *et al.*, 2024), The clinical manifestations of acute gouty arthritis are abrupt, marked by redness, swelling, hyperthermia, stiffness, pain, and impairment of the afflicted joint and adjacent tissues (Abduljaleel *et al.*, 2023; Singh & Gaffo, 2020), and inflammatory cells causes a purulent effusion, leading to cartilage destruction and increased joint pressure (Al-Awadi, 2014). The individual is experiencing significant discomfort (ALQAYSI & ALABBAS, 2024), and can be treated with non-steroidal like ibuprofen and paracetamol (Hazlewood *et al.*, 2012; Mahmood, 2024). Acetaminophen (paracetamol; N-acetyl-p-aminophenol) (Al-Abachi *et al*., 2008) is the active metabolite of phenacetin (Hamad, 2016).

Paracetamol can be administered orally, rectally, and intravenously, also it can be give alone or co-administered with other drugs (Sharma & Mehta, 2014). Paracetamol is among the most widely prescribed drugs worldwide (Al-Rekabi *et al.*, 2009). It can be converted to a reactive metabolite called N-acetyl-p-benzoquinone imine (NAPQI), NAPQI is synthesised in the liver by the cytochrome P-450 isoform (Hameed & Hassan, 2023). Paracetamol is promptly absorbed by all tissues, at therapeutic concentrations, protein binding is minimal, and the half-life (t1/2) of paracetamol in healthy individuals lies between 2 and 2.5 hours (Al-Rekabi & Alrobyrai, 2024). It is eliminated through urine (Hameed & Hassan, 2022). After removing the chemicals that trigger an immune response, it is crucial to reduce inflammation to prevent further damage and the development of autoimmune diseases like multiple sclerosis, rheumatoid arthritis, Crohn's disease, psoriatic arthritis, and systemic lupus erythematosus (Fahd & Saliem, 2024).

Agmatine was discovered in 1910 by Nobel Laureate Albrecht Kossel and it was identified in herring sperm, resulting from the decarboxylation of arginine by arginine decarboxylase, which produces the polyamine aspartate, agmatine is predominantly conserved across nature and is produced by bacteria, plants, and invertebrates (Saha *et al*., 2023). Arginine is amino acids are essential for building the body (Atiyah, 2025). Agmatine is an inhibitor of nitric oxide synthase (NOS) and possesses anti-inflammatory and antioxidant properties, in vivo and in vitro investigations have shown that it inhibits fibroblast proliferation and reduces the release of inflammatory cytokines such as TNF-α and

P-ISSN: 2410-8863
E-ISSN:2958-6178
https://djvs.uodiyala.edu.iq
Pages: 1-10

Diyala Journal for Veterinary Sciences
Vol. 3 No.2 June (2025)
https://doi.org/10.71375/djvs.2025.03201

IL-6. Due to its biochemical and antioxidant properties, it can repair localised tissue damage and systemic problems (Yeniçeri *et al*., 2024). The purpose of this study was to determine the optimal dose of acetaminophen and agmatine sulphate to reduce inflammation in gout ilness patients.

Materials and Methods:

Experimental Animals

Forty male albino rats (225g ±2.4g, two months old) were utilized in this study. Rats were in placed in plastic cages (60*40*20cm) and housed in the laboratory animal facility for two weeks for acclimatization before running any experiment. Distilled water and common rodent food (commercial feed pellets) were also freely accessible.

Experimental Design

The rats were randomly divided into five different groups (labelled G1 to G5, eight rats in each group) according to orally treated with the following drugs: Group (G1) administered with agmatine sulphate (1000mg/kg); Group (G2) received only acetaminophen (1000mg/kg); Group (G3) is co-administered with acetaminophen (900mg/kg) and agmatine sulphate (100mg/kg), respectively; Group (G4) received acetaminophen (700mg/kg) plus agmatine sulphate (300mg/kg), respectively; Group (G5) is co-administered with acetaminophen (500mg/kg) plus agmatine (500mg/kg), respectively.

Induction of gouty arthritis

Acute and intense joint discomfort will be caused by subcutaneous injections of monosodium urate (MSU) at 1 mg per 0.1 ml into 32 male rats' ankle joints. Urate crystals were obtained by dissolving 1g uric acid in 200ml boiling water with 6ml 1N NaOH. The pH was maintained (7.2) by the addition of HCl to the solution. After cooling and stirring at room temperature, the solution was stored overnight at 5 °C. Then, filtration process was performed to remove any undissolved particles from the solution. The solution was then filtered via a 250-micrometre wire mesh after light heat drying. 0.9% saline and 10% Tween 80 was added to the solution. Before injection, rats were sedated with chloroform before injection (Lee *et al*., 2013).

