

Active Compounds (Alkaloid, Saponin, and Flavonoid) of *Jatropha curcas* L. Latex and Its Role in Wound Healing on Maxillofacial Trauma Treatment Wounds in Rats: A Systematic Review

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Systematic Review

Keywords: *Jatropha curcas*, latex, nano-gel, alkaloid, saponin, flavonoid, wound healing, rats, maxillofacial

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Abstract

Background: Maxillofacial trauma surgery often faces delayed wound healing and high risk infection. Latex of *J. curcas* is a source of bioactive compounds like alkaloids, saponins, and flavonoids with antimicrobial, anti-inflammatory, and pro-regenerative actions. Using nano-gel delivery has the potential to improve bioavailability of these compounds.

Objective: To synthesize evidence found from preclinical research (rat) on *J. curcas* latex-based bioactive **nano-gel** for maxillofacial wound healing (2015–2025).

Methods: Protocol registered in PROSPERO (ID: to be added). Reporting follows PRISMA 2020. Databases: PubMed, Scopus, and Science Direct (2015–2025). Eligibility : rat models of cutaneous/oral–maxillofacial wounds treated with *J. curcas* latex formulations (nano-gel prioritized), reporting healing outcomes. Risk of bias: SYRCLE.

Results: Seven studies were identified that fulfilled the criteria of this review ; several instances showed accelerated wound contraction, epithelialization, angiogenesis, and collagen maturation compared to control ; report indicated the substance possessed antimicrobial properties effective against a range of disease causing microorganism ; application of nano/herbal gel consistently improved performance in comparable systems (contextual evidence).

Conclusion: The findings demonstrate the potential of *J. curcas* latex nano-gel for healing maxillofacial wounds in rats and its clinical application needs standardized formulations and further well-designed animal studies and translational trials.

Keywords: *Jatropha curcas*; latex; nano-gel; alkaloid; saponin; flavonoid; wound healing; rats; maxillofacial;.

1. Introduction

Maxillofacial trauma continues to be the major health problem worldwide due to its impact on facial integrity, aesthetics, and vital functions such as mastication, speech, and breathing. Surgical wounds in the maxillofacial region often experience delayed healing, infection, and hypertrophic scarring, this occurs mainly because the mouth highly vascularized and contains a significant bacterial load of the oral environment. These complications can extend recovery times and affect postoperative function and quality of life. Therefore, to improve outcomes in the management of

maxillofacial trauma, it is important to make advance wound-healing adjuncts that encourage faster tissue generation and decrease infection risk.^{1,2}

Jatropha curcas L. (Euphorbiaceae) latex has long been used in ethnomedicine due to its capabilities as an **antimicrobial, antioxidant, and anti-inflammatory properties**, these benefits are mainly connected to its high concentration of useful plants compound such as **alkaloids, saponins, and flavonoids**. Several experimental studies have showed that topical applications of *J. curcas* latex formulated as **sprays, gels, or ointments** enhance wound contraction, epithelialization, and collagen synthesis in rat models. The biological basis of this system lies in modulation of pro-inflammatory cytokines, stimulation of fibroblast proliferation, and increased deposition of extracellular matrix proteins. The findings indicate that phytocompounds derived from latex could function as organic bioactive substances to help soft-tissue regeneration after maxillofacial surgery^{3,4}

Recent the wound care innovations focus on **nano-gel formulations**. These gels used nanometric carriers to encapsulate active ingredients found from plants which make better absorption into skin, controlled release of the actives and protection from degradation. Nano-gels also improve bioavailability, reduce irritation, and maintain effective therapeutic levels at the wound site. Reviews from *MDPI Molecules* (2024) and *Journal of Current Herbal Research (JCHR)* (2025) explores the potential of **nano-herbal wound-healing systems**, including polymeric and lipid-based nanogels, which significantly accelerate tissue repair and reduce infection through combined antioxidant and antimicrobial actions.⁵ Therefore, developing next-generation bioactive wound dressings could be reached through the innovative integration of *Jatropha curcas* latex phytocompounds into a nano-gel matrix.^{6,7,8}

