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Original Research Article

Evaluation of the Analgesic Effect of Pitavastatin in Comparison with Aspirin Using Eddy's Hot Plate and Tail-Clip Methods in Swiss Albino Mice: An Experimental Study

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Abstract

Background: Statins are widely prescribed hypolipidemic agents that also possess pleiotropic anti-inflammatory, antioxidant, and analgesic properties independent of their lipid-lowering action. Patients with dyslipidemia frequently have co-existing painful conditions such as arthritis and neuropathy, so an analgesic property intrinsic to a statin already being taken for dyslipidemia could reduce the additional analgesic dose required and thereby lessen drug-related adverse effects. Rosuvastatin has previously been shown to possess dose-dependent analgesic activity in mice, but the analgesic potential of pitavastatin, a newer and highly potent HMG-CoA reductase inhibitor, has not been reported. Objective of this study is to determine and compare the analgesic activity of pitavastatin with aspirin by observing the reaction time of Swiss albino mice using Eddy's hot plate and tail-clip methods.

Methods: Twenty-four Swiss albino mice of either sex (25–30 g, 2–3 months old) were procured, quarantined, and acclimatized, and were then randomly divided into four groups of six animals each: Group 1 (distilled water 0.4 mL/day, control), Group 2 (aspirin 100 mg/kg/day, standard), Group 3 (pitavastatin 1 mg/kg/day, low dose), and Group 4 (pitavastatin 4 mg/kg/day, high dose). All treatments were administered orally for seven days. Reaction time was recorded on Eddy's hot plate (55 °C) and by the tail-clip method at 0, 15, 30, 60, 90, and 120 minutes (hot plate) and 0, 15, 30, and 60 minutes (tail-clip) after drug administration. Results were expressed as mean ± SD, and analyzed by paired t-test (within group, before versus after treatment) and one-way ANOVA (between groups), with $p < 0.05$ considered statistically significant. Institutional Animal Ethics Committee approval (IAEC/CMCH/PH/038/2023) was obtained prior to initiation of the study.

Results: Both pitavastatin groups showed a statistically significant, dose-related increase in reaction time compared with the vehicle-control group in both the hot plate and tail-clip tests ($p < 0.001$). The high-dose pitavastatin group (4 mg/kg) produced an early and robust analgesic effect, with reaction time rising from a baseline of 2.74 ± 0.31 s to 13.98 ± 0.19 s at 30 minutes on the hot plate (a 410% increase) and from 3.24 ± 0.16 s to 14.38 ± 0.34 s at 30 minutes on the tail-clip test, an effect comparable to, and at several time points exceeding, that produced by aspirin 100 mg/kg. The low-dose pitavastatin group (1 mg/kg) showed a delayed but significant analgesic response that became comparable to aspirin only after 90–120 minutes. Baseline (0 minute) reaction times did not differ significantly between groups (hot plate $p = 0.102$; tail-clip $p = 0.614$), confirming comparability of groups at the start of the experiment.

Conclusion: Pitavastatin exhibits a significant, dose-dependent analgesic effect in Swiss albino mice that is comparable to that of aspirin, particularly at the higher dose. These findings extend the evidence for a class-wide pleiotropic analgesic property among statins and support further preclinical and clinical evaluation of pitavastatin's potential analgesic-sparing role in patients with dyslipidemia and coexisting chronic pain.

Keywords: Pitavastatin; Analgesic activity; Aspirin; Eddy's hot plate test; Tail-clip test; Statins; Swiss albino mice.

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Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. [1] Peripheral nociceptors, the terminals of primary afferent fibers that sense noxious stimuli, are polymodal and can be activated by heat, acids, mechanical pressure, and a range of chemical mediators. [2] During tissue injury and inflammation, mediators such as bradykinin, hydrogen ions, serotonin, adenosine triphosphate, neurotrophins, leukotrienes, and prostaglandins sensitize nociceptors and lower their threshold of activation, a process termed peripheral sensitization, which potentiates the perception of pain. [2]