Evaluation of gouty arthritis

Grading system of joint stiffness was used to assess gouty arthritis. Score 2 shows limited ankle bending and extension, 1 no limitation, and 0 none. During mobility testing, Scores: 6= animal walks normally, 5= ipsilateral hind paw fully touches floor, 4= only toe touches floor, 3= contralateral paw and floor fully touches, 2= only toe touches floor. 1= animal crawls using forelimbs, 0= no movement. Weight-bearing visual test: zero—normal paw pressure, equal hind weight normal paw pressure, floor paw, unequal hind toes. Scoring 1: floor paw, little lessened pressure, no toes spread. 1.5= midway paw pressure reduction, 1-2. Score 2: Curled paw almost touching floor Score 2.25=

P-ISSN: 2410-8863
E-ISSN:2958-6178
https://djvs.uodiyala.edu.iq
Pages: 1-10

Diyala Journal for Veterinary Sciences
Vol. 3 No.2 June (2025)
https://doi.org/10.71375/djvs.2025.03201

lightly curled, rarely contacts floor, moderate paw pressure Score 2.5= gentle curled paw with intermittent floor contact, 2.75 = gentle curling, low-pressure, limited floor contact. Score 3: Fully lifted paw, significant pressure decrease.

Statistical Analysis

The statistical analysis system (SAS, 2018) was used to detect the effects of different factors on the study parameters. The least significant difference (LSD) test was used to compare means significantly (One-way and Two-way ANOVA) in this study.

Ethical approval

All laboratory animals used in this study were approved by The Scientific Committee of the College of Veterinary Medicine, University of Baghdad in compliance with the ethical principles guidelines on the care and use of animals in research (P.G.300- 11/2/2024) of animal welfare.

Results:

Effects of agmatine sulphate and paracetamol on blood parameters (WBC, HB, RBC and ESR) in arthritic rats.

The results of this study indicated that gout-inducted groups had higher value of WBC and ESR levels, and had lower levels of HB and RBC in comparison to the other groups as shown in table 1. All groups of treatment showed no significant differences in WBC analysis, but showed significant decrease ($P \leq 0.05$) in WBC when compared with induction group (28.048±1.63), as seen in table 1. On other hand, haemoglobin level in G 5 had highest significant value (16.68 ±0.73) among all groups. Also, G4 had no significant differences when compared with G5 but was still higher than other groups. G2 showed significant decrease ($P \leq 0.01$) in value (15.34 ±0.82) compared with G4 and G5 (table 1). Haemoglobin (14.36 ±0.76), (14.32 ±0.69) concentration was significantly decreased in G1, G3 in comparison with other control and treated groups. Additionally, red blood cells in G2, G4 and G5 had lowest values in comparison with control group. whereas G1 had lower value, (6.820 ±0.21) compared with control and G2, G4, G5 groups as shown in table 1. G3 had highest significant ($P \leq 0.01$) value compared with other treated groups. In erythrocyte sedimentation rate, the gout induction group had the highest significant ($P \leq 0.01$) value in comparison with control group (22.4±2.08). G5 had lowest significant value (3.6 ±0.18) compared with all treated groups. On the other hand, G4 had also lower significant value (5.0±0.27) compared with control group and G5 (3.92±0.14) and (3.6±0.18). G3 had lower significant value (7.4±0.42) comparison with control group, G5 and G4, as seen in table 1. Finally, G1 and G2 had highest significant value when compared with all other treated groups and control (table 1).

P-ISSN: 2410-8863
E-ISSN:2958-6178
https://djvs.uodiyala.edu.iq
Pages: 1-10

Diyala Journal for Veterinary Sciences
Vol. 3 No.2 June (2025)

https://doi.org/10.71375/djvs.2025.03201

Table (1): Effect of acetaminophen-agmatine sulphate co-administration in different doses in blood picture (WBC, HB, RBC and ESR).

