IJPSR (2026), Volume 17, Issue 6 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 08 January 2026; received in revised form, 27 January 2026; accepted, 28 January 2026; published 01 June 2026

EVALUATION OF ANALGESIC ACTIVITY OF LACTIUM (α-CASOZEPINE) IN SWISS ALBINO MICE: A COMPARATIVE STUDY WITH PENTAZOCINE

C. D. Jaypriya [*1], V. Arun Kumar [2] and B. Sharmila [1]

Department of Pharmacology [1], Government Medical College, Thiruvallur - 602001, Tamil Nadu, India.
Department of Pharmacology [2], Government Medical College, The Nilgiris - 643005, Tamil Nadu, India.

Keywords:

Lactium, α-casozepine, Analgesic activity, Hot plate method, Tail clip method, GABA receptors

Correspondence to Author:
C. D. Jaypriya MD,

Assistant Professor,
Department of Pharmacology,
Government Medical College,
Thiruvallur - 602001, Tamil Nadu, India.

E-mail: drpriyadermcare@gmail.com

ABSTRACT: Background: Pain management remains challenging with current analgesics associated with significant adverse effects. Lactium, a milk protein hydrolysate containing α-casozepine with GABA-A receptor affinity, has unexplored analgesic potential. **Methods:** Twenty-four male Swiss albino mice (20-30g) were randomly divided into four groups (n=6): control (normal saline 10ml/kg), standard (pentazocine 10mg/kg), and test groups receiving Lactium at 150mg/kg and 300mg/kg, administered orally. Analgesic activity was assessed using Eddy's hot plate method and Haffner's tail clip method at 0, 30, and 60 minute post-administration. Statistical analysis was performed using two-way repeated measures ANOVA followed by Bonferroni post-hoc test. **Results:** Lactium at 300mg/kg demonstrated statistically significant analgesic activity in both hot plate (30 min: $p=0.004$; 60 min: $p<0.001$) and tail clip ($p<0.001$ at both time points) methods. At 60 minutes, no significant difference was observed between Lactium 300mg/kg and pentazocine in hot plate ($p=1.000$) or tail clip ($p=1.000$) tests, indicating equivalent efficacy. Lactium 150mg/kg showed no significant analgesic effect. The effects were consistent across both thermal and mechanical nociception models. **Conclusion:** Lactium at 300mg/kg exhibits dose-dependent analgesic activity comparable to pentazocine at peak effect. Given its established safety profile, Lactium warrants further investigation as a potential analgesic agent.

INTRODUCTION: Pain is an unpleasant sensory and emotional experience that represents one of the most common symptoms requiring medical intervention. Despite significant advances in pain pharmacotherapy, the management of acute and chronic pain remains challenging, with many patients experiencing inadequate relief or intolerable adverse effects [1].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.17(6).1770-77

This article can be accessed online on www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.17(6).1770-77

Current analgesic regimens rely heavily on opioids for severe pain and non-steroidal anti-inflammatory drugs (NSAIDs) for moderate pain [2]. However, long-term opioid use is associated with physical dependence, constipation, tolerance, addiction, and risk of overdose, while chronic NSAID therapy carries substantial risks of gastrointestinal complications, cardiovascular events, and renal toxicity [3, 4].

These limitations necessitate the exploration of novel analgesic agents with improved safety profiles and alternative mechanisms of action [5]. γ-Aminobutyric acid (GABA) is the primary inhibitory neurotransmitter in the central nervous system and plays a fundamental role in nociceptive

processing. GABA receptors, particularly the GABA-A subtype, are abundantly expressed in pain-modulating regions including the dorsal horn of the spinal cord, periaqueductal gray matter, and rostral ventromedial medulla [6].

GABAergic neurotransmission regulates both ascending nociceptive signals and descending pain inhibitory pathways. Pharmacological enhancement of GABAergic activity through GABA-A receptor agonists has consistently demonstrated antinociceptive properties in preclinical models, establishing GABA-A receptor modulation as a validated target for analgesic drug development [7].

Lactium® is a commercially available bioactive milk protein hydrolysate derived from tryptic digestion of bovine αs1-casein, yielding a decapeptide known as α-casozepine. Extensive preclinical and clinical research has established Lactium's anxiolytic and stress-reducing properties, which are mediated through binding affinity for GABA-A receptors similar to benzodiazepines [8].