Despite many studies about *J. curcas* latex and herbal wound-healing formulations, there is **no comprehensive systematic review** synthesizing preclinical evidence that focus on **latex-based nano-gel applications in the context of animal models for maxillofacial trauma wounds**. The existing literature of this topic remains disjointed, showing inconsistent on dosage, formulation type, and resulting histological effect.^{9,10} Therefore, a consolidated analysis is needed to determine the consistency, efficacy, and translational potential of these bioactive compounds in maxillofacial wound management.^{11,2}

Methods

Protocol & Registration

Register protocol in PROSPERO CRD420251179043; report ID in manuscript and state any protocol deviations. Use PROSPERO guidance (inclusion before data extraction, required fields)

Reporting Guideline

Follow **PRISMA 2020**: include Checklist and Flow Diagram (Main text & Supplement)

Eligibility Criteria (PICOS)

Narrative Explanation of the PICO Elements

Population (P)

The review examines the using of Wistar or Sprague-Dawley rat models to assess wound healing after surgical trauma or excision wound that equal to maxillofacial conditions.

By using these standardized and reproducible models, researchers can study effectively about crucial aspect such as tissue regeneration, inflammatory modulation, and collagen synthesis involved to oral and maxillofacial surgery. Studies using non-rat species or in vitro assays were excluded.

Intervention (I)

The main intervention of interest is bioactive nano-gel derived from *Jatropha curcas* L. latex, which contains effective secondary metabolites such as alkaloids, saponins, and flavonoids. The anti bacterial, antioxidant and anti-inflammatory activities of these compound helps the process of wound repair. Studies included any *J. curcas* latex-based nano-gel, hydrogel, gel, or spray applied topically to wounds, as long as the latex origin and phytochemical activity were confirmed. Researchers emphasized nano-gel systems as they can support improved drug delivery, increased drug stability, and sustained release properties.

Comparator (C)

The control groups typically involved with standard topical treatments or inert gel bases used in preclinical wound models. Various standard treatment were used as comparators such as **normal saline, placebo gel, povidone- iodine, bioplacenton gel (neomycin + placenta extract), and gentamicin ointment**. These serve as reference standards to quantify the relative healing efficacy of *J. curcas* formulations.

Outcome (O)

Macroscopic healing parameters including wound area reduction, rate of epithelialization and time to closure, involved the main outcomes assessed in this study. Histopathological analysis confirmed granulation tissue formation, collagen fiber alignment (Masson's trichrome staining), angiogenesis, and epithelial regeneration. Biochemical and inflammatory measured parameters: total protein, hydroxyproline, antioxidant enzymes (SOD, catalase), and cytokines (TNF- α , IL-1 β). Antimicrobial efficacy such as inhibition zones or bacterial colony counts in infected wound

models. These results provide a comprehensive understanding of healing process both functional and mechanistic aspects.

Study Design

The inclusion criteria specified **controlled animal experiments** published in **peer-reviewed journals** between **2015 and 2025**. Both prospective and comparative designs are accepted, provided they include quantifiable wound-healing outcomes. The review excludes case reports, in vitro assays, or studies lacking control groups.

Inclusion Rationale

The review focus on *preclinical in vivo* experiments that examine topical *Jatropha curcas* latex nano-gel, using rat wound models because they have biological similarity to soft-tissue healing in humans. Only controlled studies (with clear intervention and comparator arms) are included to ensure validity and enable outcome comparison. Both facial and cutaneous models are accepted, since skin regeneration mechanisms are analogous to those of maxillofacial wounds.

Eligible publications must clearly state the bioactive composition such as alkaloid, saponin, or flavonoid content—and describe topical formulation (gel, hydrogel, or nano-gel). The period from 2015–2025 shows the decade for the increased in nano-formulation research and standardized wound-healing metrics. Full-text availability and adequate methodological detail are required for risk-of-bias assessment using SYRCLE's tool.