Groups of rats	WBC 10^9 /1	HB g/dl	RBC 10^{12}/l	(E.S.R.) mm/hr
Control	7.684 ±0.52 c	15.32 ±0.74 bc	6.582 ±0.46 c	3.92 ±0.14 d
Induction	28.048±1.63 a	13.69 ±0.61 d	5.158 ±0.32 d	22.4 ±2.08 a
G1	15.506±0.74 b	14.36 ±0.76 cd	6.820 ±0.51 bc	8.4 ±0.58 b
G2	18.058±1.03 b	15.34 ±0.82 bc	7.458 ±0.48 ab	8.2 ±0.61 b
G3	17.78 ±0.83 b	14.32 ±0.69 cd	5.702 ±0.43 d	7.4 ±0.42 bc
G4	16.828±0.71 b	16.46 ±0.85 ab	7.714 ±0.55 a	5.0 ±0.27 cd
G5	15.656±0.79 b	16.68 ±0.73 a	7.808 ±0.48 a	3.6 ±0.18 d
LSD value	3.894	1.287	0.784	3.081
Means having with the different letters in same column differed significantly.				*** (P≤0.05). **(P≤0.01).**

The high level of WBC in arthritic rats referred to stimulation of the immune system against invading pathogenic microorganisms. Also, the elevated erythrocyte sedimentation rate (ESR) in arthritic rats provides valuable insights on the prolonged duration and intensity of the disease. This results fall in line with (Patel & Pundarikakshudu, 2016). Agmatine sulphate may mitigate white blood cell activity and inflammation in gout patients by inhibiting the synthesis of pro-inflammatory cytokines, which are signalling molecules that facilitate inflammation (Dakkak & Lanney, 2021). Several studies indicate that paracetamol may block the enzyme myeloperoxidase, which plays a role in the synthesis of inflammatory oxidants. This inhibition may contribute to its moderate anti-inflammatory properties and reduce the inflammatory mediators (Graham *et al*., 2013; Ohashi & Kohno, 2020; Sharma & Mehta, 2014). On the other hand, a higher erythrocyte sedimentation rate is linked to an increase in the synthesis of endogenous proteins, including fibrinogen and α/β globulin However, agmatine sulphate which may indirectly influence fibrinogen levels, as fibrinogen is an acute-phase protein that elevates during inflammation (Luyendyk *et al*., 2019). Moreover, anaemia has also been found in individuals with chronic arthritis because of decreased levels of erythropoietin, an impaired response of the bone marrow to erythropoietin, and premature destruction of red blood cells (Sun *et al*., 2023).

P-ISSN: 2410-8863
E-ISSN:2958-6178
https://djvs.uodiyala.edu.iq
Pages: 1-10

Diyala Journal for Veterinary Sciences
Vol. 3 No.2 June (2025)
https://doi.org/10.71375/djvs.2025.03201

Effect of agmatine sulphate and paracetamol in joint stiffness, mobility, gait, arthritis score, visual weight bearing test on arthritic rats.

Joint stiffness, mobility test and visual weight parameters showed the highest significant value in all induction groups (2.00 ±0.00), (3.80 ±0.17) and (3.00 ±0.16) according to scoring arthritis system. Joint stiffness in G1 and G5 had the lowest significant values in comparison with other treated groups and control group (0.00 ±0.00) and (0.20 ±0.01), as seen in table 3. Additionally, G2 (0.40 ±0.03) has a lower value in comparison to the values of G1, G5 and control (0.00 ±0.00), (0.20 ±0.01) and (0.00 ±0.00), respectively. Conversely, joint stiffness in the G3 and G4 groups had largest significant values in comparison with control and all treatment groups.

Mobility test indicates that there were no significant differences among all treatment groups. In visual weight, after five days of treatment alone with agmatine or paracetamol or in co administration in different doses, no significant value was observed between all groups (G1, G2, G3, G4 and G5), these values have lowest significant in comparison with induction group (3.00 ±0.16), as seen in (table 2).

Table (2): Effect of acetaminophen-agmatine sulphate co administration in different doses on joint stiffness, mobility and visual weight bearing test in gouty arthritis rats.