Importantly, Lactium exhibits a favorable safety profile, with no reported major adverse effects in human clinical trials and was found to be safe. Studies in rats have demonstrated the absence of toxic effects even at high doses, with no evidence of dependence or habituation unlike benzodiazepines [9, 10]. Despite this well-characterized GABAergic mechanism and established safety profile, the analgesic potential of Lactium has never been systematically evaluated.

The rationale for investigating Lactium as a potential analgesic agent is compelling. First, its documented GABA-A receptor affinity provides a mechanistic basis for predicted antinociceptive activity. Second, as a food-derived bioactive peptide with good safety profile, Lactium represents a potentially safer alternative or adjunct to conventional analgesics, particularly in populations at high risk for opioid-related adverse events or NSAID-induced complications. To the best of our knowledge, this study represents the first evaluation of Lactium's analgesic properties using validated experimental pain models. This study therefore aimed to systematically evaluate the antinociceptive potential of Lactium using established thermal and mechanical pain models in mice [11, 12].

Aim and Objectives:

1. To evaluate the analgesic activity of Lactium (150 mg/kg and 300 mg/kg) in Swiss albino mice using Eddy's hot plate method and Haffner's tail clip method

2. To compare the analgesic efficacy of Lactium with pentazocine, as standard

MATERIALS AND METHODS:

Animals: Twenty-four male Swiss albino mice 6 to 8 weeks old, weighing 20-30 grams were sourced from TANUVAS, Madhavaram, Chennai and kept at Animal house of Govt medical college, Kilpauk. Sample size was selected based on previous similar analgesic studies in rodents [13]. Animals were housed in standard polypropylene cages under controlled condition with temperature maintained at 24°C and humidity at 45 to 55%. They were fed with standard pellet diet and filtered water *ad libitum*. Twelve hours light and twelve hours dark cycle was maintained for 10 days prior to the experimentation. Animals were allowed to adapt to the environment 1-2 hours before the procedure. All animals were fasted for 4 hrs before drug administration with free access to water. The study was approved by Institutional Animal Ethics Committee, Government Kilpauk Medical College, Chennai. IAEC proposal no.116/GKMC/IAEC/2020 and the meeting held on 12.08.2020. Handling of animals was done as Per Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines.

Preparation of Drugs: Lactium (α-casozepine, standardized milk protein hydrolysate) is available as 150 mg capsules, procured from Torrent Pharma (Gujarat, India) which was dissolved in normal saline. Pentazocine was available as 25 mg tablet, procured from Sun Pharma (Gujarat, India) which was crushed, and the powder was dissolved in normal saline. Drug solutions were prepared immediately before administration and were given orally using gavage needle and syringe.

Experimental Procedure: In accordance with ethical guidelines for animal experimentation, animals were divided into four groups, each containing 6 animals which were randomly allocated using computer generated random

numbers. Random allocation was done by one investigator, and the experiments were carried out by the other. Baseline test (0 minute) with both the Eddy's hot plate and Haffner's tail clip method was done and animals with extremely high baseline latency were replaced (>15s). The dose of Lactium was chosen as 150mg/kg and 300mg/kg based on the study by Dela Peña IJI *et al* (2016) [14]. Oral Pentazocine was chosen as this route has been validated for analgesic studies in rodents [15]. The four groups were listed below

1. Group 1 (Vehicle control): Normal saline 10ml/kg
2. Group 2 (Standard): Pentazocine 10mg/kg
3. Group 3 (Test 1): Lactium 150mg/kg
4. Group 4 (Test 2): Lactium 300mg/kg

Based on the group, animals were given any of the above drugs or normal saline. All groups received equal volumes (10 ml/kg) to eliminate volume-related confounders. Mice were tested at 30 min and 60 min with Eddy's hot plate first followed by Haffner's tail clip method with adequate recovery time in between.

Assessment of Analgesic Property:

Eddy's Hot Plate Method: For this procedure, each mouse was placed individually in a beaker on the hot plate, which consists of electrically heated surface. Temperature of the hot plate was maintained at 55° Celcius. Responses such as jumping off the surface, withdrawal of the paws and licking of the paws were observed.

The latency period from placing the animal on the plate and the onset of first response was recorded by stopwatch. A cut-off time of 15 seconds was followed to avoid any thermal injury to the paws [16]. **Fig. 1** Test was done at baseline then repeated at 30 and 60 minute and the reaction time was recorded.

