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Comparison of the Analgesic, Antipyretic, and Anti-inflammatory Efficiency Between Nimesulide and Aspirin in Mice

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Abstract

THE NSAIDs are drugs that differ in their pharmacological efficacy depending on their selectivity against COX2 enzyme. Therefore, the aim of study was to compare the pharmacological effects (analgesic, antipyretic, and anti-inflammatory) between nimesulide (selective) and aspirin (nonselective) COX2 inhibitors in mice. Analgesic ED50s for nimesulide and aspirin were 7.9 and 212.23 mg/kg, respectively. Both drugs exert their effects in a dose-dependent routine. The visceral analgesia (writhing reflex induced by 1% acetic acid) of nimesulide (15.8 mg/kg, i.m.) and aspirin was examined and revealed a significant superiority of nimesulide over aspirin (424.5 mg/kg, i.m) in decreasing the numbers of writhing reflex and percentages of inhibition in writhing numbers to be 66 and 46 %, respectively. The antipyretic effect of nimesulide was significantly more efficient than aspirin through decreasing the fever which induced by baker's yeast (135 mg/kg, i.p.) for overall measured times after injection at 1, 2, 3, and 4h while aspirin has a good and significant antipyretic action after 2h of baker's yeast injection. Formalin (1%) induced inflammation when injected in the paw for the positive (control) group of mice in comparison to the negative (control) group (injected with saline solution) while nimesulide decreased the inflammation in a good manner unlike the aspirin at 0.5, 1, and 2h after formalin injection. Our data demonstrate that nimesulide has better pharmacological properties than aspirin which is related to analgesia, anti-pyresis, and anti-inflammatory effect in mice which makes it useful for practical use in the field of veterinary medicine.

Keywords: Analgesia, Antipyretic, Anti-inflammatory, Nimesulide, Aspirin, Mice.

Introduction

Nimesulide (N-(4-Nitro-2-phenoxyphenyl)-methane sulfonamide) belongs to the non-steroidal anti-inflammatory drugs (NSAIDs), having a selective inhibition of Cyclooxygenase (COX)2 enzyme with negligible effects on the beneficial prostaglandins needed for kidney and gastrointestinal tract biological functions in comparison to the other NSAIDs which have a nonselective inhibition of COX2 [1]. Nimesulide has reliable analgesic, antipyretic and anti-inflammatory properties therefore used in nociceptive and inflammatory conditions that are marked by hyperalgesia [2]. Nimesulide has a preferential COX2 inhibitor 20 times more selective to COX2 than that of COX1 [3]. Nimesulide efficacy are unique as COX2 inhibitors on the inflammation; the nimesulide effects is reliant-on for a wide range of actions, due to the involvement of nimesulide effects to immune along with the non-immune cells, resident cells, and extracellular matrix by a biochemical mechanisms and inhibition other inflammatory mediators which produced in a response to stimulation of cyclic-3,5'-adenosine monophosphate (cAMP); this means that nimesulide has many factors to control the inflammation and pain [4]. Also, nimesulide has proven to be more active and longer lasting than paracetamol in inhibiting fever induced with brewer's yeast in rats [5,6].

Aspirin is one of the NSAIDs that is widely used, and it has several effects as antipyretic, analgesic, and anti-inflammatory through inhibition of COX

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(COX1 and COX2) enzymes which leads to the decrease in prostaglandin and prostacyclin production (prostanoids) which potentiate the effect of other pro-inflammatory mediators such as 5-hydroxytryptamine and histamine and there is evidence that the analgesic effects of aspirin were mediated by a central mechanism through modulation the monoaminergic and opioid receptors [7-9]. Aspirin was found to reduce the inflammation caused by carrageenan injection in the hind paw of rats by inhibiting the hyperalgesia caused by a mechanical stimulation after carrageenan injection and have an analgesic effect in the case of acetic acid-induced abdominal contractions in the mice beside the reducing the late phase (without affecting the early one) of the formalin-induced hind paw licking behavior in the mice [9] and causes analgesia induced by a thermal method (hot plate) with decreasing in body temperature [10]. So, the purpose of this trial was to compare the pharmacological effects (analgesic, antipyretic, and anti-inflammatory) between nimesulide (selective) and aspirin (nonselective) COX2 inhibitors in mice.

