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INPLASY

Agarwood (chenxiang; Aquilaria and Gyrinops spp.) for skin wound and burn repair: a systematic review of preclinical and clinical evidence, bioactive constituents and engineered delivery systems

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ADMINISTRATIVE INFORMATION

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 November 2026 and was last updated on 27 November 2026.

INTRODUCTION

Review question / Objective We conducted a systematic review with three questions. RQ1: what preclinical and clinical evidence shows that Aquilaria- or Gyrinops-derived materials promote skin wound or burn repair, and through which mechanisms? RQ2: which engineered delivery systems and biomaterials have been developed for these materials, how were they characterized, and how did they perform? RQ3 (secondary, constituent level): what in vivo evidence shows that β-caryophyllene and mangiferin promote wound or burn repair or limit scarring? We then used the findings to derive design and evaluation criteria for agarwood-based burn dressings, treating agarwood as a test case for engineering a traditional Chinese herbal medicine into a wound-repair biomaterial..

Rationale Burns remain a major global health problem.

Agarwood (chenxiang, gaharu, oud) is the resin-impregnated wood that Aquilaria and Gyrinops trees (Thymelaeaceae) form after wounding or microbial infection.
Narrative reviews often describe agarwood as a promising wound-healing agent, but none has appraised the primary evidence systematically..

Condition being studied Agarwood (chenxiang), a Chinese herbal medicine, and other Aquilaria and Gyrinops materials are often proposed for wound repair, but this evidence has not been appraised systematically. We reviewed preclinical and clinical evidence for these materials in skin wound and burn repair, their engineered delivery systems, and in vivo wound evidence for two constituents, β-caryophyllene and mangiferin.We reviewed preclinical and clinical evidence for materials in skin wound and burn repair, their engineered delivery systems, and in vivo wound evidence for two constituents, β-caryophyllene and mangiferin.skin wound or burn repair..

METHODS

Search strategy Databases: OpenAlex (OpenAlex, 2026) and PubMed
For RQ3, PubMed was searched with caryophyllene AND (wound* OR burn* OR scar* OR reepitheli* OR re-epitheli*) and with the same string for mangiferin..

Participant or population RQ1: efficacy and mechanisms
In vivo animal models of skin wounds (excision, incision, burn, diabetic or infected), scars, skin inflammation or topical irritation and sensitization; ex vivo skin and skin equivalents; keratinocytes and dermal fibroblasts with repair-relevant outcomes; humans with wounds, burns or scars
RQ2: delivery systems and biomaterials
Any, with or without biological testing
RQ3: constituent level (secondary)
In vivo skin wound, burn or scar models.

Intervention RQ1: efficacy and mechanisms
Any material derived from Aquilaria or Gyrinops (resinous wood, wood, leaves, bark, branches, flowers, fruits, seeds, roots, and their essential oils, distillates, extracts, fractions or isolated compounds), alone or formulated; topical application required for non-wound in vivo models
RQ2: delivery systems and biomaterials
Engineered delivery system or biomaterial (e.g., hydrogel, nanoemulsion, nanoparticle, nanofiber, film, patch, dressing) or conventional topical vehicle loaded with such material
RQ3: constituent level (secondary)
β-Caryophyllene or mangiferin from any source as the only active, alone or in an inert carrier.

Comparator RQ1: efficacy and mechanisms
Any (vehicle, untreated, positive control) or none
RQ2: delivery systems and biomaterials
Any (blank carrier, free payload) or none
RQ3: constituent level (secondary)
Any or none.

Study designs to be included Primary studies of any design (in vivo, ex vivo, in vitro, clinical).

Eligibility criteria RQ1: efficacy and mechanisms
E1, material not from Aquilaria or Gyrinops; E2, model neither skin-relevant nor a delivery system (including pure antimicrobial screening); E3, outcome not relevant to repair (whitening, fragrance chemistry, plant biology) or carrier designed solely for food, fragrance or commodity use without biological testing; E4, reviews, theses, conference abstracts, patents and preprints; E5, phytosynthesized inorganic nanoparticles in which the extract served only as a reducing agent, unless tested on skin; E6, duplicate reports; E7, insufficient information; E8, retracted reports
RQ2: delivery systems and biomaterials
As for RQ1
RQ3: constituent level (secondary)
Compound combined with other actives (e.g., silver, antibiotics, exosomes, other phytochemicals); in vitro only; non-wound models (e.g., chemically induced skin inflammation); insufficient information to confirm the compound as the only active.