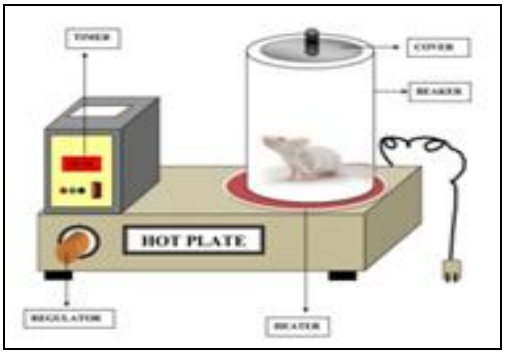

FIG. 1: EDDY'S HOT PLATE

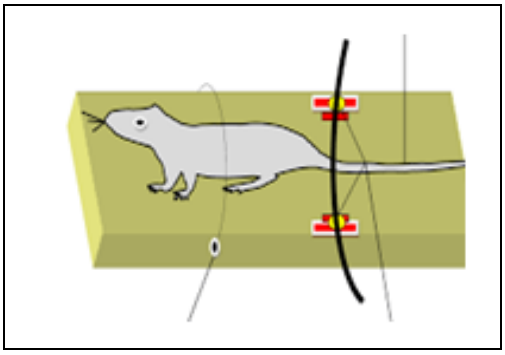

FIG. 2: HAFFNER'S TAIL CLIP

Haffner's Tail Clip Method: In this procedure, a metal artery clip with padded jaws to avoid tissue damage, is applied at the root of the tail to give uniform noxious stimulus. The animal responds to the stimulus by biting the clip or tail where the clip was placed. The reaction time between application of the clip and the response was noted using stopwatch. The procedure was done at baseline and repeated at 30 and 60 minute. A cut-off time of 15 seconds was followed to avoid any injury to the animal **Fig. 2** [17]**.**

Statistical Analysis: Data were entered in Excel and analyzed using two-way repeated measures ANOVA with treatment (four groups) and time (0, 30, 60 minute) as factors. Post-hoc pair wise comparisons were performed using Bonferroni correction for multiple comparisons. Results are expressed as mean ± standard deviation. Statistical significance was set at $p < 0.05$. All analyses were performed using SPSS for mac version 31.0 of IBM Corp.

RESULTS: In this study, 24 Swiss male albino mice were evaluated for analgesic effect using Eddy's hot plate and tail clip method. Reaction time was noted at 0 min (baseline) and at 30 and 60 minute of drug administration in the control, standard and test drug groups.

Eddy's Hot Plate Method: Table 1 presents the mean with standard deviation of reaction time in seconds in Eddy's Hot plate method with the graphical representation in **Fig. 3.**

TABLE 1: DESCRIPTIVE STATISTICS - EDDY'S HOT PLATE METHOD (MEAN ± SD)

Group	0 min	30 min	60 min
Control (n=6)	5.14 ± 0.69	5.19 ± 0.75	5.17 ± 0.40
Lactium 150mg (n=6)	5.24 ± 0.95	5.78 ± 1.72	5.60 ± 0.98
Lactium 300mg (n=6)	5.26 ± 0.54	7.71 ± 0.58	10.45 ± 0.74
Pentazocine 10mg/kg (n=6)	5.08 ± 0.67	10.08 ± 0.90	10.52 ± 1.21