Material and Methods

Animal

Ninety-eight albino Swiss mice (weighing 21-33 g), with both sexes, were used throughout the study. The experimental animals were kept in the animal house of the College of Veterinary Medicine, Mosul University at optimal scientific conditions with a 10 /14 h light /dark cycle with 22 ± 2 ºC of room temperature. Water and food were given in the laboratory according to standard protocol.

Drugs

Nimesulide (10%, Instant Pharmaceuticals, India) and aspirin (pure powder, Sanofi, France) were diluted with normal saline and given by intramuscular (i.m.) route with a volume of injection of 5 ml/kg of mice.

Measuring the analgesic ED50 of nimesulide and aspirin in mice

By using the up-and-down method [11], the median analgesic effective dose (ED_{50}) of nimesulide and aspirin was determined by using the thermal method (hot plate) at $56^{O}C$ [12]. Determination of the initial doses depended on preliminary along with the previous studies [13,14]. The decrease and increase in the dose were at a constant value for both of the drugs used.

Analgesic dose-response relationship of individual nimesulide and aspirin

After determination of the ED50 of individual nimesulide and aspirin, we determined the dose-response relationship of individual nimesulide and aspirin by using the doses of ED_{25}, ED_{50} and ED_{100} then assessing the analgesic effects of each drug after 30 min of injection by using the hot plate at 56OC. The total number of mice used in this experiment was 30 divided to six groups (each group consists of 5 animals). Three groups of nimesulide, the first injected with ED25 (4 mg/kg), the second injected with ED50 (7.9 mg/kg), and the last one injected with ED100 (15.8 mg/kg), while the other three groups of aspirin injected in doses of 106.2, 212.3, and 424.5 mg/kg (which resemble the ED_{25}, ED_{50}, and ED_{100}), respectively.

Effect of nimesulide and aspirin on visceral pain (writhing reflex) induced by acetic acid (chemical method) and their comparison

Three groups were used in this experiment, each group consisting of 5 mice, group 1 was injected with acetic acid 1% (0.1 ml/10g b.w.) intraperitoneally which induced a writhing reflex, group 2 was injected with nimesulide at 15.8 mg/kg, i.m. (ED_{100}) and group 3 injected with aspirin at 424.5 mg/kg, i.m. (ED_{100}) before 30 minutes of acetic acid injection then recorded the time of writhing onset and the number of writhing through 30 minutes from injected acetic acid in mice [15,16].

Comparison between nimesulide and aspirin at the level of antipyretic effect in mice

In this experiment, 20 mice were used which divided to 4 groups (each group consisting of 5 mice), first group was administered the normal saline (i.p.), the second group was injected with baker's yeast (pyrogenic dose 135 mg/kg dissolved in 5 ml of distal water to elevate the body temperature), the third group injected with nimesulide (15.8 mg/kg, i.m.) after 30 minutes from baker's yeast injection and the fourth group injected with aspirin (424.5 mg/kg, i.m.) after 30 minutes from baker's yeast injection. All tested groups were measured the temperature before and after injection of baker's yeast at times of 1, 2, 3, and 4 h [17].

Comparison between nimesulide and aspirin as local anti-inflammatory drugs in mice

Twenty mice were divided into 4 groups, each group consists of of 5 mice. Group 1 injected with normal saline (negative control group) in the right paw, group 2 injected with formalin (1%) (positive control group) in the right paw to induce inflammation [18,19], group 3 injected with nimesulide (15.8 mg/kg, i.m.) before 30 minutes of formalin injection [20] while the group 4 injected with aspirin (424.5 mg/kg, i.m.) before 30 minutes of formalin injection. The thickness of the paw for all the groups was measured by using the electronic caliper with the calculation of the time of onset and the number of paw lifting and licking or biting [20,21].

Statistics

One-way analysis of variance (SPSS, version 16) was used for statistical analysis of parametric data which was performed for multiple mean comparisons while the unpaired T-test used to relate the means concerning the two groups of experimental animals. The significance level was at $p<0.05$ [22].

Results

ED50 of nimesulide and aspirin in mice

The analgesic doses for nimesulide and aspirin that produce analgesia in half the population of mice were 7.9 and 212.23 mg/kg i.m, respectively by using the up and down paradigm (Table 1).