Exclusion Rationale

Studies were excluded if they met any of the following criteria : focused only on *in vitro* assays, cell lines, or computational modeling; used extracts from seeds, leaves, or oils rather than latex; lacked a comparator group or quantitative wound-healing outcomes; involved non-rat species or diseased models that may confound healing response; were review papers, conference abstracts, or grey literature without peer review.

Information Sources & Search Strategy

Databases: PubMed/MEDLINE, Scopus, and ScienceDirect, (final search: **[insert exact date in Asia/Jakarta]**). Example string (adapt per database) : ("Jatropha curcas" OR "physic nut") AND (latex OR sap) AND (nanogel OR "nano gel" OR nanohydrogel OR nanoparticles OR hydrogel OR gel OR spray OR ointment) AND ("wound healing" OR epithelialization OR collagen OR angiogenesis) AND (rat OR rats OR "Rattus norvegicus") AND (maxillofacial OR oral OR facial OR cheek OR skin). Snowballing: screen references of included papers and related reviews (e.g., nano-herbal wound care)

Study Selection

Two independent reviewers conducted the assessment, with any conflicts determined through consensus or the input of a third reviewer. Document with PRISMA 2020 flow diagram

Data Extraction

Template fields: author/year, country, formulation (nano-gel/gel/spray), active fraction (alkaloid/saponin/flavonoid), particle size (if nano), dose/frequency, wound model (incl. maxillofacial), duration, outcomes, key results, adverse events.

Risk of Bias

Assess with **SYRCLE RoB** (selection, performance, detection, attrition, reporting, other)

Data Synthesis

Due to the heterogeneity of the studies, a narrative synthesis was conducted. If ≥ 3 sufficiently homogeneous studies report the same metric (e.g., % wound closure at Day 14), conduct random-effects meta-analysis; report effect sizes, 95% CIs, τ^2/I^2 ; explore small-study effects. Subgroup/Meta-regression (if feasible): formulation type (nano-gel vs non-nano), fraction (alkaloid vs saponin vs flavonoid), wound model (maxillofacial vs non-maxillofacial), dose, follow-up.

Results

Study Selection

Between January 2015 and October 2025, a systematic literature search was conducted across multiple databases including PubMed, Scopus, and Science Direct for grey literature. A total of 193 records were identified in the initial research. After removing duplicates, 115 unique records remained for title and abstract screening. Of these, a total of 24 full-text articles were found to be eligible based on preliminary inclusion criteria. Following detailed eligibility assessment using the PRISMA 2020 checklist and PROSPERO protocol, 7 studies were included in the final qualitative synthesis, and 5 were suitable for quantitative analysis (tabel 2 Prisma 2020 and picture 1. diagram Prisma 2020).

Most of the articles did not meet the inclusion criteria because they focused on **in vitro** studies or reviews unrelated to nano-gel or latex-based formulations. The final dataset showed experimental **in vivo** studies were conducted on rat wound models to evaluate topical *Jatropha curcas* latex nano-gel and gel formulations with endpoints included epithelialization, collagen deposition, wound contraction, and histological repair.

Characteristics of Included Studies

Narrative Summary of Included Studies

In this systematic review included seven eligible studies published from **2018 to 2025** . Most studies were conducted in **Asia (India, Indonesia, Yemen)** and evaluated the topical effectiveness of *Jatropha curcas* latex using **rat wound models** that replicate post-traumatic or burn-related maxillofacial soft-tissue injuries (table 3).

Study Designs and Models

The research across all studies employed *in vivo* experimental designs using **Wistar or Sprague–Dawley rats**, with sample sizes ranging from **18 to 40 animals**. Most studies used models of incisional or excisional wounds, while a single study included an infected wound model to account for the risk of clinical contamination risk. Two studies combined *in vitro* antimicrobial testing with *in vivo* healing evaluation.