Values expressed as Mean ± Standard Deviation; Reaction time in seconds

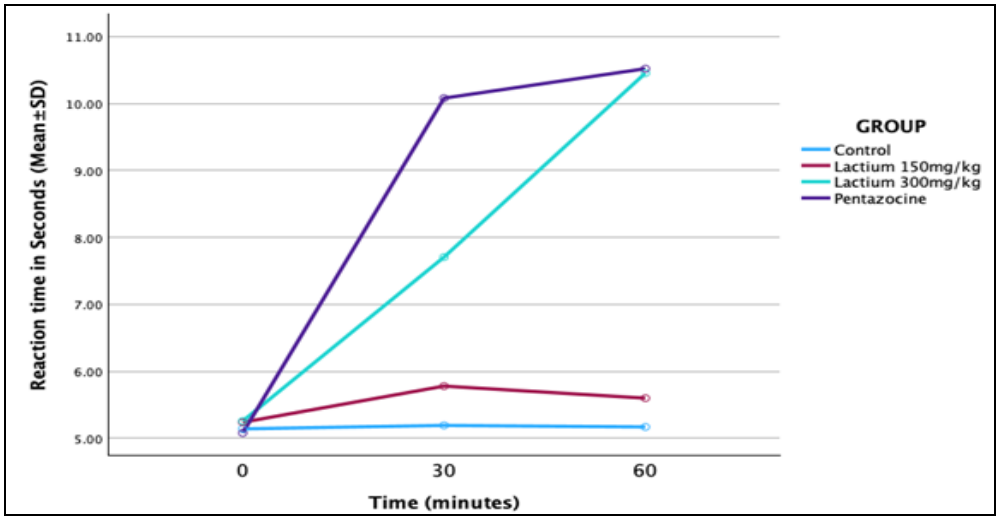

FIG. 3: EFFECT OF DIFFERENT DOSES OF LACTIUM AND PENTAZOCINE ON REACTION TIME IN EDDY'S HOT PLATE METHOD OVER TIME. Values are expressed as mean ± SD (n = 6). Data analyzed using two-way repeated measures ANOVA followed by Bonferroni post-hoc test.

Two-way repeated measures ANOVA shown in **Table 2** revealed significant main effects of Time ($F_{2,40} = 561.103$, $p < 0.001$, $\eta^2_p = 0.966$) and Group ($F_{3,20} = 21.708$, $p < 0.001$, $\eta^2_p = 0.765$), with a highly significant Time × Group interaction ($F_{6,40} = 180.297$, $p < 0.001$, $\eta^2_p = 0.964$), indicating differential treatment responses over time.

TABLE 2: TWO-WAY REPEATED MEASURES ANOVA SUMMARY -EDDY'S HOT PLATE METHOD

Source	df	F	p-value	Partial η^2
Within-Subjects Effects				
Time	2, 40	561.103	<0.001	0.966
Time × Group	6, 40	180.297	<0.001	0.964
Between-Subjects Effects				
Group	3, 20	21.708	<0.001	0.765

Sphericity assumed (Mauchly's W = 0.932, p = 0.512)

Table 3 illustrates the Post-hoc pairwise comparisons with Bonferroni correction. It demonstrates that there are no significant differences between any groups at baseline (all p = 1.000) **Table 3A**.

In a similar manner, Lactium 150 mg/kg produced no significant analgesic effect at any time point (all p > 0.05 vs control). Whereas, Lactium 300 mg/kg significantly increased hot plate latency compared to control at both 30 minute (mean difference: 2.51 sec, 95% CI: 0.69-4.34, p = 0.004) and 60 minute (mean difference: 5.28 sec, 95% CI: 3.79-6.78, p < 0.001). At 30 minute, pentazocine demonstrated superior analgesic efficacy compared to Lactium 300 mg/kg (mean difference: 2.37 sec, p = 0.007) **Table 3B**. However, at 60 minute (peak effect), there was no significant difference between Lactium 300 mg/kg (10.45 ± 0.74 sec) and pentazocine (10.52 ± 1.21 sec; mean difference: 0.07 sec, p = 1.000), indicating statistically equivalent analgesic efficacy at this time point **Table 3C**.

Both treatments produced highly significant increases compared to control (p < 0.001 for both), representing approximately 102% and 104% increases in latency, respectively.

TABLE 3A: POST-HOC PAIRWISE COMPARISONS - EDDY'S HOT PLATE METHOD AT BASELINE (0 MINUTE)

Comparison	Mean Diff (sec)	95% CI	p-value
Control vs Lactium 150mg	-0.10	-1.33 to 1.13	1.000 (NS)
Control vs Lactium 300mg	-0.12	-1.35 to 1.11	1.000 (NS)
Control vs Pentazocine	0.06	-1.17 to 1.30	1.000 (NS)
Lactium 150mg vs Lactium 300mg	-0.02	-1.25 to 1.21	1.000 (NS)
Lactium 150mg vs Pentazocine	0.16	-1.07 to 1.40	1.000 (NS)
Lactium 300mg vs Pentazocine	0.18	-1.05 to 1.41	1.000 (NS)

TABLE 3B: POST-HOC PAIRWISE COMPARISONS - EDDY'S HOT PLATE METHOD AT 30 MINUTE

Comparison	Mean Diff (sec)	95% CI	p-value
Control vs Lactium 150mg	-0.59	-2.41 to 1.24	1.000 (NS)
Control vs Lactium 300mg	-2.51	-4.34 to -0.69	0.004**
Control vs Pentazocine	-4.89	-6.71 to -3.06	<0.001***
Lactium 150mg vs Lactium 300mg	-1.93	-3.75 to -0.10	0.035 (NS)
Lactium 150mg vs Pentazocine	-4.30	-6.13 to -2.47	<0.001***
Lactium 300mg vs Pentazocine	-2.37	-4.20 to -0.55	0.007**

