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ORIGINAL RESEARCH

Analgesic Efficacy of a Novel Traditional Chinese Medicine Ointment Against Mechanical Allodynia in Rat Models

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Video Abstract

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Background: Effective management of procedure-related pain, such as venipuncture, is a critical clinical need. The Eutectic Mixture of Local Anesthetics (EMLA) cream is a standard topical analgesic but has limitations including contraindications and potential adverse effects. The Cortex Erythrinae formula recorded in the Golden Mirror of Medicine is traditionally used to dispel wind-dampness, unblock collaterals, and relieve arthralgia.

Objective: This study aimed to develop a novel Traditional Chinese Medicine (TCM) ointment based on classical prescriptions and to evaluate its efficacy against mechanical allodynia, using EMLA cream as a positive control.

Methods: Fifty male Sprague-Dawley rats were randomly allocated to five groups (n=10). Mechanical allodynia was induced; the mechanical withdrawal threshold (MWT), pain-related behaviors, skin irritation, and systemic toxicity were assessed following topical application of low-, medium-, or high-concentration TCM ointment, EMLA cream, or blank vehicle.

Results: High-concentration TCM ointment significantly elevated MWT ($P < 0.001$ vs EMLA) and reduced paw-licking and writhing responses, without inducing skin irritation or systemic toxicity.

Conclusion: The high-concentration TCM ointment provided rapid (within 20 min), superior, and cost-effective analgesia with an excellent safety profile, suggesting its promise as an alternative to EMLA for managing mechanical allodynia.

Plain Language Summary: This study developed a new Traditional Chinese Medicine (TCM) ointment inspired by a classical formula. Tested in a rat model of pain, this high-concentration ointment provided faster and stronger pain relief compared to the commonly used EMLA cream, without causing skin irritation or other safety concerns. The results suggest this TCM ointment could be a promising, safe, and cost-effective alternative topical analgesic.

Keywords: EMLA, herbal medicine, mechanical allodynia, topical analgesia, traditional chinese medicine, von Frey test

Introduction

Pain is a major source of physiological and psychological stress, frequently leading to anxiety, panic, and heightened anticipation of future painful experiences, all of which can negatively impact treatment outcomes.[1] Recognized as the "fifth vital sign" by the American Pain Society, effective pain management remains a critical component of comprehensive patient care.[2]

Mechanical allodynia, characterized by the perception of pain in response to normally non-painful stimuli, presents a significant clinical challenge in various conditions, including neuropathies, postoperative states, and inflammatory

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disorders.[3] It severely impairs quality of life and functional recovery, creating a substantial unmet therapeutic need. This is particularly relevant in the context of procedural pain. For instance, venipuncture is one of the most common clinical procedures, yet it consistently ranks highly as a source of fear and anxiety in both children and adults, often leading to avoidance of necessary medical care. Current topical analgesics, such as the eutectic mixture of local anesthetics (EMLA) cream, are effective,[4] but have limitations. These include contraindications in patients with amide-type anesthetic allergies, the risk of methemoglobinemia, age restrictions, and the potential for contact dermatitis.[5,6] These drawbacks highlight the necessity for developing safer and more universally applicable alternatives. Traditional Chinese Medicine (TCM) offers a rich repository of topical analgesics historically used for conditions like cervical spondylosis, frozen shoulder, lumbar disc herniation, and gout.[7] These therapies often employ multi-component formulations targeting multiple pathways, aligning with a holistic treatment approach. However, scientific validation of their efficacy against mechanical allodynia remains limited. Furthermore, notable TCM analgesics such as Aconitum carmichaelii are constrained by inherent toxicity and a lack of standardized formulations.[8] Therefore, there is an urgent need to develop natural analgesics with minimal side effects through rigorous scientific evaluation and standardized preparation.

From a mechanistic perspective, mechanical allodynia involves peripheral and central sensitization, driven by inflammatory mediators, ion channel dysregulation (eg, sodium channels, TRP channels), and neuroimmune interactions. This complex pathophysiology underscores the potential utility of a multi-target therapeutic strategy, as often embodied in TCM formulations, which may offer superior efficacy by simultaneously modulating these interconnected pathways.

In this study, we developed a novel TCM analgesic ointment based on the classical Cortex Erythrinae formula from the *Golden Mirror of Medicine*.[9] This formula is traditionally understood to dispel wind-dampness, unblock collaterals, and relieve pain. We aimed to evaluate its effects on mechanical allodynia thresholds in rats and compare its efficacy and safety to EMLA cream, thereby providing preclinical evidence for its potential as a topical analgesic alternative to EMLA for procedure-related pain management.