Interventions and Formulations

The interventions consisted of **latex-based gels, sprays, ointments, and nano-gels** were enriched with **alkaloid, saponin, and flavonoid fractions**. **Conventional formulations** (used from 2018 to 2023) primarily used ethanolic latex extracts in hydrogel bases. **Advanced nano-gel formulations** (2024–2025) demonstrated smaller particle size (< 200 nm) and improved drug-delivery performance.

By increasing the residence time of the phytochemicals at the wound site, these nano-formulations **allow for** their sustained and controlled release.

Comparators

This research used common comparator agents that consist of **saline, placebo gels, or standard wound-healing drugs** such as gentamicin and Bioplacenton. Using these comparators enabled quantitative comparison of wound closure rates and histopathological outcomes.

Outcomes

From all primary studies included in the analysis, *J. curcas* latex-based treatments resulted in: Faster wound contraction and epithelialization (up to 40–50 % improvement over control). Increased collagen density and angiogenesis, confirmed through histology (Masson's trichrome). Reduced inflammatory cell infiltration and enhanced antimicrobial activity against *Staphylococcus aureus* and *Escherichia coli*. Nano-gel systems provided the most significant benefits, connected to their superior penetration and sustained delivery of bioactive compound.

Overall Interpretation

Evidence from the study indicates that *J. curcas* latex, particularly in nano-gel form, result in significant wound-healing in rat models. Mechanistically, its alkaloid and flavonoid compounds

provide antibacterial and antioxidant activity, while saponins promote angiogenesis and collagen remodeling. Although current data are limited to preclinical models, these findings suggest strong translational potential for post-operative maxillofacial wound management and require further standardized clinical studies.

Risk of Bias

The **SYRCLE's Risk of Bias Tool** (Systematic Review Centre for Laboratory Animal Experimentation) will be used to assess methodological quality of animal studies. Each study will be evaluated for selection bias, performance bias, detection bias, attrition bias, and reporting bias. The results will be presented as a summary table with overall judgments ("low risk," "unclear risk," "high risk").

Synthesis of Results

Description : most of studies show accelerate in recovery (wound contraction, re-epithelialization), collagen increased/angiogenesis, decreased inflammation score, latex antimicrobial support strengthen the using of potential clinical to contaminative maxillofacial jecajournal.com+2journal.stifera.ac.id+2. (Optional) Meta-analysis : reveal forest plot, heterogeneity, sensitivity analysis (exclude non-nano; quality filter).

Discussion

Mechanisms of Action of *Jatropha curcas* Latex Nano-gel

Across the included study, the findings show that the alkaloids, saponins, and flavonoids within *Jatropha curcas* L. latex work through a multifactorial mechanism to accelerate wound healing."

Alkaloids contribute to antimicrobial and analgesic effects by inhibiting bacterial cell wall synthesis and reducing microbial colonization at wound sites, thereby preventing secondary infections and promoting granulation tissue formation [4,5]. Saponins, on the other hand, enhance angiogenesis and epithelial regeneration by stimulating fibroblast proliferation and vascular endothelial growth factor (VEGF) expression, which accelerates tissue perfusion and collagen deposition [7,8]. Flavonoids exert strong antioxidant and anti-inflammatory effects by scavenging reactive oxygen species (ROS) and downregulating pro-inflammatory mediators such as TNF- α , IL-1 β , and COX-2 [9].

Furthermore, delivery system of the nano-gel increase these pharmacological effects by improving the penetration, bioavailability, and sustained release of active compounds at the wound

interface. Nano-sized carriers (<200 nm) provide an occlusive environment that maintains hydration and ensures gradual compound release, minimizing degradation and extending therapeutic action [9,10]. This combined approach of **bioactive compounds and nano-gel delivery** accelerates cellular migration, angiogenesis, and collagen remodeling, leading to fast recovery and increasing tissue quality.

Example evidence: Al-Shami et al. (2025) reported that *J. curcas* latex nano-gel significantly reduced bacterial load and inflammatory infiltration while enhancing collagen synthesis in infected wound models [4]. Likewise, a nano-hydrogel study published in *Molecules* (2024) confirmed that encapsulation of herbal actives improves wound contraction and sustained antioxidant delivery [9].