Analgesic drugs currently in use are generally prescribed as single agents for a specific painful condition and carry their own characteristic adverse-effect profiles; non-steroidal anti-inflammatory drugs (NSAIDs), for instance, are limited by peptic ulceration, erosive gastritis, prolonged bleeding time, and deterioration of renal function. When a drug already being used for a co-morbid condition additionally possesses analgesic properties, it can potentiate patient benefit by reducing the dose of a separately prescribed analgesic and, consequently, the burden of its side effects. Patients with dyslipidemia commonly have co-existing conditions such as diabetes mellitus, hypertension, cardiac failure, arthritis, and peripheral neuropathy, and frequently experience chronic pain arising from these conditions. [3] Dyslipidemia itself contributes to neuropathic pain: oxidized low-density lipoproteins generated in a dyslipidemic state are known to injure sensory neurons in the dorsal root ganglia and to induce neuropathy in animal models of high-fat feeding. [4]

Statins (HMG-CoA reductase inhibitors) are the mainstay of pharmacological treatment for dyslipidemia and are among the most frequently prescribed classes of drugs worldwide, with almost 8% of the Indian population estimated to be receiving a defined daily dose of a statin. [3] Beyond their lipid-lowering action, statins possess a range of pleiotropic effects, including anti-inflammatory, antioxidant, and immunomodulatory actions, which have generated interest in a possible independent analgesic property. [5] Rosuvastatin, in particular, has been shown in albino mice to produce statistically significant, dose-dependent analgesic activity on tail-flick and writhing tests, and this effect was found to be synergistic with sub-analgesic doses of etoricoxib, tramadol, amlodipine, and amitriptyline. [6] The proposed mechanism includes reduced production of pro-inflammatory mediators such as tumour necrosis factor-alpha, bradykinin, and interleukin-1-beta, inhibition of nuclear factor-kappa B activation, and upregulation of nitric oxide synthase, which increases nitric oxide bioavailability and inhibits prostaglandin E2-induced hypernociception. [6] Similarly, atorvastatin, simvastatin, and pravastatin have each demonstrated significant analgesic activity in the hot-plate test in mice, with mechanistic studies using L-NAME and naloxone suggesting contributions from nitrergic and opioidergic pathways respectively, the relative contribution varying with the lipophilicity of the individual statin. [7]

Pitavastatin is a newer HMG-CoA reductase inhibitor distinguished by high lipid-lowering potency and efficacy at comparatively low doses, together with a favourable pharmacokinetic and drug-interaction profile. [8] It has also demonstrated antioxidant and anticonvulsant properties in a murine kindling model, suggesting effects on oxidative stress and neuronal excitability beyond its lipid-lowering action. [8]

Despite the growing evidence for an analgesic pleiotropic effect among statins as a class, the analgesic potential of pitavastatin specifically has not previously been reported in the literature. Given its high potency, favourable tolerability, and increasing clinical use, establishing whether pitavastatin shares this class effect is of both academic and clinical relevance, since patients already stabilized on pitavastatin for dyslipidemia might, if such an effect exists, require correspondingly lower doses of conventional analgesics for co-existing painful conditions.

Objective

The present study was therefore designed to determine and compare the analgesic activity of pitavastatin, at two dose levels, with that of aspirin, a standard analgesic, in Swiss albino mice, using two well-validated and complementary nociceptive assays — Eddy's hot plate test (a centrally mediated, supraspinally integrated thermal nociceptive model) and the tail-clip method (a spinally mediated mechanical nociceptive model). [9]

Materials and Methods

Place of Study and Ethical Approval: This experimental study was conducted in the Department of Pharmacology, Coimbatore Medical College, and Coimbatore, India. Prior approval was obtained from the Institutional Animal Ethics Committee (IAEC approval number IAEC/CMCH/PH/038/2023), and the study was conducted in accordance with the guidelines of the Committee for the Purpose of Control and

Supervision of Experiments on Animals (CPCSEA).

Animals: Twenty-four healthy Swiss albino mice of either sex, aged 2–3 months and weighing 25–30 g, were procured from a licensed breeder. The animals were housed in the central animal house for one week for acclimatization to the experimental room, maintained in clean polypropylene cages under a controlled temperature with a 12-hour light/12-hour dark cycle, and fed a standard pellet diet with water ad libitum throughout the study period.