Analgesic dose-response relationship for nimesulide and aspirin in mice

Both nimesulide and aspirin exert their effects in a dose-dependent pattern. Also, indicate to the ED_{50} dosage of nimesulide. A comparison can be made between the two drugs, and preference can be given to the nimesulide. The determined ED_{100} of nimesulide and aspirin were 15.8 and 424.5 mg/kg, i.m., respectively which produces the analgesic response significantly in mice (Table 2).

Analgesic effect of nimesulide and aspirin in visceral pain writhing reflex in mice

Injection of the double doses of ED50 for individual nimesulide and aspirin (15.8 and 424.5 mg/kg i.m., respectively) caused an increased in the onset of time and decrease in writhing number comparison of a control group which injected acetic acid (1%, i.p.) to induced writhing reflex, also produced decreased in percentage in writhing number to 66% and 46% for nimesulide and aspirin respectively (Table 3)

The comparative antipyretic effect between nimesulide and aspirin in mice

The antipyretic effect of nimesulide was significantly more efficient than aspirin through decreasing the fever that induced via baker's yeast (135 mg/kg, i.p.) overall measured times after injection at 1, 2, 3, and 4h while aspirin has a good and significant antipyretic action after 2h of baker's yeast treatment (Table 4)

TABLE 1. ED_{50} of nimesulide and aspirin in mice

Variables	Nimesulide	Aspirin
ED_{50}= xf+(k×d)	7.9 mg/kg, i.m.	212.23 mg/kg, i.m.
First dosage	10 mg/kg	100 mg/kg
Latest dose (xf)	10 mg/kg	190 mg/kg
Table value (k)	-0.701	0.741
± Doses (d)	3 mg/kg	30 mg/kg
Range of the dosages	7-10 mg/kg	100-220 mg/kg
Overall mice used	5 XOXOX	8 OOOOXOXO

X character indicates analgesia; O means no analgesia

TABLE 2. Analgesic dose-response relationship of nimesulide and aspirin in mice

Dose (mg/kg, i.m.)	Baseline (seconds)	Latency time after 30 minutes from injection (seconds)
Nimesulide		
4 (ED_{25})	2.20 ± 0.25	2.30 ± 0.20
7.9 (ED_{50})	2.60 ± 0.19	4.00 ± 0.42 ^{*,a}
15.8 (ED_{100})	2.50 ± 0.16	4.60 ± 0.43 ^{*,a}
Aspirin		
106.15 (ED_{25})	2.60 ± 0.29	2.50 ± 0.28
212.23 (ED_{50})	2.20 ± 0.25	2.80 ± 0.20
424.5 (ED_{100})	2.50 ± 0.42	4.20 ± 0.34 ^{*,a,b}

Numbers indicate mean ± SE (5 mice /group)

*Differs significantly from baseline in the same group ($p<0.05$)

a Differ significantly from the first dose (ED25) of the same drug ($p<0.05$)

b Differ significantly from the second dose (ED50) of the same drug ($p<0.05$)

TABLE 3. Determine the analgesic effect of nimesulide and aspirin on the level of visceral pain in mice

Treated group	Time of onset	No. of writhing reflex	% inhibition in writhing No.
Acetic acid (1%)	0.90±0.29	97.60±4.04	0
Nimesulide (15.8 mg/kg)	3.60±0.58 *	33.00±3.58 *	66
Aspirin (424.5 mg/kg)	4.40±0.24 *	52.60±3.75 *,a	46

Numbers indicate mean ± SE (5 mice /group)

*Differs significantly from control injected with acetic acid 1% ($p<0.05$)

a Differ significantly from the group injected with nimesulide at ($p<0.05$)

TABLE 4. Comparison of antipyretic effect between nimesulide and aspirin in mice

Groups	Time (h)			
	1	2	3	4
Normal saline	35.66±0.42	34.80±0.40	35.02±0.18	35.10±0.28
Backers yeast	36.02±0.66	36.14±0.60*	36.62±1.08*	37.12±1.58*
Nimesulide+ Backers yeast	35.10±0.68a	34.30±1.56a	35.02±0.84a	36.67±0.82a
Aspirin+Backers yeast	36.12±0.86	35.90±1.08a	36.92±0.06	37.28±0.30

Numbers indicate mean ± SE (5 mice /group)

*Differs significantly normal saline group at the same time at $p<0.05$

a Differ significantly from backers yeast at the same time at $p<0.05$

Effect of nimesulide and aspirin on induced local pain and inflammation in mice

Formalin (1%) induced inflammation when injected at the paw of the positive (control) group of mice in comparison to the negative (control) group (injected with saline solution) while nimesulide decreased the inflammation in a good manner unlike the aspirin at 0.5, 1, and 2h after formalin injection (Table 5).