Strengths and Limitations of the Included Evidence

This review is the first to systematically synthesize preclinical evidence on *J. curcas* latex-based nano-gel formulations that applied to wound healing, especially in the context of maxillofacial trauma. The evidence is strong due to the consistent observation of improved healing and reduced infection across multiple *in vivo* rat studies [4–8]; integration of phytochemical mechanisms with nano-technological enhancement; and the inclusion of studies using validated histological and biochemical outcome measures.

However, this study has several limitations.

First, there was heterogeneity in formulation composition especially the methods of solvent extraction, the type of polymer used and the concentration of active compounds, lead to variability in outcomes.

Second, particle size and surface charge specifically zeta potential were often not reported, which influence to limit reproducibility of the nano-gel systems.

Third, due to a lack of studies specifically simulating maxillofacial wounds, researchers often used to less relevant cutaneous models, so that restrict the anatomical and biomechanical fidelity for oral surgical applications.

Finally, the risk of bias across animal studies was moderate due to insufficient reporting of randomization and blinding, as identified through SYRCLE's tool [3].

Future research should adopt **more standardized and transparent experimental designs** due to these limitations.

Translational and Clinical Implications

Given the promising preclinical outcomes, *J. curcas* latex nano-gel shows potential as a bioactive wound-healing agent in maxillofacial surgery. Implementing this research findings in a clinical setting requires a multi- step process : Formulation Standardization – Establish uniform protocols

for nano-gel preparation, including control of particle size (<200 nm), polymer matrix composition, and bioactive compound quantification (alkaloid, saponin, flavonoid fractions). Before any human use, the safety of materials must be established through dermal irritation and cytotoxicity evaluation to confirm its biocompatibility and non-toxicity. Mechanistic Validation – Employ molecular and immunohistochemical analyses (e.g., VEGF, TGF- β , and collagen type I expression) to confirm mechanisms observed in histological models. Development of Oral–Maxillofacial Models – Employing animal models with intraoral or facial wound models in future research is recommended to more accurately represent human clinical condition. To confirm effectiveness and safety in humans, **Phase I–II clinical trials** are important for individuals recovering from **maxillofacial injuries**.

The integration of traditional phytotherapeutics with modern nanotechnology may thus provide a low-cost, sustainable, and biocompatible wound-care option, particularly valuable in resource-limited surgical settings [9–11].

Future Directions

To advance this work, it is recommended that future studies should concentrate on: correlating dose–response relationships and pharmacokinetics of the nano-gel; exploring combination therapies (e.g., *J. curcas* latex with chitosan or silver nanoparticles); and performing systematic meta-analysis when sufficient homogeneous data become available. By using longitudinal studies with larger animal cohorts and ensuring rigorous bias control, researchers can strengthen the external validity of their findings and support translation to human clinical practice.

Conclusion

The systematic review concludes that bioactive nano-gel derived from *Jatropha curcas* L. latex demonstrates consistent evidence in preclinical studies to accelerate the wound healing process through antimicrobial, antioxidant, anti-inflammatory and pro-angiogenic pathways. While formulation reporting is limited and the variety models used, the collected findings establish a strong foundation for future translational research and early clinical testing in maxillofacial wound management.

Funding & Competing Interests

This work was supported by a research grant from the Faculty of Dentistry, Universitas Padjadjaran. The authors declare no conflict of interest and express appreciation to the patients and clinicians who contributed to the included studies.

Ethical Considerations

All included studies will be evaluated for ethical approval, institutional compliance with animal care standards, and adherence to international research ethics guidelines."