Information sources OpenAlex (OpenAlex, 2026) and PubMed were searched from inception to 22 November 2026. OpenAlex was chosen because it indexes many regional and open-access journals and conference proceedings from the countries where agarwood is produced. Europe PMC was planned but could not be queried because of repeated access failures, and Scopus, Web of Science, Embase and CNKI were not available to the review team. Searches combined an agarwood block (aquilaria, agarwood, gaharu, gyrinops) with a wound and skin block (wound, burn, scar, ulcer, healing, cicatrix, skin, cutaneous, dermal, dermatitis, epidermal, keratinocyte, HaCaT, fibroblast, re-epithelialization, psoriasis, eczema, atopic) and a delivery and formulation block (nanoemulsion, emulsion, nanoparticle, nanocapsule, liposome, encapsulation, hydrogel, dressing, nanofiber, electrospun, scaffold, transdermal, ointment, cream, gel, topical, patch, film). Because the interfaces limit query length, the Boolean string was split into partitions that shared the agarwood block, and the results were merged; the union of the partitions is logically equivalent to the full string. OpenAlex queries were applied to titles and abstracts. PubMed queries used All Fields, which also triggers automatic term mapping. Exact strings, run dates, interface hit counts and exported records for every partition are reported in Supplementary Table S1..

Main outcome(s) RQ1: efficacy and mechanisms
Primary: wound closure, healing time, re-epithelialization, histological repair, scar outcomes, burn healing.
RQ2: delivery systems and biomaterials
Structure and morphology, physicochemical properties, loading, release or skin permeation, stability, sterility, fluid handling, cytocompatibility, bioactivity, skin- or wound-relevant testing, in vivo testing
RQ3: constituent level (secondary)
Wound closure, re-epithelialization, histology, inflammatory, angiogenic and matrix markers, scar or flap outcomes.

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Additional outcome(s) RQ1: efficacy and mechanisms
Secondary: inflammatory, oxidative, angiogenic and matrix markers; skin-cell viability, proliferation and migration; antimicrobial activity of dressings; material properties; safety
RQ2: delivery systems and biomaterials.

Data management Data were extracted into a structured sheet covering bibliographic details, country and funding; species, plant part, preparation, solvent and standardization; formulation or carrier, composition and physicochemical data; model, species, sex, group size, wound induction, treatment regimen and duration; comparators; outcomes with direction and magnitude; and safety. Reports describing the same experiments were linked and counted as one study. Missing information was recorded as not reported, and authors were not contacted..

Quality assessment / Risk of bias analysis Animal studies were assessed with the SYRCLE risk-of-bias tool (Hooijmans et al., 2014), the controlled human study with ROBINS-I (Sterne et al., 2016), and in vitro and ex vivo skin studies with the in vitro module of ToxRTool, which assigns reliability categories from 1 (reliable without restriction) to 4 (not assignable) (Schneider et al., 2009). The reporting of delivery systems was mapped against 12 domains derived from the MIRIBEL standard for bio-nano research (Faria et al., 2018) and from wound-dressing requirements: payload identity and standardization; structure, size and morphology; physicochemical properties; loading or encapsulation; release or skin permeation; storage or cycling stability; sterility; fluid handling; cytocompatibility with a blank-carrier control; bioactivity; skin- or wound-relevant testing; and in vivo testing. Each domain was scored as reported, partially reported or not reported, and a completeness score was calculated as (reported + 0.5 × partially reported)/ 12..

Strategy of data synthesis Because models, materials and outcomes were heterogeneous and no outcome was measured in comparable models by three or more studies, meta-analysis was not performed, as specified in the protocol. Studies were grouped by question, then by model (in vivo wound or burn; topical in vivo non-wound; skin cells and ex vivo skin; delivery systems) and by material (leaves; resinous wood or heartwood; essential oil or distillate). The direction of effect for each outcome was tabulated against the study's vehicle or untreated control; we did not vote-count on p-values. Evidence directness was graded as Level A (agarwood material in an in vivo wound or burn model or in human wounds), Level B (agarwood material in skin cells, ex vivo skin or a topical in vivo non-wound model), Level C (delivery system or material characterized without skin or wound testing) and Level D (constituent from a non-Aquilaria source; RQ3). Certainty was judged qualitatively from risk of bias, indirectness, imprecision and inconsistency. Risk of bias due to missing results was not assessed formally because no quantitative synthesis was performed; selective outcome reporting was judged within the risk-of-bias tools..

Subgroup analysis Not applicable.

Sensitivity analysis Not applicable.

Language restriction Targeted web searching in English, Indonesian, Malay and Chinese.

Country(ies) involved Romania.

Keywords agarwood, Aquilaria, burn wound, wound dressing, drug delivery system, β-caryophyllene, mangiferin, traditional Chinese medicine.

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