TABLE 3C: POST-HOC PAIRWISE COMPARISONS - EDDY'S HOT PLATE METHOD AT 60 MINUTE

Comparison	Mean Diff (sec)	95% CI	p-value
Control vs Lactium 150mg	-0.43	-1.92 to 1.07	1.000 (NS)
Control vs Lactium 300mg	-5.28	-6.78 to -3.79	<0.001***
Control vs Pentazocine	-5.35	-6.85 to -3.85	<0.001***
Lactium 150mg vs Lactium 300mg	-4.86	-6.35 to -3.36	<0.001***
Lactium 150mg vs Pentazocine	-4.92	-6.41 to -3.42	<0.001***
Lactium 300mg vs Pentazocine	-0.07	-1.56 to 1.43	1.000 (NS)

NS = Not significant; **p < 0.01; ***p < 0.001. Bonferroni correction applied for multiple comparisons.

Haffner's Tail Clip Method: Table 4 presents the mean with standard deviation of reaction time in seconds in Haffner's tail clip method with the graphical representation in **Fig. 4.**

TABLE 4: DESCRIPTIVE STATISTICS -HAFFNER'S TAIL CLIP METHOD (MEAN ± SD)

Group	0 min	30 min	60 min
Control (n=6)	1.52 ± 0.50	1.20 ± 0.37	1.18 ± 0.37
Lactium 150mg (n=6)	1.44 ± 0.50	1.56 ± 0.50	1.58 ± 0.50
Lactium 300mg (n=6)	1.32 ± 0.47	4.34 ± 0.74	5.54 ± 0.96
Pentazocine 10mg/kg (n=6)	1.32 ± 0.47	6.04 ± 0.57	5.66 ± 0.94

Values expressed as Mean ± Standard Deviation; Reaction time in seconds.

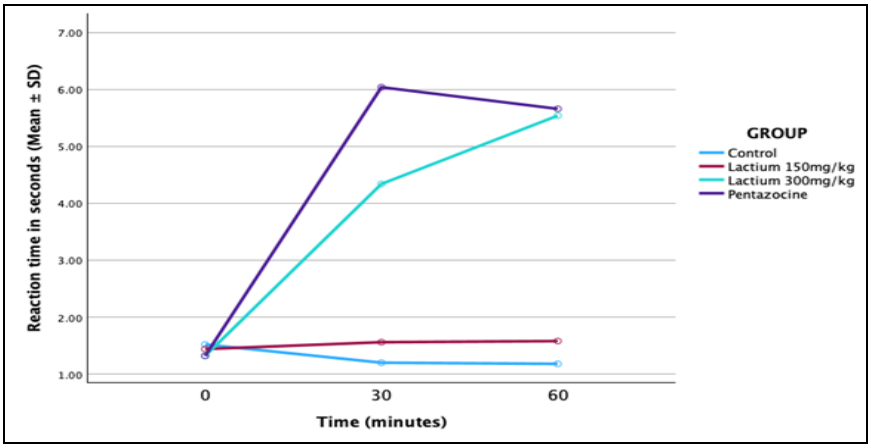

FIG. 4: EFFECT OF DIFFERENT DOSES OF LACTIUM AND PENTAZOCINE ON REACTION TIME IN HAFFNER'S TAIL CLIP METHOD OVER TIME. Values are expressed as mean ± SD (n = 6). Data analyzed using two-way repeated measures ANOVA followed by Bonferroni post-hoc test

Two-way repeated measures ANOVA **Table 5** revealed significant main effects of Time ($F_{1.107,22.133}$= 1025.87, $p < 0.001$, $\eta^2_p = 0.981$) and Group ($F_{3,20} = 40.97$, $p < 0.001$, $\eta^2_p = 0.860$), with a

highly significant Time × Group interaction ($F_{3.320,22.133}$= 408.23, p < 0.001, η^2_p = 0.984), indicating differential treatment responses over time. Mauchly's test indicated violation of sphericity (W = 0.193, p < 0.001); therefore, Greenhouse-Geisser corrected values are reported (ε = 0.553).