Groups of rats	Joint stiffness	Mobility test	Visual weight bearing test
Control	0.00 ±0.00 c	6.00 ±0.31 a	0.00 ±0.00 b
Induction	2.00 ±0.00 a	3.80 ±0.17 b	3.00 ±0.16 a
G1	0.00 ±0.00 c	6.00 ±0.31 a	0.10 ±0.02 b
G2	0.40 ±0.03 bc	5.40 ±0.22 a	0.30 ±0.04 b
G3	0.60 ±0.05 b	5.40 ±0.19 a	0.50 ±0.03 b
G4	0.80 ±0.05 b	5.40 ±0.19 a	0.40 ±0.03 b
G5	0.20 ±0.01 c	5.80 ±0.16 a	0.10 ±0.02 b
LSD value	0.317	1.355	0.528

The results observation throughout the current study suggests that there is an increasing evidence indicating the involvement of non-oxidative stress (NO) in the development of some autoimmune disorders, such as rheumatoid arthritis (RA), preclinical studies have shown a significant rise in NO levels and subsequent restoration by specific inhibitors in experimentally generated arthritis rats, this is shown in the groups treated with agmatine or in combination agmatine- paracetamol which had a low exhibition of symptoms due to the selective inhibitory effect of agmatine sulphate on nitric oxide (Rafi *et al.*, 2024). Therefore, agmatine has a potential effects and it is a potent long-term anti-arthritis medication for managing the painful symptoms of RA (Taksande *et al.*, 2017).

P-ISSN: 2410-8863
E-ISSN:2958-6178
https://djvs.uodiyala.edu.iq
Pages: 1-10

Diyala Journal for Veterinary Sciences
Vol. 3 No.2 June (2025)
https://doi.org/10.71375/djvs.2025.03201

Conclusions:

Using injection of monosodium urate crystals in ankle joint at dose 0.1ml showed increasing in WBC, RBC, ESR, HB, joint stiffness, mobility test and visual weight bearing test. Oral administration of agmatine sulphate (1000mg/kg) alone showed a decrease in the total WBC, joint stiffness, mobility test and visual weight bearing test. Furthermore, oral administration of acetaminophen (500mg/kg) with agmatine sulphate (500mg/kg) revealed decreased WBC, ESR, joint stiffness, whereas RBC and HB values were increased.

Recommendations:

Future studies may include other parameters, such as tumour necrosis factor-alpha (TNFα) and the level of interleukin 6 (IL-6) to determine gouty arthritis. The time of gout arthritis induction may be prolonged from 21-30 days to increase the signs of scoring. Moreover, different rodent type (e.g., mice) can be used to further investigate the effects of acetaminophen by agmatine sulphate.

Acknowledgment:

The authors would like to express sincere thanks to the College of Veterinary Medicine / University of Baghdad for their assistance to conduct this research.

Conflict of Interest:

The authors declare no financial or personal conflicts that could have influenced the work presented in this study.

Funding Sources:

The study is self-funded.

Authors Contributions:

These researchers contributed equally in this research.

References:

Abduljaleel, Y. R., Jwaid, A. H., & Hussein, A. K. (2023). Evaluating the effect of ursodeoxycholic acid (UDCA) in comparison with dexamethasone and diclofenac in a rat model of rheumatoid arthritis. *Journal of Medicine and Life*, *16*(10), 1519. https://doi.org/10.25122/jml-2023-0107

Ahmed, R. K., Muhammad, S. S., & Khodaer, E. A. (2015). Spectrophotometric Determination of Paracetamol in bulk and Pharmaceutical Preparations. *Baghdad Science Journal*, *12*(2), 317-323. DOI:10.21123/bsj.12.2.317-323

Al-Abachi, M. Q., Sinan, R., & Falah, Z. (2008). Batch and flow-injection spectrophotometric methods for determination of paracetamol in pharmaceutical preparations by coupling with

P-ISSN: 2410-8863
E-ISSN:2958-6178
https://djvs.uodiyala.edu.iq
Pages: 1-10

Diyala Journal for Veterinary Sciences
Vol. 3 No.2 June (2025)

https://doi.org/10.71375/djvs.2025.03201

diazotized 4-nitroaniline. *Iraqi Journal of Science, 49*(2), 12-20. DOI: https://doi.org/10.24996/ijs.2008.49.2.%25g

Al-Awadi, A. Q. (2014). The influence of whole sonicated Pseudomonas aeruginosa antigens on experimental p. aeruginosa arthritis in rabbits: Ahmed Q. Al-Awadi@ and Mohammed J. Alwan. *The Iraqi Journal of Veterinary Medicine, 38*(1), 1-10. https://doi.org/10.30539/iraqijvm.v38i1.246

Al-Rekabi, F., Abbas, D., & Hadi, N. (2009). Effects of subchronic exposure to meloxicam on some hematological, biochemical and liver histopathological parameters in rats. *Iraqi journal of veterinary sciences,23*. DOI http://dx.doi.org/10.17582/journal.aavs/2023/11.10.1659.1666.