Materials and Methods

Experimental Materials and Ointment Preparation

The TCM ointment was formulated by modifying the classical Cortex Erythrinae formula.[9] It contained the following herbs: Cortex Erythrinae (Hai Tong Pi) 30 g, Speranskia tuberculata (Tou Gu Cao) 30 g, Clematis chinensis (Wei Ling Xian) 30 g, Aconitum carmichaelii (prepared Chuanwu) 10 g, Aconitum kusnezoffii (prepared Caowu) 10 g, Zanthoxylum bungeanum (Hua Jiao) 10 g, Cyathula officinalis (Chuan Niu Xi) 30 g, Angelica sinensis (Dang Gui) 20 g, Luffae Fructus (Si Gua Luo) 10 g, Spatholobus suberectus (Ji Xue Teng) 20 g, Glycyrrhiza uralensis (Gan Cao) 6 g, and the penetration enhancer laurocapram (Azone) 5.4 g.

The preparation procedure was as follows: Aconitum carmichaelii and Aconitum kusnezoffii (20 g total, 1:1) were steam-distilled for 1 h to collect volatile components. Concurrently, the remaining herbs (excluding laurocapram) were immersed in 1 L of water for 1 h and then decocted with an additional 200 mL of water for 1 h, yielding approximately 360 mL of decoction. This decoction was concentrated to 45 mL in a 60°C water bath, and 0.9 g laurocapram was added to produce the high-concentration formulation (9.16 g/mL). Medium- (4.58 g/mL) and low-concentrations (3.05 g/mL) formulations were prepared by adjusting the final volume and laurocapram amount. All herbal materials were procured from certified commercial suppliers and complied with the quality standards of the Pharmacopoeia of the People's Republic of China (2020 Edition). As a representative example, the monarch drug Cortex Erythrinae (Hai Tong Pi, Batch A220501) underwent and passed comprehensive quality control testing, including screening for 33 prohibited pesticides (see Supplementary Material for the complete quality control reports). The identity of all materials was verified by TCM pharmacists at the Maternal and Child Health Hospital of Hubei Province. Representative voucher specimens have been deposited in the hospital's herbarium for reference. The geographical origins of all herbs are documented in the Supplementary Material.

Animals and Experimental Design

Fifty male Sprague-Dawley rats (250 ± 20 g) were obtained from the Animal Experiment Center of Wuhan University. The rats were housed under controlled conditions: temperature 18–22°C, humidity 40–70%, and a 12-h light/dark cycle, with ad libitum access to food and water. After 1-week of acclimation, the rats were randomly assigned to five groups (n=10 per group) using a computer-generated sequence: (1) Blank Control (Group C); (2) EMLA Cream Control (Group P); (3) Low-concentration TCM (Group L); (4) Medium-concentration TCM (Group M); (5) High-concentration TCM (Group H).

The experimental design adhered to the ARRIVE guidelines 2.0. Key elements included: randomization of animals to groups using a computer-generated sequence; partial blinding of outcome assessors; pre-defined primary outcome (Mechanical Withdrawal Threshold at 20 min); and a pre-specified sample size justification. The sample size of ten rats per group was determined based on established protocols from prior mechanical allodynia studies,[3,10] and was further justified by a prospective power analysis performed using G*Power 3.1 software ($\alpha = 0.05$, power = 0.95, estimated effect size f = 1.2). A post-hoc power analysis, based on the observed large effect size for the key comparison (Group H vs Group P) in MWT at 20 minutes, confirmed a statistical power > 0.99.

The animal study protocol was approved by the Ethics Committee of the Maternal and Child Health Hospital of Hubei Province and received final ethical approval (Approval No. WP20230084) from the Wuhan University Center for Animal Experiment, where the experiments were conducted. All procedures were performed in accordance with the institutional animal welfare guidelines. At the end of the experiment, all rats were euthanized humanely by an overdose of intraperitoneal sodium pentobarbital (150 mg/kg) in accordance with the American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia of Animals.