TABLE 5: TWO-WAY REPEATED MEASURES ANOVA SUMMARY – HAFFNER'S TAIL CLIP METHOD

Source	df	F	p-value	Partial η²
Within-Subjects Effects				
Time	1.11, 22.13	1025.87	<0.001	0.981
Time × Group	3.32, 22.13	408.23	<0.001	0.984
Between-Subjects Effects				
Group	3, 20	40.97	<0.001	0.860

NOTE: Sphericity violated (Mauchly's W = 0.193, p < 0.001); Greenhouse-Geisser correction applied (ε = 0.553).

Post-hoc pairwise comparisons in **Table 6A** confirmed no significant differences between any groups at baseline (all p = 1.000). Likewise, Lactium 150 mg/kg produced no significant analgesic effect at any time point. In contrast, Lactium 300 mg/kg significantly increased tail clip reaction time at both 30 minute (p < 0.001) and 60 minute (p < 0.001) compared to control. At 30 minute, pentazocine demonstrated superior efficacy compared to Lactium 300 mg/kg (p < 0.001) **Table 6B**. However, at 60 minute (peak effect), there was no significant difference between Lactium 300 mg/kg and pentazocine (mean difference: 0.12 sec, p = 1.000), indicating statistically equivalent analgesic efficacy **Table 6C**. This finding corroborates the hot plate results, demonstrating consistent analgesic equivalence between Lactium 300 mg/kg and pentazocine across both thermal and mechanical nociception models.

TABLE 6A: POST-HOC PAIRWISE COMPARISONS – HAFFNER'S TAIL CLIP METHOD AT BASELINE (0 MINUTE)

Comparison	Mean Diff (sec)	95% CI	p-value
Control vs Lactium 150mg	0.08	-0.74 to 0.90	1.000 (NS)
Control vs Lactium 300mg	0.20	-0.62 to 1.02	1.000 (NS)
Control vs Pentazocine	0.20	-5.79 to 1.02	1.000 (NS)
Lactium 150mg vs Lactium 300mg	0.12	-0.70 to -0.94	1.000 (NS)
Lactium 150mg vs Pentazocine	0.12	-0.70 to -0.94	1.000 (NS)
Lactium 300mg vs Pentazocine	0.00	-0.82 to 0.82	1.000 (NS)

TABLE 6B: POST-HOC PAIRWISE COMPARISONS – HAFFNER'S TAIL CLIP METHOD AT 30 MINUTE

Comparison	Mean Diff (sec)	95% CI	p-value
Control vs Lactium 150mg	-0.36	-1.31 to 0.59	1.000 (NS)
Control vs Lactium 300mg	-3.14	-4.09 to -2.19	<0.001***
Control vs Pentazocine	-4.84	-5.79 to -3.89	<0.001***
Lactium 150mg vs Lactium 300mg	-2.78	-3.73 to -1.83	<0.001***
Lactium 150mg vs Pentazocine	-4.48	-5.43 to -3.53	<0.001***
Lactium 300mg vs Pentazocine	-1.70	-2.65 to -0.75	<0.001***

TABLE 6C: POST-HOC PAIRWISE COMPARISONS – HAFFNER'S TAIL CLIP METHOD AT 60 MINUTE

Comparison	Mean Diff (sec)	95% CI	p-value
Control vs Lactium 150mg	-0.40	-1.65 to 0.85	1.000 (NS)
Control vs Lactium 300mg	-4.36	-5.61 to -3.11	<0.001***
Control vs Pentazocine	-4.48	-5.73 to -3.23	<0.001***
Lactium 150mg vs Lactium 300mg	-3.96	-5.21 to -2.71	<0.001***
Lactium 150mg vs Pentazocine	-4.08	-5.33 to -2.83	<0.001***
Lactium 300mg vs Pentazocine	-0.12	-1.37 to 1.13	1.000 (NS)

NS = Not significant; ***p < 0.001. Bonferroni correction applied for multiple comparisons.

DISCUSSION: Analgesics are drugs that act on peripheral or central nervous system to selectively relieve pain without significantly altering consciousness [18]. Centrally acting analgesics act by raising the threshold for pain and by altering the physiological responses to pain whereas

peripherally acting analgesics act by inhibiting the impulse generation at the chemoreceptor site [19].