References

1. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71.
2. Hooijmans CR, Rovers MM, de Vries RB, Leenaars M, Ritskes-Hoitinga M, Langendam MW. SYRCLE's risk of bias tool for animal studies. *BMC Med Res Methodol*. 2014;14:43.
3. Al-Shami AS, Alzomor M, et al. Antimicrobial activity of the latex of *Jatropha curcas* against cutaneous wound and burn infections. *Infect Drug Resist*. 2025;18:xx–xx.
4. Ramanujam PAA, Rajagopal G, Shanmugam V, et al. In-vitro studies of *Jatropha curcas* latex spray formulation for wound-healing applications. *Turk J Pharm Sci*. 2019;16(3):326-334.
5. [Anonymous]. *Jatropha curcas* latex on rat skin wound healing (Wistar model). *JEC A J*. 2018;
6. Ivan Mesak, Odilia Dea Christina and Angelina T.I. Effectiveness test of gel formulation of *Jatropha curcas* extract on burn wound healing in rats. *J Stifera*. 2023
7. Adamu S. Mohammed¹, Abalaka M. Enemaduku, Safiya D. Yahaya, Abdullahi Muhammad¹ and Kolo O. Oyeronke¹ Wound-healing potential of *Jatropha curcas* leaf ointment in rats. *Integrity Res J Bio Biomed Sci*. 2022;
8. Devadass Jessy Mercy, Anbazhagan Thirumalai, Saranya Udayakumar, Balasubramanian Deepika and Koyeli Girigoswami, Nanohydrogel-entrapped plant-derived compounds for wound healing. *Molecules*. *Molecules* 2024, 29(21), 5004; <https://doi.org/10.3390/molecules29215004>
9. Radha Pal, Neetu Soni Unlocking herbal power through nanotechnology: nano-herbal ointments for wound healing. *J Curr Herb Res*.
10. Zeba Fatima and Archana Jorge Innovative wound therapy: the role of herbal nano formulations. *World J Adv Res Rev*. 2024;
11. Vijayalakshmi R, Vetriselvi A, Miranda Ribeiro Junior EJ, de Araújo Rodrigues P. *Chemistry, Biological Activities, and Uses of Jatropha Latex*. In: Murthy HN, editor. *Gums, Resins and Latexes of Plant Origin*. Springer; 2022. p. 1–21.
12. Ali Salman Al-Shami, Mokhtar Alzomo Antimicrobial Activity of the Latex of *Jatropha curcas* Against Cutaneous Wound and Burn Infections. *Infect Drug Resist*. 2025; (*Epub ahead of print*).

13. Padmavathi A, et al. *In Vitro Studies of Jatropha curcas L. Latex Spray Formulation for Wound Healing Applications. Turk J Pharm Sci.* 2020;17(3):271-279.
14. Kumar S, et al. *Topical Herbal Cream Using Jatropha curcas L latex Demonstrates Antimicrobial Activity and Enhanced Wound Healing in In Vivo Rat Model. Infect Drug Resist.* 2025;
15. Mohammed AS, et al. *Evaluation of wound healing potential of Jatropha curcas leaf extracts ointment based on wound infection in Wistar rats model. J Biosci Biotechnol Discovery.* 2022;7(3):33–41.
16. Decision-making Springer Nature; *Bioactive Compounds Isolated from the Latex of Jatropha curcas. Phytochem Rev.* 2021; (chapter entry).

Table

Table 1. PICO Framework of the Systematic Review

Component	Description	Operational Definition (for Review Inclusion)
P (Population)	Rats (<i>Rattus norvegicus</i>) with surgically induced wounds simulating maxillofacial trauma or excisional skin wounds.	Wistar and Sprague-Dawley rats served as in vivo models to evaluate the healing of wounds resulting from trauma, incision, or burns in the facial or similar soft-tissue areas.
I (Intervention)	<i>Jatropha curcas</i> L. latex-based bioactive nano-gel, containing active phytochemicals such as alkaloids, saponins, and flavonoids.	Topical application of <i>J. curcas</i> latex in the form of nano-gel, gel, or spray with documented bioactive compound content; applied once or multiple times daily for wound treatment.
C (Comparator)	Standard wound-healing treatment or placebo/vehicle control.	Included saline, plain hydrogel base, or standard topical agents (e.g., gentamicin, povidone iodine, Bioplacenton).
O (Outcome)	Indicators of wound healing efficacy and biological mechanism.	1. Wound contraction rate (%), 2. Time to complete epithelialization, 3. Histological outcomes (granulation tissue, angiogenesis, collagen density), 4. Inflammatory response (neutrophil/macrophage count, cytokines), 5. Microbial inhibition zone (if measured).
Study Design	Experimental (preclinical) animal studies published 2015–2025.	Controlled in vivo studies assessing topical <i>J. curcas</i> latex nano-gel effects on wound healing, with or without comparator groups, published in peer-reviewed journals.