Behavioral and Toxicity Assessments

Mechanical Withdrawal Threshold (MWT)

The MWT was assessed using a standardized set of calibrated von Frey filaments (Stoelting Co., USA) ranging from 0.4 g to 15.0 g, following the well-validated "up-down" method described by Chaplan et al.[10] Rats were placed individually in transparent Plexiglas chambers (20×25×15 cm) on an elevated stainless-steel wire mesh grid, allowing full access to the plantar surface of the hind paws. The testing room was maintained in a quiet environment with consistent lighting. After a 20-min acclimation period, the filaments were applied perpendicularly to the mid-plantar surface of the left hind paw until slight buckling occurred, each stimulus being held for approximately 6–8 seconds. A positive response was defined as a rapid paw withdrawal, flinching, or licking upon stimulus application.

The testing sequence began with the 2.0 g filament. In the absence of a response, the next higher force filament was applied; following a positive response, the next lower force filament was used. This pattern continued until six responses were recorded in the immediate vicinity of the withdrawal threshold. The 50% paw withdrawal threshold (in grams) was calculated using the formula: 50% threshold (g) = $(10^{(Xf + \kappa\delta)}) / 10{,}000$, where Xf is the log value of the final filament used, κ is the tabular value for the specific response pattern, and δ is the mean difference between stimuli (0.224).[11] All behavioral tests were conducted by the same experimenter, who was trained to apply consistent force, to minimize inter-observer variability.

Pain-Related Behaviors

Pain responses were evaluated using two complementary methods. The number of paw licks was counted over 20-min following application. For the acetic acid-induced writhing test, abdominal hair was removed 24 h before testing; After seven days of daily abdominal application, 0.2 mL of 0.3% acetic acid was injected intraperitoneally 20 min after the final application. The latency to the first writhe and the total number of writhes were recorded over 20-min observation period.[12]

Skin Irritation Assessment

Cutaneous tolerance was evaluated using a bilateral comparison model. The investigational formulation was applied to a 2×2 cm area on both intact (left flank) and damaged (needle-scratched until bleeding) skin, covered with 3M dressings

for 24 h. Erythema and edema were scored at 1, 24, 48, and 72 h after removal using a standardized scale (0–4 for erythema, 0–4 for edema, maximum score 8).[13]

Systemic Toxicity Evaluation

The rats in TCM groups received oral administration of the ointment (14 g/kg/day) for 14 days.[14,15] Body weight was recorded weekly. General health, behavior, signs of poisoning, and mortality were monitored throughout the study period.

Quality Control in Behavioral Assessment

To ensure the reproducibility and consistency of behavioral data, several quality control measures were implemented: (1) All von Frey filaments were calibrated before and after the study period. (2) The experimenter performing the behavioral tests underwent standardized training using the protocol outlined by Chaplan et al[10] until consistent application technique and scoring were achieved. (3) Testing was conducted at the same time of day (±2 hours) to control for circadian influences. (4) The testing chambers and mesh grid were cleaned thoroughly between animals to remove olfactory cues.

Statistical Analysis

Data were analyzed using SPSS 26.0 and GraphPad Prism 10.0. The normality of distribution for all continuous variables was confirmed using the Shapiro–Wilk test, and homogeneity of variances was assessed using Levene's test. All datasets met the assumptions for parametric analysis. For comparisons of MWT and pain behavior scores across the five experimental groups at specific time points, one-way analysis of variance (ANOVA) was employed. When a significant main effect was found ($P < 0.05$), Fisher's Least Significant Difference (LSD) post hoc test was used for multiple comparisons. The use of LSD was justified by the exploratory nature of the study and the need to minimize Type II errors in this preclinical efficacy comparison. Within-group comparisons between baseline and post-treatment time points were performed using paired Student's t-tests. Continuous variables are presented as mean ± standard deviation (SD). A two-tailed P value < 0.05 was considered statistically significant. The specific statistical test used for each analysis is indicated in the respective figure legends.

Blinding Protocol

Group allocation was performed by an independent statistician. Treatment administrators were aware of group assignments due to visible differences between the formulations. Behavioral outcome assessors were partially blinded to the specific TCM concentrations but could distinguish between TCM and control formulations. Skin-irritation scoring was conducted by a clinician blinded to all group assignments. Data analysts were fully blinded through the use of anonymized datasets.

Results

The High-Concentration TCM Ointment Significantly Elevates Mechanical Allodynia Threshold

No significant differences in baseline mechanical withdrawal thresholds were observed among the groups (C: 4.974 ± 0.151, P: 5.016 ± 0.156, L: 5.0 ± 0.174, M: 4.960 ± 0.220, H: 5.077 ± 0.262; $P > 0.05$). At 20 minutes post-application, all treatment groups exhibited significantly increased thresholds compared to their respective baseline (L: 5.151 ± 0.148, $P < 0.05$; P: 5.614 ± 0.086, M: 5.366 ± 0.166, H: 5.80 ± 0.451, $P < 0.01$). Critically, the high-concentration TCM group (H) demonstrated significantly greater analgesia than the EMLA group (P) ($P < 0.001$, Figure 1).