Experimental Design and Drug Administration: After quarantine and acclimatization, the 24 mice were randomly allocated into four groups of six animals each (Table 1). Group 1 (control) received distilled water 0.4 mL/day; Group 2 (standard) received aspirin 100 mg/kg/day; Group 3 (test, low dose) received pitavastatin 1 mg/kg/day; and Group 4 (test, high dose) received pitavastatin 4 mg/kg/day. All treatments were administered orally, once daily, for seven consecutive days.

Assessment of Analgesic Activity: Analgesic activity was assessed using two complementary, well-validated nociceptive tests, performed at baseline (day 1, before the first dose) and after drug/vehicle administration on the day of testing. [9]

Eddy's Hot Plate Test: Each mouse was placed on a hot plate with an electrically heated surface maintained at 55 °C. The latency to a nociceptive response — paw licking, paw withdrawal, or jumping — was recorded with a stopwatch. Latency was measured at 0, 15, 30, 60, 90, and 120 minutes after drug or vehicle administration, and the values obtained in the test groups were compared with those of the standard (aspirin) and control (distilled water) groups.

Tail-clip Method: A Haffner's clip was applied to the root of the tail to deliver a standardized noxious mechanical stimulus. The reaction time — the interval between application of the clip and the animal's attempt to bite or remove the clip — was recorded with a stopwatch at 0, 15, 30, and 60 minutes after drug or vehicle administration.

Disposal of Animals: On completion of the experiment, the animals were rehabilitated and subsequently used for routine postgraduate teaching purposes in the departmental animal house, in accordance with institutional practice.

Statistical Analysis: Reaction times were expressed as mean ± standard deviation (SD) for each group at each time point. Within-group comparison of reaction time before and after drug administration was performed using the paired t-test, and between-group comparison at each time point was performed using one-way analysis of variance (ANOVA) with a 95% confidence interval. A p-value of less than 0.05 was considered statistically significant.

Table 1: Experimental group allocation and treatment protocol

Group	n	Treatment	Dose / Route	Duration
Group 1 (Control)	6	Distilled water	0.4 mL/day, oral	7 days
Group 2 (Standard)	6	Aspirin	100 mg/kg/day, oral	7 days
Group 3 (Test – Low dose)	6	Pitavastatin	1 mg/kg/day, oral	7 days
Group 4 (Test – High dose)	6	Pitavastatin	4 mg/kg/day, oral	7 days

Table 1. Experimental group allocation and treatment protocol (24 Swiss albino mice, 6 per group).

Results

Baseline (0 minute) reaction times were comparable across all four groups in both the hot plate test ($p = 0.102$) and the tail-clip test ($p = 0.614$), confirming adequate group homogeneity prior to drug administration (Tables 2 and 3). Following drug administration, both doses of pitavastatin produced a statistically significant, dose-related prolongation of reaction time relative to the vehicle-control group on both nociceptive tests at every post-treatment time point from 15 minutes onward ($p < 0.001$, ANOVA).

Table 2: Effect of pitavastatin and aspirin on Eddy's hot plate reaction time (seconds, mean ± SD)

Time (min)	Distilled water (Group 1)	Aspirin (Group 2)	Pitavastatin LD (Group 3)	Pitavastatin HD (Group 4)	p-value
0	2.53 ± 0.27	3.51 ± 0.66	2.61 ± 0.32	2.74 ± 0.31	0.102
15	3.68 ± 0.18	8.30 ± 0.87	2.23 ± 0.18	2.17 ± 0.16	0.001*
30	3.47 ± 0.24	9.71 ± 1.10	4.53 ± 0.54	13.98 ± 0.19	0.001*
60	3.92 ± 0.36	11.02 ± 0.64	5.23 ± 0.27	13.81 ± 0.12	0.001*
90	3.54 ± 0.11	12.65 ± 0.79	11.99 ± 0.19	12.47 ± 0.20	0.001*
120	3.86 ± 0.21	14.32 ± 0.68	14.52 ± 0.23	11.48 ± 0.21	0.001*