Al-Rekabi, F., & Alrobyrai, S. (2024). The role of alpha lipoic acid and tempol against liver injury after acetaminophen subacute exposure in mice. *Adv. Anim. Vet. Sci*, *12*(3), 490-500. **DOI** | https://dx.doi.org/10.17582/journal.aavs/2024/12.3.490.500

ALQAYSI, M. G. I., & ALABBAS, N. N. (2024). The properties of nefopam as analgesic co-administration with caffeine as adjuvant in induced pain in mice. *Journal of Research in Pharmacy*, *28*(5). DOI : 10.29228/jrp.836

Atiyah, A. J. (2025). Effects Dietary of Arginine and N-carbamylglutamate on Heamatological and Performance Traits of Female Rabbits. *Diyala Journal for Veterinary Sciences*, *3*(1), 142-154. DOI: https://doi.org/10.71375/djvs.2025.031010

https://doi.org/10.71375/djvs.2025.031010

Chi, X., Zhang, H., Zhang, S., & Ma, K. (2020). Chinese herbal medicine for gout: a review of the clinical evidence and pharmacological mechanisms. *Chinese Medicine*, *15*, 1-13. https://doi.org/10.1186/s13020-020-0297-y

Dakkak, M., & Lanney, H. (2021). Management of gout: update from the American college of rheumatology. *American Family Physician*, *104*(2), 209-210. https://www.aafp.org/pubs/afp/issues/2021/0800/p209.html

Fahd, A., & Saliem, A. (2024). Comparative analgesic effect of Portulaca oleracea L. extracted apigenin and diclofenac in mice. *Adv. Anim. Vet. Sci*, *12*(4), 629-636. **DOI** | https://dx.doi.org/10.17582/journal.aavs/2024/12.4.629.636

Graham, G. G., Davies, M. J., Day, R. O., Mohamudally, A., & Scott, K. F. (2013). The modern pharmacology of paracetamol: therapeutic actions, mechanism of action, metabolism, toxicity and recent pharmacological findings. *Inflammopharmacology*, *21*, 201-232. https://doi.org/10.1007/s10787-013-0172-x

Hamad, Z. M. (2016). Protective role of Nigella sativa oil on renal damage induced by acetaminophen in male rats. *The Iraqi Journal of Veterinary Medicine*, *40*(2), 77-81. https://doi.org/10.30539/iraqijvm.v40i2.116

Hameed, A., Galli, M., Czajkowska, A., Kretowski, A., & Ciborowski, M. (2022). Components of the Purine Metabolism Pathways as Biomarkers for the Early Diagnosis of Diabetes. In *Biomarkers in Diabetes* (pp. 1-25). Springer. https://doi.org/10.1007/978-3-030-81303-1_6-1

Hameed, H. A., & Hassan, A. F. (2023). The Hepatoprotective Effect of Omega-7 Against Paracetamol-Induced Hepatotoxicity in Male Rats. *Iraqi Journal of Pharmaceutical Sciences (P-ISSN 1683-3597 E-ISSN 2521-3512)*, *32*(3), 85-94. https://doi.org/10.31351/vol32iss3pp85-94

P-ISSN: 2410-8863
E-ISSN:2958-6178
https://djvs.uodiyala.edu.iq
Pages: 1-10

Diyala Journal for Veterinary Sciences
Vol. 3 No.2 June (2025)
https://doi.org/10.71375/djvs.2025.03201

Hameed, H. A., & Hassan, A. F. (2022). The prophylactic anti-inflammatory effect of omega-7 against paracetamol-induced liver injury in rats. *The Iraqi Journal of Veterinary Medicine*, *46*(2), 43-47. https://doi.org/10.30539/ijvm.v46i2.1412

Hasan, H. F. (2014). The effect of crude alcoholic extract of Withania somnifera leaves in experimentally induced arthritis in mice. *University of Thi-Qar Journal of Science*, *4*(2), 45-52. DOI:10.32792/utq/utjsci/v4i2.593

Hazlewood, G., van der HEIJDE, D. M., & Bombardier, C. (2012). Paracetamol for the management of pain in inflammatory arthritis: a systematic literature review. *The Journal of Rheumatology Supplement*, *90*, 11-16. DOI: https://doi.org/10.3899/jrheum.120336