TCM Ointment Reduces Pain-Related Behaviors

All treatment groups showed a significant reduction in pain-related behaviors compared to the blank control ($P < 0.001$). The frequency of paw-licking was markedly decreased (C: 10.5 ± 1.58; P: 6.1 ± 0.88; L: 8.0 ± 0.82; M: 7.0 ± 0.82; H: 4.8 ± 0.92). Similarly, the latency to the first writhe was prolonged (C: 171 ± 3.90; P: 327 ± 4.48; L: 302 ± 4.06; M: 318 ± 2.77; H: 353 ± 9.5) and the number of writhes was reduced (C: 35 ± 1.25; P: 18 ± 1.2; L: 31 ± 8.80; M: 25 ± 1.77; H: 11.6 ± 1.51). The high-concentration TCM group (H) performed superiorly to the EMLA group (P) in both writhing latency and frequency ($P < 0.001$, Figure 2).

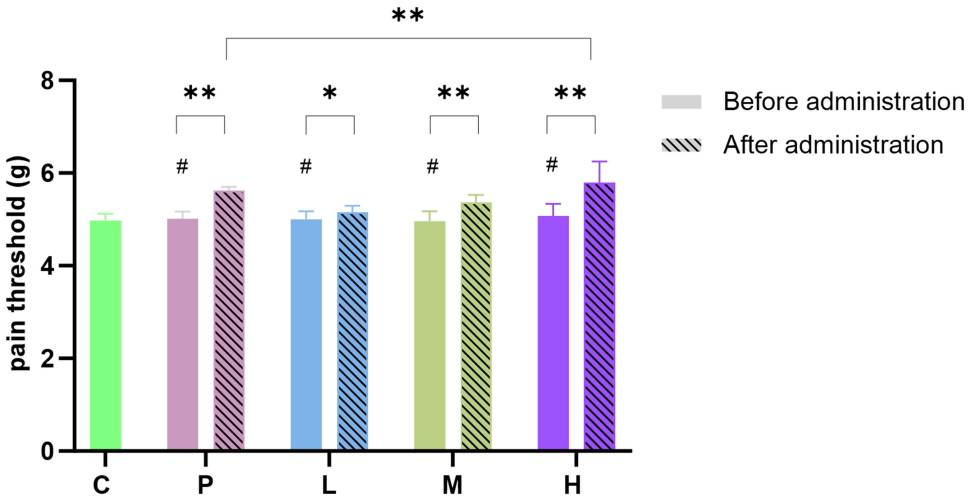

Figure 1 Effects of topical treatments on mechanical withdrawal threshold (MWT). Data are presented as mean ± SD (n=10). *$P < 0.05$, **$P < 0.01$, # $P>0.05$ vs own baseline.
Abbreviations: C, Blank Control; P, EMLA Cream; L, Low-concentration TCM; M, Medium-concentration TCM; H, High-concentration TCM.