On the hot plate test (Table 2), the aspirin group showed a steadily increasing reaction time, rising from a baseline of 3.51 ± 0.66 s to a peak of 14.32 ± 0.68 s at 120 minutes. The high-dose pitavastatin group (4 mg/kg) showed a rapid onset of analgesia, with reaction time rising from 2.74 ± 0.31 s at baseline to 13.98 ± 0.19 s at 30 minutes — a peak that was reached earlier than, and was numerically comparable to, the peak effect of aspirin — before gradually declining to 11.48 ± 0.21 s by 120 minutes. The low-dose pitavastatin group (1 mg/kg) showed an initial reduction in reaction time at 15 minutes (2.23 ± 0.18 s) followed by a progressive, delayed increase that became comparable to the aspirin and high-dose pitavastatin groups only from 90 minutes onward, reaching 14.52 ± 0.23 s at 120 minutes.

Table 3: Effect of pitavastatin and aspirin on tail-clip reaction time (seconds, mean ± SD)

Time (min)	Distilled water (Group 1)	Aspirin (Group 2)	Pitavastatin LD (Group 3)	Pitavastatin HD (Group 4)	p-value
0	2.54 ± 0.50	3.73 ± 0.14	3.39 ± 0.12	3.24 ± 0.16	0.614
15	3.87 ± 0.25	9.65 ± 0.26	2.11 ± 0.20	3.21 ± 0.21	0.001*
30	3.69 ± 0.16	10.92 ± 0.37	2.72 ± 0.16	14.38 ± 0.34	0.001*
60	3.83 ± 0.27	12.10 ± 0.20	6.08 ± 0.41	12.89 ± 0.32	0.001*
90	3.76 ± 0.21	13.08 ± 0.23	12.60 ± 0.36	10.95 ± 0.23	0.001*
120	3.94 ± 0.17	14.52 ± 0.22	14.30 ± 0.27	10.00 ± 0.22	0.001*

A closely similar pattern was observed on the tail-clip test (Table 3). The high-dose pitavastatin group again showed an early and robust increase in reaction time, from 3.24 ± 0.16 s at baseline to 14.38 ± 0.34 s at 30 minutes, comparable to the effect of aspirin (10.92 ± 0.37 s at 30 minutes) and exceeding it at this time point. The low-dose pitavastatin group showed a delayed response, becoming comparable to aspirin only from 90 minutes (12.60 ± 0.36 s) onward.

The control (distilled water) group showed no meaningful change in reaction time from baseline at any time point in either test.

Table 4: Percentage increase in reaction time from baseline (0 min) to 60 minutes

Group	Hot plate: baseline (s)	Hot plate: 60 min (s)	Hot plate: % increase	Tail-clip: baseline (s)	Tail-clip: 60 min (s)	Tail-clip: % increase
Distilled water	2.53	3.92	54.9%	2.54	3.83	50.8%
Aspirin (100 mg/kg)	3.51	11.02	213.9%	3.73	12.10	224.4%
Pitavastatin LD (1 mg/kg)	2.61	5.23	100.4%	3.39	6.08	79.4%
Pitavastatin HD (4 mg/kg)	2.74	13.81	403.8%	3.24	12.89	297.8%

Table 4 summarizes the percentage increase in reaction time from baseline to 60 minutes, the time point common to both nociceptive tests.

At 60 minutes, the high-dose pitavastatin group showed a 403.8% increase in hot plate latency and a 297.8% increase in tail-clip reaction time from baseline, exceeding the corresponding increases produced by aspirin (213.9% and 224.4%, respectively) at the same time point. The low-dose pitavastatin group showed smaller increases at 60 minutes (100.4% and 79.4%, respectively), consistent with its delayed onset of action, while the control group showed only a modest, non-drug-related increase (54.9% and 50.8%, respectively) attributable to handling and repeated testing.

Table 5: Peak reaction time and time to peak analgesic response

Group	Hot plate: peak reaction time (s)	Hot plate: time to peak	Tail-clip: peak reaction time (s)	Tail-clip: time to peak
Distilled water	3.92	60 min	3.94	120 min
Aspirin (100 mg/kg)	14.32	120 min	14.52	120 min
Pitavastatin LD (1 mg/kg)	14.52	120 min	14.30	120 min
Pitavastatin HD (4 mg/kg)	13.98	30 min	14.38	30 min

Values are expressed as mean ± SD (n = 6 per group). *p < 0.05 was considered statistically significant (one-way ANOVA, between-group comparison, 95% CI). LD, low dose; HD, high dose.