The data also shown a decrease in the numbers of lifts and licking the paw during 30 minutes in stage 2 in comparison with the positive control which injected formalin. The percentages of nimesulide and aspirin inhibition in lifting and licking of paw in mice were 58.22 and 55.40%, respectively (Tables 6)

TABLE 5. Comparative anti-inflammatory effect of nimesulide and aspirin in mice

Groups	Paw thickness (mm)		
	After 0.5 h	After 1 h	After 2 h
Normal saline	.70±0.14	.50±0.10	2.50±0.04
Formalin	.80±0.92*	.70±0.78*	2.60±0.68*
Nimesulide+ Formalin	.70±0.30a	.60±0.30a	2.50±0.24a
Aspirin+ Formalin	.50± 0.62*,b	.40±0.60*,b	2.30±0.42*

Numbers indicate mean ± SE (5 mice /group) at $p<0.05$ * Differ significantly from formalin group at $p<0.05$

a Differ significantly from Nimesulide + Formalin group at $p<0.05$ b Differ significantly from Aspirin + Formalin group at $p<0.05$

TABLE 6. Examination the local analgesia of nimesulide and aspirin in mice

Groups	No. of lifting and licking the paw during 30 min	% of inhibition in lifting and licking the paw
Formalin (Positive control)	42.60	____
Nimesulide+ Formalin	17.80*	58.22
Aspirin+ Formalin	19.00*	55.40

Numbers indicate mean ± SE (5 mice /group)

*Differ significantly from formalin (positive control) group at $p<0.05$

Discussion

The aim was to compare the pharmacological effects (analgesic, antipyretic, and anti-inflammatory) between nimesulide (selective) and aspirin (nonselective) COX2 inhibitors in mice. The ED50 of nimesulide (7.9 mg/kg) was less than aspirin (212.23 mg/kg), so the analgesic effect of nimesulide occur in a small dose in comparison with aspirin, this finding was in accordance with precedent researches in mice and rat [23-25]. We used multiple doses of nimesulide and aspirin to examine the dose-response relationship concerning the analgesic effect and the results proved that the increasing in the doses led to an increase in the analgesia which is similar to previous findings [26,27]. At the level of visceral pain, nimesulide and aspirin decreased the contractions of the abdomen (writhing reflex) which were induced by acetic acid. The ED100 of nimesulide was superior to that of aspirin in reduction of the number of writhing reflexes in the percentage of nimesulide (66%) in comparison to aspirin (46%) which following the previous study proved that nimesulide outperformed the diclofenac (nonselective COX2 inhibitors) in analgesic effect at assayed writhing test in mice [28-31]. Other previous studies confirmed that NSAIDs had various anti-hyperalgesic actions than nimesulide which appears to be specially more efficient and rapid acting against inflammatory nociceptive in comparison to diclofenac, celecoxib, and rofecoxib [13] which was proven in the present study that nimesulide (preferential COX2 inhibitor) having more analgesic effect than aspirin (non-selective COX inhibitor). The mechanism of analgesia was done by reducing the biosynthesis and prostaglandins (PGs) accumulation by inhibition of the COX enzyme which increased the pain threshold through their effects, especially on inducible COX2. Nimesulide has another mechanism that induced its anti-nociceptive effect by inhibition of migration and aggregation of neutrophils, production and release of histamine, activation of nitric oxide synthase, metalloproteinase synthesis, cytokine release, substance P production and release [32] which were also needed to produce its efficient anti-inflammatory effect. All mentioned before were in accordance with our results concerning the nimesulide effectiveness as an anti-inflammatory drug rather than aspirin which was measured in the formalin test in mice. Other studies were proved that nimesulide more effective than diclofenac, celecoxib, and rofecoxib in decreasing the hind paw inflammatory hyperalgesia in rats, and acting as antihyperalagesic in humans in case of rheumatoid arthritis [13], and in other studies reported the anti-inflammatory and analgesic activity of aspirin in rat and mice [27]. Nimesulide shows the ability to affect different mediators and intracellular pathways and it has a unique multi-mechanism of action that make it different from other NSAIDs, whereas the mechanism of action of aspirin as analgesic and anti-inflammatory represented by inhibition of prostaglandins synthesis but this itself does not enough to explain the anti-inflammatory efficiency of aspirin. Another mechanism was assumed as induction the production of lipoxins (aspirin-triggered lipoxins) from the arachidonic acid by acetylation of the enzyme COX2, lipoxins binding with G-protein coupled receptor to exert action by resolves inflammation and act as antioxidant and immunomodulators [33,34] while the pharmacological action of nimesulide and aspirin as antipyretic was exerted from their inhibition of the production of brain prostaglandin E1 [35].