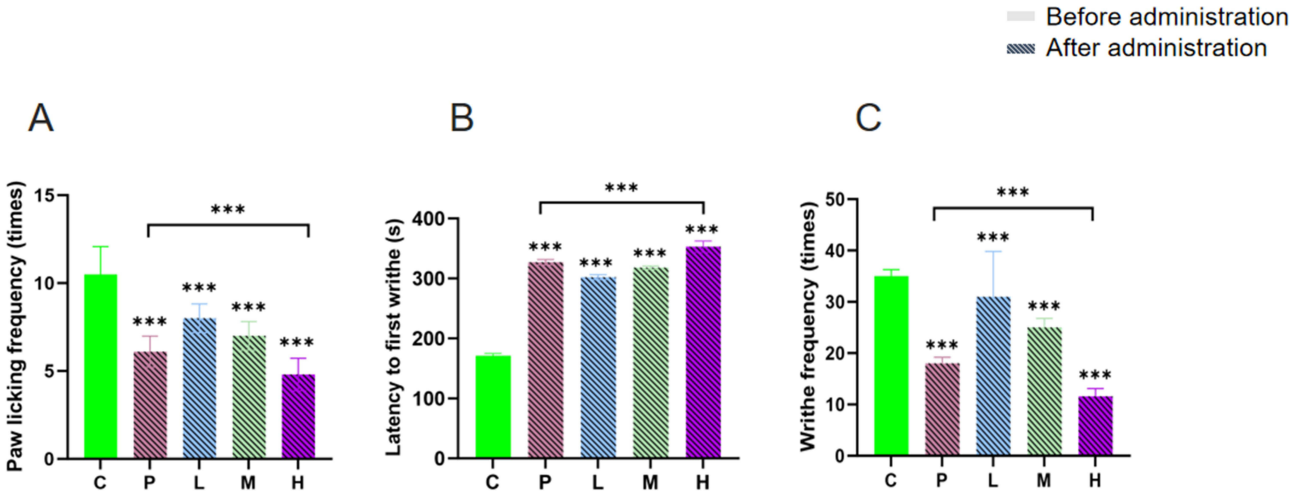

Figure 2 Effects of topical treatments on pain-related behaviors. (**A**) Number of paw-licks within 20 minutes after application. (**B**) Latency to the first writhe following acetic acid injection. (**C**) Total number of writhes within 20 minutes after acetic acid injection. Data are presented as mean ± SD (n=10). ***P < 0.001 vs Blank Control group (**C**) or vs EMLA group (P).
Abbreviations: C, Blank Control; P, EMLA Cream.

TCM Ointment Shows Excellent Skin Safety Profile

Transient, mild erythema (score < 0.5) was observed at the 1-hour time point in only two rats from the EMLA-treated group on damaged skin; this resolved spontaneously within 24 hours (Table 1). In contrast, no skin reactions were observed in any of the TCM groups on either intact or damaged skin at any time point.

No Systemic Toxicity Observed

No abnormalities or mortality were observed in TCM groups during the 14-day observation period. All rats maintained a normal appearance, behavior, and steady body weight gain, with no signs of toxicological reactions.

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Table 1 Skin Irritation Scores Following Application of EMLA Cream and TCM Ointments on Intact and Abraded Skin

Skin Type	Treatment Group	Mean Irritation Score (Mean±SD)				Irritation Intensity
		1 h	24 h	48 h	72 h	
Intact Skin	EMLA Cream	0	0	0	0	Non-irritating
	Low-concentration TCM	0	0	0	0	Non-irritating
	Medium-concentration TCM	0	0	0	0	Non-irritating
	High-concentration TCM	0	0	0	0	Non-irritating
Abraded Skin	EMLA Cream	<0.5	0	0	0	Non-irritating
	Low-concentration TCM	0	0	0	0	Non-irritating
	Medium-concentration TCM	0	0	0	0	Non-irritating
	High-concentration TCM	0	0	0	0	Non-irritating

Notes: Data are presented as the mean score for each group (n=10). The irritation score was evaluated according to a standardized scale (0–4 for erythema, 0–4 for edema, maximum score 8). A score of <0.5 indicates negligible irritation that resolved spontaneously.
Abbreviations: EMLA, Eutectic Mixture of Local Anesthetics; TCM, Traditional Chinese Medicine.

Discussion

Main Findings of the Study

This study developed a novel TCM ointment based on the classical Cortex Erythrinae formula[9] and evaluated its topical analgesic efficacy. The key finding is that the high-concentration TCM formulation significantly elevated the mechanical withdrawal threshold (MWT) within 20 minutes of application, demonstrating superior efficacy compared to the standard EMLA cream ($P < 0.001$). This primary analgesic effect was corroborated by significant reductions in pain-related behaviors, including paw-licking frequency and acetic acid-induced writhing. Critically, the TCM ointment exhibited an excellent safety profile, with no observable skin irritation or systemic toxicity throughout the study period.

Correlation Between Findings and Objectives

These results directly fulfill the primary study objective. We have developed a TCM-based topical agent that provides rapid and superior analgesia relative to the active control (EMLA) in a validated model of mechanical allodynia. The complete absence of local or systemic adverse effects strongly aligns with the goal of creating a safer alternative for procedural pain management.[4–6] The data robustly support the hypothesis that a rationally designed, multi-herbal formulation can achieve potent analgesia through synergistic mechanisms.