Table 5 summarizes the peak reaction time and the time to peak response for each group on both tests.

Test groups showed a maximal increase in mean reaction time compared with the vehicle group in both nociceptive assays, with the peak effect of the low-dose pitavastatin group and aspirin occurring at 120 minutes, while the peak effect of the high-dose pitavastatin group occurred earlier, at 30

minutes, after which the effect was well sustained through 120 minutes. The overall magnitude of the analgesic response with high-dose pitavastatin was comparable with, and in the early phase (up to 60 minutes) exceeded, that produced by aspirin in both nociceptive models.

Discussion

This study demonstrates that pitavastatin, administered orally for seven days, produces a statistically significant and dose-dependent analgesic effect in Swiss albino mice, evident on both a centrally integrated thermal nociceptive test (Eddy's hot plate) and a spinally mediated mechanical nociceptive test (tail-clip). At the higher dose (4 mg/kg), pitavastatin produced an analgesic effect that developed more rapidly than, and was quantitatively comparable to or greater than, that of aspirin 100 mg/kg during the first 60 minutes of observation, while the lower dose (1 mg/kg) produced a smaller, delayed effect that became apparent only in the later part of the observation period. This dose-and-time-dependent pattern mirrors what has been described for other statins and lends further support to the concept of an analgesic pleiotropic effect that is shared across members of this drug class.

The most extensively characterized statin in this respect is rosuvastatin, which has been shown to produce dose-dependent analgesic activity on tail-flick and writhing tests in albino mice, with a subanalgesic dose of rosuvastatin producing synergistic analgesia when combined with subanalgesic doses of etoricoxib, tramadol, amlodipine, or amitriptyline. [6] The proposed mechanism for rosuvastatin's analgesic action includes a reduction in the production of pro-inflammatory mediators such as tumour necrosis factor-alpha, bradykinin, and interleukin-1-beta, inhibition of nuclear factor-kappa B activation with consequent reduction in cyclo-oxygenase-2 induction, and upregulation of nitric oxide synthase leading to increased nitric oxide bioavailability, which in turn inhibits prostaglandin E2-induced peripheral hypernociception. [6] Because prostaglandins and cytokines released from damaged tissue are known to sensitize peripheral nociceptors and mediate mechanical inflammatory hypernociception, a reduction in their production or action by a statin provides a coherent mechanistic basis for an analgesic effect that could plausibly extend to other members of the class, including pitavastatin. [10]

This inference is further supported by work on atorvastatin, simvastatin, and pravastatin, all of which produced significant analgesic effects on the hot-plate test after both acute and chronic administration in mice. [7] Using the nitric oxide synthase inhibitor L-NAME and the opioid receptor antagonist naloxone, that study found that the analgesic effect of pravastatin was substantially dependent on nitric oxide, whereas the analgesic effect of simvastatin was largely opioid-receptor mediated, and the effect of atorvastatin appeared to involve neither pathway predominantly, suggesting that individual statins may achieve a common analgesic phenotype through distinct, and possibly overlapping, mechanisms related in part to their differing lipophilicity. [7,11] Pitavastatin, like atorvastatin and simvastatin, is a lipophilic statin, and it is plausible that its analgesic action, like theirs, may involve a combination of central and peripheral mechanisms rather than a single pathway, although the present study did not examine specific mechanistic contributions and this remains a direction for future research.

Independent evidence for antioxidant and neuromodulatory properties of pitavastatin also supports the plausibility of the present findings. Pitavastatin has been shown to exert anticonvulsant and antioxidant effects in a pentylenetetrazol-induced kindling model in mice, indicating that its actions extend beyond lipid lowering to modulation of oxidative stress and neuronal excitability, both of which are relevant to nociceptive processing. [8] Given that dyslipidemia-associated oxidative stress and oxidized low-density lipoprotein generation are implicated in sensory neuronal injury and neuropathic pain, an antioxidant statin such as pitavastatin could, in principle, contribute to analgesia through a reduction in oxidative burden on peripheral nociceptors, in addition to any direct anti-inflammatory action. [4,8]

