



Is *Quercus infectoria* Ready for Perioperative Pain Management? A Clinical Commentary

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Received: February 10, 2026; **Accepted:** February 25, 2026; **Published:** April 8, 2026

Abstract

Karimian et al. investigated the anti-inflammatory and analgesic effects of the hydroalcoholic extract of *Quercus infectoria* fruit hulls (Jaft-e-Baloot) in male mice using a formalin-induced pain and inflammation model. The study demonstrated a dose-dependent reduction in paw edema and nociceptive behavior, with the 200 mg/kg dose showing effects comparable to those of diclofenac, suggesting that bioactive compounds modulate inflammatory mediators. However, translational relevance to surgical settings is limited, as postoperative pain involves tissue injury, ischemia-reperfusion, immune activation, and wound healing—factors not captured by the formalin model. Critical perioperative considerations, such as hemostasis, wound repair, infection risk, and interactions with anesthetic agents, were not addressed. Additionally, the study's exclusive use of male NMRI mice and intraperitoneal administration limits generalizability and clinical translation. For anesthesiology, the extract's effects on central analgesic pathways, sedative properties, and cardiovascular or respiratory safety remain unknown. Overall, while promising, the findings are exploratory. Future research should include surgical pain models, pharmacokinetics, safety profiling, and evaluation within multimodal analgesic regimens to establish clinical relevance.

Keywords: Analgesia; Herbal Medicine; Perioperative Pain; *Quercus infectoria*; Research; Translational

In the Study “The Effect of the Hydroalcoholic Extract of *Quercus infectoria* Fruit Hulls (Jaft-E-Baloot) on Formalin-Induced Inflammation and Pain in Male Mice,” Karimian et al. provide valuable experimental evidence supporting the anti-inflammatory and analgesic effects of the hydroalcoholic extract of *Quercus infectoria* fruit hulls using a formalin-induced pain and inflammation model in male mice (1). The authors are to be commended for addressing an

ethnopharmacologically relevant medicinal plant and for attempting to scientifically validate its traditional use.

From a preclinical pharmacological perspective, the findings demonstrate a dose-dependent reduction in both paw edema and nociceptive behavior, particularly at the 200 mg/kg dose, which showed effects comparable to diclofenac. These results suggest that bioactive compounds within the fruit hulls may modulate inflammatory



mediators involved in the biphasic formalin response.

Translational Limitations from a Surgical Perspective

Pain and inflammation following surgical procedures are complex and multifactorial. They involve tissue incision, ischemia-reperfusion injury, immune system activation, wound healing dynamics, and systemic stress responses, all of which contribute to complex molecular and cellular disturbances affecting surgical outcomes and tissue viability in reconstructive procedures (2). While the formalin model is well-established for evaluating peripheral inflammatory and nociceptive mechanisms, it does not adequately replicate postoperative pain or surgical inflammation, which are heavily influenced by mechanical tissue disruption and repair processes (as evidenced by the predominant use of incision-based models, such as the plantar incision model for surgical pain studies) (3).

Moreover, the current study does not address whether *Q. infectoria* extract affects hemostasis and bleeding risk, wound healing or fibroblast activity, and infection susceptibility. These factors are critical for any agent proposed as an alternative or adjunct to conventional anti-inflammatory drugs in surgical settings. Therefore, although the extract demonstrates promising anti-edematous activity, its extrapolation to perioperative use should be approached with caution.

Considerations from an Anesthesiology and Pain Management Perspective

From an anesthesiology viewpoint, postoperative pain is a multidimensional phenomenon involving peripheral, spinal, and supraspinal pathways, requiring integrated and multimodal management strategies for optimal outcomes (4). Preclinical pain models, including the formalin test, are extensively used to evaluate nociceptive and inflammatory mechanisms. However, the

formalin model primarily reflects peripheral inflammatory pain and spinal sensitization, and does not fully capture the complexity of postoperative hyperalgesia, opioid-sparing effects, or interactions within multimodal analgesia protocols.

While diclofenac often serves as a positive control, the absence of comparisons with centrally acting analgesics (e.g., opioids or $\alpha 2$ -agonists) limits interpretation of the extract's potential in contemporary perioperative analgesic regimens. Additionally, many studies fail to report critical parameters, including sedative or central nervous system depressant effects, respiratory or cardiovascular safety, and potential interactions with anesthetic agents.

Overall, these limitations underscore the need for rigorous preclinical evaluation, including comprehensive pharmacokinetic profiling, safety assessment, and comparison with established analgesics. Such studies are essential before considering the extract as a potential adjunct or alternative in perioperative pain management.

Methodological and Experimental Considerations

The exclusive use of male NMRI mice may limit generalizability, as sex-related differences in inflammatory and pain responses are well documented, and omission of females can bias outcomes and reduce translational relevance (Sex/Gender Biases in Pain Research and Clinical Practice; Intraperitoneal Route of Drug Administration). Furthermore, the intraperitoneal route of administration and lack of pharmacokinetic or human-equivalent dose analysis restrict clinical translation, given the limited pharmacokinetic data available for IP administration compared with human routes of drug delivery (Intraperitoneal Route of Drug Administration) (5).

Conclusion and Future Directions

In summary, Karimian et al.'s study adds meaningful evidence supporting the anti-inflammatory and analgesic potential of *Quercus infectoria*. Nevertheless, from a surgical and anesthesiology perspective, the findings should be interpreted as preclinical and exploratory rather than directly applicable to the management of clinical pain or inflammation.

Future studies incorporating surgical pain models, comprehensive safety and toxicity profiling, pharmacokinetic analyses, and comparative evaluation within multimodal analgesic frameworks will be essential to determine the translational relevance of this promising herbal candidate in perioperative settings.

Conflict of Interest

The authors declared no conflicts of interest.

Author Contributions

Both authors contributed equally to the conception and design of the review, literature search, analysis and interpretation of the available evidence, drafting and critical revision of the manuscript, and final approval of the version to be published. Both authors agreed to be accountable for all aspects of the work.

Statement Ethical

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Data Availability Statement

The datasets generated and analyzed during the current study are available from the corresponding authors upon reasonable request.

Acknowledgment

The authors express their gratitude to the officials of Lorestan University of Medical Sciences (LUMS), Khorramabad, Iran for their support.

Consent for Publications

All authors approved the manuscript for publication.

Funding Statement

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Artificial Intelligence Statement

Artificial intelligence tools were used solely for language editing, grammar correction, and improving the clarity and readability of the manuscript. No artificial intelligence tool was used to generate scientific content, analyze or interpret data, or make scientific conclusions. The authors remain fully responsible for the content and accuracy of the manuscript.

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