In the present study, we have compared the analgesic activity of different doses of Lactium with control and standard (Pentazocine) using Swiss albino mice. The methods employed for screening of analgesic activity in this study are Haffner's tail clip and Eddy's hot plate method. Both methods are useful in illustrating centrally mediated antinociceptive responses which focus generally on changes above the spinal cord level. While the tail clip method mediates a spinal reflex to a nociceptive stimulus, hot plate method involves higher brain functions and is regarded as a supraspinally organized response [20].

Lactium, αs1- Casein hydrolysate at a dose of 150mg/kg did not produce any significant analgesia at 30 minute or even 60 minute when compared to control. At 30 minute of drug administration, mice in the Lactium 300mg/kg group, showed significantly higher latency period than control but lower than that of Pentazocine. Surprisingly, at a dose of 300mg/kg the latency period of Lactium was comparable to that of Pentazocine.

In a study by Carrillo *et al.* (2018), the antinociceptive activity of casein hydrolysate using acetic acid-induced writhing in the mouse model demonstrated antinociceptive activity at 30mg/kg [21]. Where as in our study the antinociceptive effect is significant only at 300mg/kg. This may be attributed to the level of active ingredient in the given drug.

The latency period between the exposure to painful stimuli and the onset of response is considered as analgesic effect, one may consider that the effect observed might be due to motor slowing by GABA-A activation. Dela Peña IJI *et al* (2016) [14] found that though Lactium has sleep enhancing effects, it doesn't cause any significant motor alteration. Additionally, this study evaluated only acute pain models. Chronic pain models and assessment of different pain modalities (neuropathic, inflammatory) are needed to fully characterize Lactium's analgesic profile.

Limitations: The study was not blinded, which may introduce observer bias in latency measurements. Future studies should employ blinded outcome assessment. An important limitation of this study is the absence of motor function assessment. The increased latency observed could potentially be due to sedation or motor impairment rather than analgesia. Future studies should include rotarod test or open field assessment to exclude nonspecific behavioral slowing and confirm genuine antinociceptive activity while assessing centrally acting analgesics.

CONCLUSION: This study provides preliminary evidence that Lactium at 300 mg/kg exhibits antinociceptive activity in acute pain models in mice. The effect was comparable to pentazocine at 60 minute in both thermal and mechanical nociception tests. Given the established safety profile of Lactium in previous studies, [22] further investigation into its analgesic potential is warranted. Future research should include chronic pain models, motor function assessment, dose-response studies, and elucidation of the mechanism of action through receptor binding and antagonist studies.

ACKNOWLEDGEMENT: The authors acknowledge the support provided by the Department of Pharmacology and the Animal House, Government Kilpauk Medical College, Chennai for providing support for this study. The authors are grateful to IAEC for giving the permission to do this experiment on mice.

Funding: No external funding was received for this study.

CONFLICTS OF INTEREST: The authors declare no conflicts of interest.

REFERENCES:

1. Tripathi KD: Essentials of Medical Pharmacology. Jaypee Brothers Medical Publishers Pvt. Ltd; 9th Edition 2025.
2. Da Costa BR, Pereira TV and Saadat P: Effectiveness and safety of non-steroidal anti-inflammatory drugs and opioid treatment for knee and hip osteoarthritis: network meta-analysis. BMJ 2021; 375: 2321. doi:10.1136/bmj.n2321
3. Benyamin R, Trescot AM and Datta S: Opioid complications and side effects. Pain Physician 2008; 11(2): 105-120.
4. Bindu S, Mazumder S and Bandyopadhyay U: Non-steroidal anti-inflammatory drugs (NSAIDs) and organ damage: A current perspective. Biochem Pharmacol 2020; 180: 114147. doi:10.1016/j.bcp.2020.114147
5. Pulskamp TG, Johnson LM and Berlau DJ: Novel non-opioid analgesics in pain management. Pain Manag 2024; 14(12): 641-651. doi:10.1080/17581869.2024.2442292