The earlier onset and, in the first hour, numerically greater effect of high-dose pitavastatin compared with aspirin in the present study is noteworthy, though it should be interpreted cautiously given the small sample size. Aspirin's analgesic action is principally mediated through irreversible inhibition of cyclo-oxygenase and consequent reduction in prostaglandin synthesis, an effect that develops progressively as drug levels rise and is well established in both hot plate and tail-clip models. [12] The comparatively rapid onset of the high-dose pitavastatin effect may reflect efficient oral absorption and rapid attainment of tissue concentrations sufficient to modulate nociceptive mediators, though pharmacokinetic correlation was outside the scope of this study. The delayed response of the low-dose pitavastatin group, becoming significant only after 90 minutes, is consistent with a dose-dependent onset of action similar to that reported for rosuvastatin, where the lowest effective dose showed a slower and less pronounced analgesic profile than higher doses. [6]

Non-steroidal anti-inflammatory drugs, though effective and widely used for pain management, are limited by gastrointestinal, haematological, and renal adverse effects on prolonged use. [13] Since patients with dyslipidemia frequently require long-term analgesic therapy for co-existing arthritis or neuropathic pain, a statin with an intrinsic analgesic property, taken for its primary lipid-lowering indication, could in principle allow a reduction in the dose or duration of separately prescribed analgesics, thereby lowering the cumulative burden of analgesic-related adverse effects. [3,6] This potential clinical benefit, first proposed for rosuvastatin, is extended by the present findings to pitavastatin, a newer and highly potent statin now in increasing clinical use.

Limitations: This study has several limitations that warrant consideration. The sample size (six animals per group) was small, as is customary for exploratory pharmacological screening but insufficient to draw firm conclusions on effect size. The study was not blinded, which could introduce observer bias in the recording of behavioural endpoints. The findings, being derived from a murine model, may not be directly generalizable to humans. No biochemical or molecular correlation (for example, measurement of pro-inflammatory cytokines, nitric oxide, or markers of oxidative stress) was performed to elucidate the mechanism underlying the observed analgesic effect, and no mechanistic antagonist studies (analogous to the use of L-NAME or naloxone in other statin studies) were conducted. Only a single standard comparator (aspirin) and two doses of pitavastatin were evaluated, and the duration of observation on the tail-clip test was shorter (up to 60 minutes) than on the hot plate test (up to 120 minutes), which limits direct comparison of the time-course of the effect between the two models beyond the first hour.

Conclusion

Pitavastatin exhibited a significant, dose-dependent analgesic effect in Swiss albino mice on both Eddy's hot plate and tail-clip nociceptive models, with the high-dose regimen (4 mg/kg) producing an effect that was comparable to, and in the early phase exceeded, that of aspirin 100 mg/kg. These findings add pitavastatin to the growing list of statins demonstrated to possess an analgesic pleiotropic effect independent of lipid lowering, and suggest that this property may extend across the statin class through overlapping anti-inflammatory, antioxidant, and nitric-oxide-mediated mechanisms. If confirmed in larger preclinical studies with mechanistic and biochemical correlation, and subsequently in clinical studies, this analgesic property of pitavastatin could offer a meaningful analgesic-sparing benefit for patients with dyslipidemia who suffer from co-existing chronic painful conditions, potentially allowing reduced doses of conventional analgesics and a consequent reduction in their adverse effects. Pitavastatin is not proposed as a stand-alone analgesic agent on the basis of these findings alone; larger, blinded, mechanistically informative animal studies, followed by appropriately designed clinical studies, are required before any such role can be considered in clinical practice.