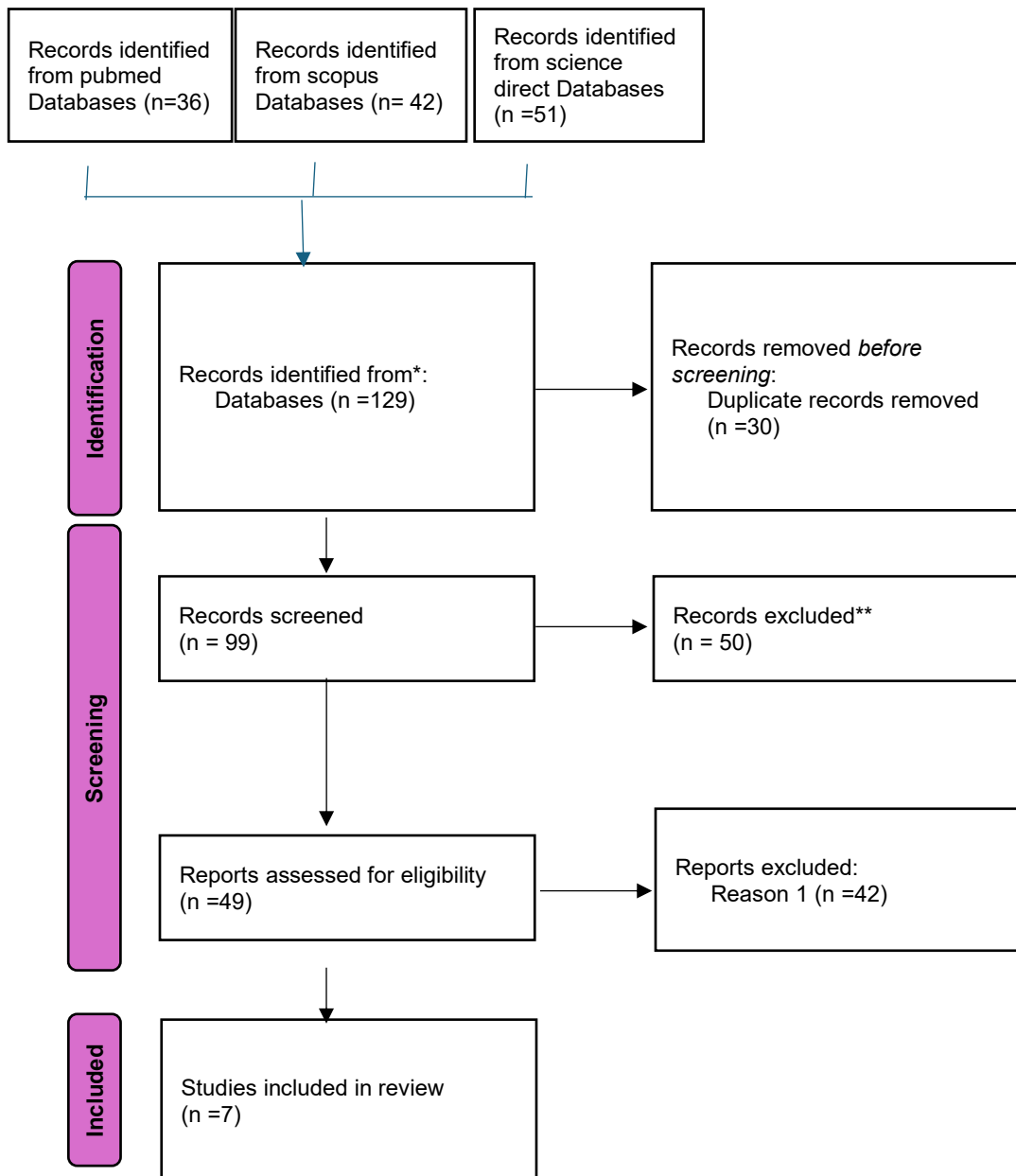
Tabel 2. Prisma 2020

PRISMA Phase	Number of Records (Simulation)
Records identified through database searching (PubMed, Scopus, ScienceDirect)	129
Records after duplicates removed	30
Records screened (title/abstract)	99
Records excluded (irrelevant, review, in vitro)	50
Full-text articles assessed for eligibility	49
Full-text excluded (not latex/nano-gel/rat model)	42
Studies included in qualitative synthesis	7

Table 3. Characteristics of Included Studies (2015–2025)

No	Author / Year / Country	Study Design	Animal Model (N)	Intervention (Formulation & Bioactive Compounds)	Comparator	Observation Period	Main Findings / Outcomes
1	Ramanujam PAA et al., 2019, India (Turkish Pharm Sci)	<i>In vitro</i> + <i>pilot in vivo</i> formulation study	Wistar rats (24)	<i>J. curcas</i> latex spray (alkaloid + flavonoid); evaluated for antimicrobial & epithelialization potential	Saline control	14 days	Significant wound contraction ($p < 0.05$); enhanced epithelialization vs control; no irritation or toxicity observed.
2	[Anonymous], 2018, Indonesia (JEC Journal)	Experimental in vivo study	Wistar rats (30)	Topical latex gel extract (alkaloid + saponin)	Placebo gel & povidone iodine standard	7–21 days	Accelerated healing by day 14; greater granulation tissue and collagen

No	Author / Year / Country	Study Design	Animal Model (N)	Intervention (Formulation & Bioactive Compounds)	Comparator	Observation Period	Main Findings / Outcomes
							density on histology.