Clinical Relevance of Mechanical Allodynia for Procedural Pain

Mechanical allodynia—pain evoked by a normally innocuous mechanical stimulus—is a core translational phenotype in pain research.[3,10] In the clinical context of procedures like venipuncture, it manifests as the tenderness and heightened sensitivity in the skin surrounding a needle puncture site. This results from local tissue injury, inflammation, and subsequent peripheral sensitization of nociceptors.[11] The von Frey filament model used herein is a well-established surrogate for this clinical phenomenon.[10] Therefore, the rapid reversal of mechanical allodynia by our TCM ointment indicates a direct action on the key pathological processes (eg, neurogenic inflammation, peripheral sensitization) that underpin post-procedural pain, ensuring high phenotypic relevance to the target application.

Clinical Context and Translational Implications

EMLA cream remains a cornerstone for procedural analgesia but has recognized limitations: a required application time of approximately 60 minutes, contraindications in patients with amide-type anesthetic allergies, a risk (albeit low) of methemoglobinemia, and potential for contact dermatitis.[4–6,16,17] Our TCM ointment presents several distinct translational advantages for procedural pain management:

1. Rapid Onset of Action (~20 minutes): Aligns better with fast-paced clinical workflows where prolonged waiting is impractical.
2. Exceptional Local Tolerability: The absence of irritation on both intact and experimentally damaged skin[13] suggests a favorable safety profile for use on fragile or compromised skin, including in pediatric populations.
3. Cost-Effectiveness: The estimated direct material cost is approximately one-fourth that of EMLA, enhancing its accessibility and potential for use in resource-conscious settings.

These attributes position the TCM ointment as a promising, fast-acting, and safe alternative for pre-procedural topical analgesia, specifically for indications like venipuncture.

Integrated Mechanism of Action: A Multi-Target Strategy

The efficacy of the formulation is grounded in a rational design that integrates traditional TCM principles with modern pharmacology. The prescription is structured to dispel wind-dampness, unblock collaterals, and relieve pain.[9] The monarch drugs, Cortex Erythrinae and Speranskia tuberculata, initiate this action. Modern studies confirm the analgesic and anti-inflammatory properties of Speranskia tuberculata extract,[18] and Cortex Erythrinae has been shown to inhibit key pro-inflammatory cytokines (TNF-α, IL-6) and NF-κB signaling,[19] thereby countering peripheral sensitization.

The ministerial drugs, processed Aconitum species and Clematis chinensis, powerfully enhance analgesia. Aconitum alkaloids provide central analgesia by blocking voltage-gated sodium channels[20] and modulating the PI3K-Akt pathway,[21] Clematis chinensis and its active component AR-6 suppress TNF-α, IL-6, and NF-κB,[22] creating a synergistic anti-inflammatory effect.

The adjuvant herbs refine the therapeutic action. Zanthoxylum bungeanum contributes local anesthesia and anti-inflammatory effects, partly via TRP channel modulation,[23] Cyathula officinalis,[24] Spatholobus suberectus,[25] and Angelica sinensis[26] work in concert to promote blood circulation and resolve stasis, concepts correlating with improved microcirculation and tissue repair. Crucially, Glycyrrhiza uralensis harmonizes the formula and detoxifies the Aconitum species through alkaloid complexation[27] and modulation of endogenous metabolism.[28] The penetration enhancer laurocapram ensures efficient transdermal delivery.[29]

We propose an integrated mechanism: 1) suppression of peripheral inflammation via cytokine and NF-κB inhibition;[18,19,22] 2) direct blockade of pain signaling through sodium and TRP channel modulation;[20,23] and 3) improvement of the local tissue environment via enhanced microcirculation.[24–26] This multi-pronged, synergistic strategy likely underlies its superior performance over single-mechanism drugs like EMLA.[4]

Study Limitations and Future Perspectives

This study has limitations. First, the sample size (n=10/group), while justified by a post-hoc power analysis for the primary outcome, may be underpowered for secondary endpoints. Second, full blinding was challenging due to formulation appearance, risking performance bias. Third, manual extraction introduces variability; automated, standardized production is needed for clinical translation. Fourth, using only male rats precludes assessment of sex-based differences in analgesic response. Notwithstanding these limitations, we have reported this study in accordance with the ARRIVE 2.0 guidelines to enhance transparency and reproducibility, particularly detailing randomization, blinding procedures, and outcome assessment. Future studies should prioritize: 1) conducting pharmacokinetic studies to characterize the transdermal absorption and bioavailability of key active compounds; 2) elucidating the molecular mechanisms through proteomic or transcriptomic analyses; and 3) initiating phased clinical trials to evaluate efficacy and safety in human subjects.