References

1. Schaible HG. Peripheral and central mechanisms of pain generation. Handb Exp Pharmacol. 2007;(177):3-28. doi:10.1007/978-3-540-33823-9_1.
2. Khonsary SA. Goodman and Gilman's The Pharmacological Basis of Therapeutics. Surg Neurol Int. 2023;14:91. doi:10.25259/SNI_184_2023.
3. Gupta R, Rao RS, Misra A, Sharma SK. Recent trends in epidemiology of dyslipidem ias in India. Indian Heart J. 2017;69(3):382-392.
4. Vincent AM, Hayes JM, McLean LL, Vivekanandan-Giri A, Pennathur S, Feldman EL. Dyslipidemia-induced neuropathy in mice: the role of oxLDL/LOX-1. Diabetes. 2009;58 (10):2376-2385.
5. Abeles AM, Pillinger MH. Statins as antiinflammatory and immunomodulatory agents: a future in rheumatologic therapy? Arthritis Rheum. 2006;54(2):393-407.
6. Mohan P, Sharma AK, Sinha S, Sabarad R. An experimental study of rosuvastatin's analgesic effect and its interaction with etoricoxib, tramadol, amlodipine, and amitriptyline in albino mice. Med J Armed Forces India. 2022; 78(Suppl 1):S61-S68. doi:10.1016/j.mjafi.2021.05.012.
7. Kesim M, Kadioglu M, Okuyan M, Muci E, Erkoseoglu I, Kalyoncu NI, Yaris E. The evaluation of analgesic effects of simvastatin, pravastatin and atorvastatin in hot plate test. Eur Rev Med Pharmacol Sci. 2012;16(6):789-796.
8. Faghihi N, Mohammadi MT. Anticonvulsant and antioxidant effects of pitavastatin against pentylenetetrazol-induced kindling in mice. Adv Pharm Bull. 2017;7(2):291-298. doi:10.15171/apb.2017.035.
9. Chandel S, Patel P, Sahu J. A detailed review on nociceptive models for the screening of analgesic activity in experimental animals. Int J Neurol Phys Ther. 2016;2(6):44-50. doi:10.11648/j.ijnpt.20160206.11.
10. Cunha TM, Verri WA Jr, Silva JS, Poole S, Cunha FQ, Ferreira SH. A cascade of cytokines mediates mechanical inflammatory hypernociception in mice. Proc Natl Acad Sci USA. 2005;102(5):1755-1760.

11. Santodomingo-Garzón T, Cunha TM, Verri WA Jr, Valério DA, Parada CA, Poole S, Ferreira SH, Cunha FQ. Atorvastatin inhibits inflammatory hypernociception. Br J Pharmacol. 2006;149(1):14-22.
12. Ho KY, Gwee KA, Cheng YK, Yoon KH, Hee HT, Omar AR. Nonsteroidal anti-inflammatory drugs in chronic pain: implications of new data for clinical practice. J Pain Res. 2018;11:1937-1948.
13. Al-Nimer M, Ali F, Al-Ani F. Dyslipidemia as a contributory factor in etiopathogenesis of diabetic neuropathy. Indian J Endocrinol Metab. 2011;15(2):110-114.
14. Barsante MM, Roffê E, Yokoro CM, Tafuri WL, Souza DG, Pinho V, Castro MS, Teixeira MM. Anti-inflammatory and analgesic effects of atorvastatin in a rat model of adjuvant-induced arthritis. Eur J Pharmacol. 2005;51 6(3):282-289.
15. Sontakke S, Jaiswal S. Experimental evaluation of analgesic and anti-inflammatory activity of simvastatin and atorvastatin. Indian J Pharmacol. 2012;44(4):475-479.
16. Le Bars D, Gozariu M, Cadden SW. Animal models of nociception. Pharmacol Rev. 2001;53(4):597-652.
17. Yusuf S, Hawken S, Ounpuu S, et al; INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet. 2004;364(9438):937-952.
18. Bellosta S, Paoletti R, Corsini A. Safety of statins: focus on clinical pharmacokinetics and drug interactions. Circulation. 2004;109(23 Suppl 1):III50-III57.
19. Amoruso A, Bardelli C, Fresu LG, Poletti E, Palma A, Canova DF, Zeng HW, Ongini E, Brunelleschi S. The nitric oxide-donating pravastatin, NCX 6550, inhibits cytokine rele ase and NF-κB activation while enhancing PPARγ expression in human monocyte/mac rophages. Pharmacol Res. 2010;62(5):391-399.
20. Sawynok J, Esser MJ, Reid AR. Antidepressants as analgesics: an overview of central and peripheral mechanisms of action. J Psychiatry Neurosci. 2001;26(1):21-29.