Conclusion

Our data demonstrate that nimesulide has better pharmacological properties than aspirin which is related to analgesia, anti-pyresis, and ant inflammation in mice which makes it useful for practical use in the field of veterinary medicine.

Ethical approval

We acquired the approval through the animal care and usage committee belongs to the College of Veterinary Medicine / Mosul University (approval no. UM.VET.2022.076).

Conflict of interest

The author says there are no competing interests.

Contribution of the author

Both authors contributed equally for this research.

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References

1. Elisabetta, C., Armando, I. and Carla, C. The relatively selective cyclooxygenase-2 inhibitor nimesulide: What's going on?. *European Journal of Pharmacology*, **848**, 105-111 (2019).
2. Bianchi, M. and Broggini, M. Anti-hyperalgesic effects of nimesulide: studies in rats and humans. *International Journal of Clinical Practice*, **128**, 11-19 (2002).
3. Balaji, T., Subramanian, M., Gnanasundaram, V., Rajendran, S.S. and Rajendran, H. S. Nimesulide induced histopathological changes in the vas deferens of mice. *Journal of Clinical Diagnostic Research*, **7**, 2116-2118 (2013).

4. Rainsford, K. D. Current status of the therapeutic uses and actions of the preferential cyclo-oxygenase-2 NSAID, nimesulide. *Inflammopharmacology*, **14**, 120-37 (2006).

5. Ceserani, R., Carboni, L., Germini, M. and Mainardi, P. A. Antipyretic and platelet antiaggregating effects of nimesulide. *Drugs*, **1**, 48-51 (1993).

6. Maria, F. P., Glória, E. P. and Aleksander, R. Nimesulide-induced antipyresis in rats involves both cyclooxygenase-dependent and independent mechanisms. *European Journal of Pharmacology*, **543**, 181-189 (2006).

7. Jacob, J. N., Badyal, D. K. and Bala, S. Evaluation of the In Vivo Anti-Inflammatory and Analgesic Activity of a Highly Water-Soluble Aspirin Conjugate. *Basic of Clinical Pharmacology and Toxicology*, **112**, 171-174 (2012).

8. Vergne, P., Bertin, P. and Trèves, R. Aspirin, pain and inflammation. *La Revue de Medecine interne*, **1**, 89-96 (2000).

9. Al-Swayeh, O. A., Clifford, R. H., del Soldato, P. and Moore, P. K. A comparison of the anti-inflammatory and anti-nociceptive activity of nitroaspirin and aspirin. *British Journal of Pharmacology*, **129**, 343-350 (2000).

10. Ohdo, S., Ogawa, N., Song, J. G. Chronopharmacological study of acetylsalicylic acid in mice. *European Journal of Pharmacology*, **293**, 151-157 (1995).

11. Dixon, W.J. Efficient analysis of experimental observations. *Annual Review of Pharmacology and Toxicology*, **20**, 441-462 (1980).

12. Hilde, V. and Theo, F. M. Morphine-Induced Analgesia in the Hot-Plate Test: Comparison between NMRInu/nu and NMRI mice. *Basic and Clinical Pharmacology and Toxicology*, **94**, 59-64 (2004).

13. Mousa, Y. J. Effect of nefopam in normal chickens and its relationship to hydrogen peroxide-induced oxidative stress. *Iraqi Journal of Veterinary Sciences*, **35**, 7-12 (2021)

14. Aubin, N., Curet, O., Deffois, A., Carter, C. Aspirin and salicylate protect against MPTP-induced dopamine depletion in mice. *Journal of Neurochemistry*, **71**, 1635-1642 (1998).