Conclusion

This study provides compelling preclinical evidence that our novel, high-concentration TCM ointment is both highly effective and safe, offering rapid (within 20 min) and superior analgesia compared to EMLA cream. Its multi-target mechanism and excellent safety profile, combined with a substantial cost advantage, position it as a promising alternative

for managing procedure-related pain such as venipuncture. Future work should focus on formula standardization, mechanistic elucidation, and validation in clinical trials.

Abbreviations

EMLA, Eutectic Mixture of Local Anesthetics; TCM, Traditional Chinese Medicine.

Data Sharing Statement

The datasets generated and analyzed during the current study are available from the corresponding author, Yongqun Hu, upon reasonable request.

Ethical Statement

The animal study was conducted as a collaborative project between the Maternal and Child Health Hospital of Hubei Province and the Wuhan University Center for Animal Experiment. The study protocol was reviewed and approved by the Ethics Committee of the Maternal and Child Health Hospital of Hubei Province (as indicated on the pre-review document). The animal experiments were performed at the Wuhan University Center for Animal Experiment, and the final protocol received ethical approval from its Institutional Animal Care and Use Committee (IACUC) (Approval No. WP20230084). All procedures were conducted in strict accordance with the animal welfare guidelines and regulations of both institutions and the ARRIVE guidelines.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

References

1. Susam V, Friedel M, Basile P, Ferri P, Bonetti L. Efficacy of the Buzzy system for pain relief during venipuncture in children: a randomized controlled trial. *Acta Biomed*. 2018;89(6–S):6–16. doi:10.23750/abm.v89i6-S.7378
2. Neshat H, Aslani K, Jamshidi M, Aslanabadi S, Ghorbani F. Comparison of the effect of massage and EMLA cream on children's physiological indices during venipuncture: a factorial clinical trial. *J Perianesth Nurs*. 2020;35(6):619–624. doi:10.1016/j.jopan.2020.04.005
3. Shen L, Fang LC, Yu JP, et al. Research progress on rat pain models. *Chongqing Med*. 2013;42(10):1166–1169.
4. Fetzer SJ. Reducing venipuncture and intravenous insertion pain with eutectic mixture of local anesthetic: a meta-analysis. *Nurs Res*. 2002;51(2):119–124. doi:10.1097/00006199-200203000-00008
5. Tan Q. Research progress on the application of compound lidocaine cream in pain-free nursing. *Chin J Mod Nurs*. 2013;19(26):3302–3304.
6. Varsha Gowda VM, Shenoi SD, Augustine KM. Anaphylactic shock secondary to topical EMLA. *J Cutan Aesthet Surg*. 2025;18(2):120–122. doi:10.4103/JCAS.JCAS_30_23
7. Feng F, Fang Y, Chen RG, et al. Randomized,double-blind,parallel controlled, multicenter clinical trial of effectiveness and safety of Shexiang Zhuifeng Zhitong Ointment in alleviating pain in knee osteoarthritis (syndrome of cold-dampness obstruction). *Zhongguo Zhong Yao Za Zhi*. 2024;49(9):2512–2521. doi:10.19540/j.cnki.cjcmm.20240202.501
8. Liang X, Su W, Zhang W, et al. An overview of the research progress on Aconitum carmichaelii Debx.: active compounds, pharmacology, toxicity, detoxification, and applications. *J Ethnopharmacol*. 2025;337(Pt 2):118832. doi:10.1016/j.jep.2024.118832
9. Wu Q. *Golden Mirror of Medicine (Yi Zong Jin Jian)*. People's Medical Publishing House; 1981.