6. Enna SJ and McCarson KE: The role of GABA in the mediation and perception of pain. Adv Pharmacol 2006; 54: 1-27. doi:10.1016/s1054-3589(06)54001-3
7. Luo Y and Balle T: GABAA receptors as targets for anaesthetics and analgesics and promising candidates to help treat coronavirus infections: A mini-review. Basic Clin Pharmacol Toxicol 2022; 131(6): 443-451. doi:10.1111/bcpt.13798
8. Miclo L, Perrin E and Driou A: Characterization of alpha-casozepine, a tryptic peptide from bovine alpha (s1)-casein with benzodiazepine-like activity. FASEB J Off Publ Fed Am Soc Exp Biol 2001; 15(10): 1780-1782. doi:10.1096/fj.00-0685fje
9. Messaoudi M, Lalonde R, Schroeder H and Desor D: Anxiolytic-like effects and safety profile of a tryptic hydrolysate from bovine alpha s1-casein in rats. Fundam Clin Pharmacol 2009; 23(3): 323-330. doi:10.1111/j.1472-8206.2009.00672.x
10. Beata C, Beaumont-Graff E and Coll V: Effect of alpha-casozepine (Zylkene) on anxiety in cats. J Vet Behav. 2007; 2(2): 40-46. doi:10.1016/j.jveb.2007.02.002
11. Bannon AW and Malmberg AB: Models of nociception: hot-plate, tail-flick, and formalin tests in rodents. Curr Protoc Neurosci 2007; Chapter 8: Unit 8.9. doi:10.1002/0471142301.ns0809s41
12. Kasap M and Can ÖD: Opioid system mediated anti-nociceptive effect of agomelatine in mice. Life Sci 2016; 163: 55-63. doi:10.1016/j.lfs.2016.08.031
13. Yimer T, Birru EM, Adugna M, Geta M and Emiru YK: Evaluation of Analgesic and Anti-Inflammatory Activities of 80% Methanol Root Extract of Echinops kebericho M. (Asteraceae) . J Inflamm Res 2020; 13: 647-658. doi:10.2147/JIR.S267154
14. Dela Peña IJI, Kim HJ and de la Peña JB: A tryptic hydrolysate from bovine milk αs1-casein enhances pentobarbital-induced sleep in mice *via* the GABAA receptor. Behav Brain Res 2016; 313: 184-190. doi:10.1016/j.bbr.2016.07.013
15. Vyas S, Agrawal RP, Solanki P and Trivedi P: Analgesic and anti-inflammatory activities of *Trigonella foenum-graecum* (seed) extract. Acta Pol Pharm 2008; 65(4): 473-476.
16. Eddy NB and Leimbach D: Synthetic analgesics. ii. dithienylbutenyl- and dithienylbutylamines. J Pharmacol Exp Ther 1953; 107(3): 385-393. doi:10.1016/S0022-3565(25)05180-8
17. Bianchi C and Franceschini J: Experimental observations on haffner's method for testing analgesic drugs. Br J Pharmacol Chemother 1954; 9(3): 280-284. doi:10.1111/j.1476-5381.1954.tb01681.x
18. Fan SH, Ali NA and Basri DF: Evaluation of Analgesic Activity of the Methanol Extract from the Galls of *Quercus infectoria* (Olivier) in Rats. Evid-Based Complement Altern Med ECAM 2014; 2014: 976764. doi:10.1155/2014/976764
19. Shreedhara CS, Vaidya VP, Vagdevi HM, Latha KP, Muralikrishna KS and Krupanidhi AM: Screening of *Bauhinia purpurea* Linn. for analgesic and anti-inflammatory activities. Indian J Pharmacol 2009; 41(2): 75-79. doi:10.4103/0253-7613.51345
20. Gabra BH and Sirois P: Beneficial effect of chronic treatment with the selective bradykinin B1 receptor antagonists, R-715 and R-954, in attenuating streptozotocin-diabetic thermal hyperalgesia in mice. Peptides 2003; 24(8): 1131-1139. doi:10.1016/j.peptides.2003.06.003
21. Carrillo W, Monteiro KM, Spindola H, Ramos M and de Carvalho JE: Antiulcerative and Antinociceptive Activities of Casein and Whey Proteins. J Med Food 2018; 21(6): 605-611. doi:10.1089/jmf.2017.0090
22. Chang CM, Tsai IJ, Yang CC, Liu WC and Yang CP: The impact of Alpha-s1 Casein hydrolysate on chronic insomnia: A randomized, double-blind controlled trial. Clin Nutr 2024; 43(12): 275-284. doi:10.1016/j.clnu.2024.10.039

How to cite this article:
Jaypriya CD, Kumar VA and Sharmila B: Evaluation of analgesic activity of lactium (α-casozepine) in swiss albino mice: a comparative study with pentazocine. Int J Pharm Sci & Res 2026; 17(6): 1770-77. doi: 10.13040/IJPSR.0975-8232.17(6).1770-77.