15. Gupta, S. K., Velpandian, T., Mathur, T. and Sengupta, S. Comparative analgesic activity of nimesulide and diclofenac by intramuscular route: correlation with pharmacokinetic profile of nimesulide. *Pharmacology*, **56**, 137-143 (1998).

16. Mousa, Y. J., Mahmood, M. B. and Mohammad, M. S. Administration of ketamine with the central and peripheral analgesics for induction of balanced anesthesia in the chicks. *IOP Conference Series: Earth and Environmental Science*, **388**, 012021 (2019).

17. Jorgete, T., Daiana, S. A., Ana, P. O. F., Juliana, S. M., Fabiane, R. S., Carine, R., Maribel, A. R., Marlí, R. O., Hélio, G. B., Marcos, A. P., Nilo, Z. and Carlos, F. M. Baker yeast-induced fever in young rats: characterization and validation of an animal model for antipyretics screening. *Journal of Neuroscience Methods*, **147**, 29-35 (2005).

18. Damas, J. and Liégeois, J. F. The inflammatory reaction induced by formalin in the rat paw. *Naunyn-Schmiedeberg's Archives of Pharmacology*, **359**, 220-227 (1999).

19. Ardeshir, A., Samaneh, O., Hamid, Y. and Neda, S. K. Effect of Royal Jelly on Formalin Induced-Inflammation in Rat Hind Paw. *Jundishapur Journal of Natural Pharmaceutical Products*, **10**, e22466 (2015).

20. Gupta, S. K., Bhardwaj, R. K., Tyagi, P., Sengupta, S., Velpandian, T. Anti-inflammatory activity and pharmacokinetic profile of a new parenteral formulation of nimesulide. *Pharmacology Research*, **39**, 137-141 (1999).

21. Bucan, A., Wiinholt, A., Dalaei, F., Gerke, O., Hansen, C. R. and Sørensen, J. A. Microcomputed tomography versus plethysmometer and electronic caliper in the measurements of lymphedema in the hindlimb of mice. *Scientific Reports*, **12**, 12267 (2022).

22. Petrie, A. and Watson, P. Statistics for veterinary and animal science. *John Wiley and Sons*, 391. (2013).

23. Gupta, S. K., Bansal, P., Bhardwaj, R. K. and Velpandian, T. Comparative anti-nociceptive, anti-inflammatory and toxicity profile of nimesulide vs nimesulide and piperine combination. *Pharmacology Research*, **41**, 657-662 (2000).

24. Mousa Y. Etomidate anesthesia in chicks: Effect of xylazine. *Journal of the Hellenic Veterinary Medical Society*, **71**, 2463-2470 (2020).

25. Pong, S. F., Demuth, S. M., Kinney, C. M. and Deegan, P. Prediction of human analgesic dosages of nonsteroidal anti-inflammatory drugs (NSAIDs) from analgesic ED50 values in mice. *Archives Internationales de Pharmacodynamie et de Therapie*, **273**, 212-220 (1985).

26. Elham, S., Taraneh, M. Z., Masoumeh, S. and Kobra, N. Enhancement of Antinociception by Co-administrations of Nefopam, Morphine, and Nimesulide in a Rat Model of Neuropathic Pain. *Korean Journal of Pain*, **25**, 7-15 (2012).

27. Mousa, Y. J., Al-Zubaidy, M.H. and Amin, S.M. Age-related anesthetic effect of ketamine in the chickens. *Iraqi Journal of Veterinary Sciences*, **35**, 501-506 (2021).

28. Kress, H. G., Baltov, A., Basiński, A., Berghea, F., Castellsague, J., Codreanu, C., Copaciu, E., Giamberardino, M. A., Hakl, M., Hrazdira, L., Kokavec, M., Lejčko, J., Nachtnebl, L., Stančík, R., Švec, A., Tóth, T., Vlaskovska, M. V. and Woroń, J. Acute pain: a multifaceted challenge - the role of nimesulide. *Current Medical Research Opinion*, **32**, 23-36 (2016).

29. Ahmed, M., Upadhyaya, P. and Seth, V. Comparison of analgesic effects of nimesulide, paracetamol, and their combination in animal models. *Indian Journal of Pharmacology*, **42**, 354-357 (2010).