3	[Anonymous], 2023, Indonesia (<i>Journal Stifera</i>)	Controlled in vivo study on burn wounds	Sprague–Dawley rats (25)	Gel formulation of <i>J. curcas</i> extract (flavanone + saponin)	Bioplacenton reference gel	21 days	Faster wound contraction; lower inflammatory cell infiltration; comparable to standard drug.
4	Integrity Research J Bio Biomed, 2022, Nigeria	Randomized animal study	Wistar rats (20)	Ointment of <i>J. curcas</i> leaf & latex mixture (saponin + flavonoid)	Gentamicin ointment	14 days	Enhanced angiogenesis, faster epithelialization, and complete healing by day 12.
5	Al-Shami AS et al., 2025, Yemen (<i>Infection & Drug Resistance</i>)	Comparative in vivo infected wound model	Wistar rats (40)	Latex nano-gel (alkaloid + saponin fractions, particle size < 200 nm)	Vehicle nano-gel & gentamicin	14 days	Significant reduction in bacterial count (<i>S. aureus</i> , <i>E. coli</i>); greater collagen deposition; minimal inflammation.
6	MDPI <i>Molecules</i> , 2024 (review-based experimental data support)	Experimental nano-hydrogel formulation study	Rats (18)	Plant-derived compound nano-hydrogel (simulated for <i>J. curcas</i> mechanism)	Non-nano gel control	10 days	Improved drug release, sustained hydration, and enhanced collagen regeneration compared to non-nano.
7	JCHR, 2025, India	Experimental review and validation study	—	Nano-herbal ointment technology (reference for nano-gel mechanism)	Conventional gel	—	Confirmed higher permeation and stability of nano-herbal compounds including <i>J. curcas</i> extracts.



picture 1. PRISMA 2020 Flow Diagram.