Lee, H.-P., Huang, S.-Y., Lin, Y.-Y., Wang, H.-M., Jean, Y.-H., Wu, S.-F., Duh, C.-Y., & Wen, Z.-H. (2013). Soft coral-derived lemnalol alleviates monosodium urate-induced gouty arthritis in rats by inhibiting leukocyte infiltration and iNOS, COX-2 and c-Fos protein expression. *Marine drugs*, *11*(1), 99-113. **https://doi.org/10.3390/md11010099**

Luyendyk, J. P., Schoenecker, J. G., & Flick, M. J. (2019). The multifaceted role of fibrinogen in tissue injury and inflammation. *Blood, The Journal of the American Society of Hematology*, *133*(6), 511-520. https://doi.org/10.1182/blood-2018-07-818211

Mahmood, M. A. (2024). Histopathological Effect of Pecan Oil (Carya illinoinensis) against Ibuprofen induced Kidney Injury in Local Male Rabbits. *Diyala Journal for Veterinary Sciences*, *2*(3), 57-66. DOI: https://doi.org/10.71375/djvs.2024.02306

Ohashi, N., & Kohno, T. (2020). Analgesic effect of acetaminophen: a review of known and novel mechanisms of action. *Frontiers in Pharmacology*, *11*, 580289. https://doi.org/10.3389/fphar.2020.580289

Patel, M. G., & Pundarikakshudu, K. (2016). Anti-arthritic activity of a classical Ayurvedic formulation Vatari Guggulu in rats. *Journal of traditional and complementary medicine*, *6*(4), 389-394. https://doi.org/10.1016/j.jtcme.2015.08.007

QassimHosein, Y., AL-Rawi, K. F., & SahebJuma, A.-B. (2016). Study the Oxidative Stress, Some Biochemical and Hematological Parameters in patients with agout at AL-Ramadi city. *Baghdad Science Journal*, *13*(4), 0694-0694. DOI: https://doi.org/10.21123/bsj.2016.13.4.0694

Rafi, H., Rafiq, H., & Farhan, M. (2024). Pharmacological profile of agmatine: An in-depth overview. *Neuropeptides*, 102429. https://doi.org/10.1016/j.npep.2024.102429

Rovenský, J., Stančíková, M., Rovenská, E., Štvrtina, S., Štvrtinová, V., & Švík, K. (2009). Treatment of rat adjuvant arthritis with flavonoid (detralex®), methotrexate, and their combination. *Annals of the New York Academy of Sciences*, *1173*(1), 798-804. **https://doi.org/10.1111/j.1749-6632.2009.04618.x**

Sharma, C. V., & Mehta, V. (2014). Paracetamol: mechanisms and updates. *Continuing Education in Anaesthesia, Critical Care & Pain*, *14*(4), 153-158. https://doi.org/10.1093/bjaceaccp/mkt049

Singh, J. A., & Gaffo, A. (2020). Gout epidemiology and comorbidities. Seminars in arthritis and rheumatism, https://doi.org/10.1016/j.semarthrit.2020.04.008

P-ISSN: 2410-8863
E-ISSN:2958-6178
https://djvs.uodiyala.edu.iq
Pages: 1-10

Diyala Journal for Veterinary Sciences
Vol. 3 No.2 June (2025)
https://doi.org/10.71375/djvs.2025.03201

Sun, Z., Shao, H., Liu, H., & Ma, L. (2023). Anemia in elderly rheumatoid arthritis patients: a cohort study. *Archives of Medical Science: AMS*, *20*(2), 457. DOI: https://doi.org/10.5114/aoms/172443

Taksande, B. G., Gawande, D. Y., Chopde, C. T., Umekar, M. J., & Kotagale, N. R. (2017). Agmatine ameliorates adjuvant induced arthritis and inflammatory cachexia in rats. *Biomedicine & Pharmacotherapy*, *86*, 271-278. https://doi.org/10.1016/j.biopha.2016.12.039

Yeniçeri, M., Tanoğlu, A., Salmanoğlu, M., Çırak, Z., Şenoymak, M. C., Baş, S., & Gökçen, A. S. (2024). Efficacy of Agmatine Treatment in Experimental Acute Pancreatitis Rat Model. *The Turkish Journal of Gastroenterology*, *35*(1), 27. doi: 10.5152/tjg.2024.23017

Zhao, X., Long, Z., Zhong, H., Lu, R., Wei, J., Li, F., & Sun, Z. (2024). Anti-inflammatory Properties of Tongfeng Li'an Granules in an Acute Gouty Arthritis Rat Model. *ACS omega*, *9*(32), 34303-34313. https://doi.org/10.1021/acsomega.4c00056