10. Chaplan SR, Bach FW, Pogrel JW, et al. Quantitative assessment of tactile allodynia in the rat paw. *J Neurosci Methods*. 1994;53(1):55–63. doi:10.1016/0165-0270(94)90144-9
11. Zimmermann M. Pathobiology of neuropathic pain. *Eur J Pharmacol*. 2001;429(1–3):23–37. doi:10.1016/S0014-2999(01)01303-6
12. Chen Q. *Pharmacological Research Methodology of Chinese Medicine*. People's Medical Publishing House; 2000:627–629.
13. Shuyun X, Rulian B, Xiu C, et al. *Pharmacological Experiment Methodology*. 3rd edn ed. People's Medical Publishing House; 2002:1331.
14. Deng Y, Luo S, He F, et al. Acute toxicity of Jiaomu oil in SD rats by intragastric administration. *J Hunan Univ Chin Med*. 2023;43(1):27–33. doi:10.19540/j.cnki.cjcmm.20240202.501
15. Zhang L, Li T, Wang R, et al. Evaluation of long-time decoction-detoxified Hei-Shun-Pian (processed Aconitum carmichaelii lateral root with peel) for its acute toxicity and therapeutic effect on mono-iodoacetate-induced osteoarthritis. *Front Pharmacol*. 2020;11:1053. doi:10.3389/fphar.2020.01053
16. Stoltz P, Manworren RCB. Comparison of children's venipuncture fear and pain: randomized controlled trial of EMLA® and J-Tip needleless injection system®. *J Pediatr Nurs*. 2017;37:91–96. doi:10.1016/j.pedn.2017.08.025
17. Yu Z, Zhou Y, Xu X, Lin L, Le Q, Gu Y. Pharmacological and non-pharmacological interventions in management of peripheral venipuncture-related pain: a randomized clinical trial. *BMC Pediatr*. 2023;23(1):58. doi:10.1186/s12887-023-03855-z
18. Zhou YX, Wang SJ, Li Y, et al. Evaluation of analgesic, anti-inflammatory, and antipyretic activities of the ethanol extract from Speranskia tuberculata. *Afr J Tradit Complement Altern Med*. 2015;12(4):1–8.
19. Kim MC, Ds K, Sj K, et al. Eucommiae cortex inhibits TNF-α and IL-6 through the suppression of caspase-1 in lipopolysaccharide-stimulated mouse peritoneal macrophages. *Am J Chin Med*. 2012;40(2):315–329. doi:10.1142/S0192415X12500115
20. Ameri A. The effects of Aconitum alkaloids on the central nervous system. *Prog Neurobiol*. 1998;56(2):211–235. doi:10.1016/S0301-0082(98)00037-9
21. Chen Z, Zhou L, Ge Y, et al. Fuzi decoction ameliorates pain and cartilage degeneration of osteoarthritic rats through PI3K-Akt signaling pathway. *Phytomedicine*. 2022;100:154071. doi:10.1016/j.phymed.2022.154071
22. Wang X, Zhou D, Zhou W, et al. Clematichinenoside AR inhibits the pathology of rheumatoid arthritis by blocking the circPTN/miR-145-5p/FZD4 signal axis. *Int Immunopharmacol*. 2022;113(Pt A):109376. doi:10.1016/j.intimp.2022.109376
23. Wei L, Zong W, Zeng QH, et al. Network pharmacology analysis and experimental verification of Zanthoxylum bungeanum anti-inflammatory and analgesic effects. *China J Chin Mater Med*. 2021;46(12):3034–3042. doi:10.19540/j.cnki.cjcmm.20210305.401
24. Huang YH, Qiu L, Peng Y, et al. Ecdysteroid-enriched fraction of Cyathula officinalis suppresses synovial proliferation and inflammation to ameliorate RA by inhibiting the AKT/PI3K/mTOR signaling pathway. *J Asian Nat Prod Res*. 2025:1–23. doi:10.1080/10286020.2025.2492357.
25. Zhang F, Ganesan K, Liu Q, Chen J. A review of the pharmacological potential of Spatholobus suberectus Dunn on cancer. *Cells*. 2022;11(18):2885. doi:10.3390/cells11182885
26. Tian Y, Shen X, Hu T, et al. Structural analysis and blood-enriching effects comparison based on biological potency of Angelica sinensis polysaccharides. *Front Pharmacol*. 2024;15:1405342. doi:10.3389/fphar.2024.1405342
27. Peter K, Schinnerl J, Felsinger S, et al. A novel concept for detoxification: complexation between aconitine and liquiritin in a Chinese herbal formula (Sini Tang). *J Ethnopharmacol*. 2013;149(2):562–569. doi:10.1016/j.jep.2013.07.022
28. Sun B, Wang X, Cao R, et al. NMR-based metabonomics study on the effect of Gancao in the attenuation of toxicity in rats induced by Fuzi. *J Ethnopharmacol*. 2016;193:617–626. doi:10.1016/j.jep.2016.10.042
29. Liao Z, Zhu C, Tan J, et al. Effects of different transdermal penetration enhancers applied to herbal cake-partitioned moxibustion on liver lipids, HSL and HMG-CoA reductase in hyperlipidemia rabbits. *J Acupunct Tuina Sci*. 2020;18(1):157–164. doi:10.1007/s11726-020-1174-z