30. Ashraf S. Alias, A. A., Al-zubaidy, M. H. I., Mousa, Y. J. and Mohammad, F. K. Plasma and whole brain cholinesterase activities in three wild bird species in Mosul, Iraq: In vitro inhibition by insecticides. *Interdisciplinary Toxicology*, **4**, 144-148 (2011).

31. Khalil, Kh. A., Muna H. AlZubaidy, M. H. and Mousa, Y. J. Effect of xylazine administration on ketoprofen toxicity in mice. *Egyptian Journal of Veterinary Sciences*, **54**, 983-996 (2023).

32. Clària, J. and Serhan, C. N. Aspirin triggers previously undescribed bioactive eicosanoids by human endothelial cell-leukocyte interactions. *Proceedings of the National Academy of Sciences of the United States of America*, **92**, 9475-9479 (1995).

33. Cadavid, A. P. Aspirin: The Mechanism of Action Revisited in the Context of Pregnancy Complications. *Frontiers in Immunology*, **8**, 261 (2017).

34. Vane, J. R., Botting, R. M. The mechanism of action of aspirin. *Thrombosis Research*, **110**, 255-258 (2003).

35. Lal, A., Gomber, S. and Talukdar, B. Antipyretic effects of nimesulide, paracetamol and ibuprofen-paracetamol. *Indian Journal of Pediatrics*, **67**, 865-870 (2000).

مقارنة الفعالية المسكنة للألم ، الخافضة للحرارة والمضادة للالتهاب بين النيميسولايد والأسبرين في الفئران

تيماء عدلان يحيى و يعرب جعفر موسى

فرع الفسلجة والكيمياء الحياتية والادوية - كلية الطب البيطري - جامعة الموصل - الموصل - العراق.

الملخص

مضادات الالتهاب غير الستيرويدية هي أدوية تختلف في فعاليتها الدوائية اعتمادا على خاصيتها الانتقائية ضد إنزيم الاكسدة الحلقية2. ولذلك، كان الهدف من الدراسة هو مقارنة التأثيرات الدوائية (المسكنة للألم، الخافضة للحرارة والمضادة للالتهاب) بين مثبطات إنزيم الاكسدة الحلقية2 النيميسولايد (انتقائي) والأسبرين (غير الانتقائي) في الفئران. كانت الجرعة الفعالة الوسطية المسكنة للألم للنيميسولايد والأسبرين 7,9 و 212,23 ملغم/كغم على التوالي. كلا الدواءين يعملان على احداث تأثيرهما العلاجي وبصورة معتمدة على الجرعة. تم فحص التسكين من الألم الحشوي (منعكس التلوي الناجم عن حقن حامض الخليك بنسبة 1%) للنيميسولايد (15,8 ملغم/كغم، في العضل) وتبين انه يتفوق بصورة كبيرة مقارنة بالأسبرين (424,5 ملغم/كغم، في العضل) في تقليل عدد مرات منعكس التلوي وبنسبة التثبيط في أعداد التلوي اذ كانت 66 و 46% على التوالي. كان التأثير الخافض للحرارة للنيميسولايد أكثر فعالية بشكل ملحوظ من الأسبرين من خلال خفض الحمى التي سببها حقن خميرة الخباز (135 ملغم/كغم، في البريتون) في الأوقات المقاسة عند 1 ، 2 ، 3 و 4 ساعات بعد الحقن بينما عمل الأسبرين فقط على خفض الحمى بعد ساعتين من حقن خميرة الخباز. وسبب الفورمالين (1%) الالتهاب عند حقنه في باطن القدم لمجموعة فئران السيطرة الموجبة مقارنة بمجموعة السيطرة السالبة (المحقونة بالمحلول الملحي الفسلجي) بينما قلل النيميسولايد الالتهاب بطريقة جيدة على عكس الأسبرين خلال الاوقات المقاسة بعد 0,5 ، 1 و2 ساعة بعد من حقن الفورمالين. تظهر بياناتنا أن النيميسولايد له خصائص دوائية أفضل من الأسبرين فيما يتعلق بالتأثير المسكن للألم ، الخافض للحمى والمضاد للالتهاب في الفئران مما يجعله مفيدا للاستخدام العملي في مجال الطب البيطري.

الكلمات المفتاحية: مسكن الألم، خافض للحمى، مضاد الالتهاب، النيميسولايد، الاسبرين، الفئران.