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Review

Pequi (*Caryocar* spp.) Oil as an Antimicrobial and Antibiotic-Modifying Natural Product Against *Staphylococcus aureus*: A Scoping Review and Research Agenda for Plasma Activation

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Abstract

Pequi oil, obtained from *Caryocar* species, is a Brazilian natural product with reported antimicrobial activity, but the pathogen-specific evidence for fruit-derived fixed oil against *Staphylococcus aureus* remains incompletely characterised. This scoping review followed the Joanna Briggs Institute (JBI) methodology and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR). PubMed, Embase, MEDLINE via the Virtual Health Library (VHL), Web of Science, and Scopus were searched without language or date restrictions; plasma-treated oil and lipid studies were mapped separately as contextual evidence. Four in vitro studies met the inclusion criteria. All evaluated *C. coriaceum* from Ceará, Brazil, all share authors, and none evaluated fruit-derived *C. brasiliense* fixed oil with a clearly stated species and fruit fraction. Intrinsic activity against *S. aureus* was weak to moderate (minimum inhibitory concentration, MIC, 512 to ≥1024 µg/mL), and biofilm evidence, based on crystal-violet biomass and high-concentration oil preparations (10–100 mg/mL test solutions), came from a single study. Two studies with overlapping authors reported reductions in aminoglycoside MICs in the presence of oil (50–99.8% in one report), without fractional inhibitory concentration indices (FICIs) from checkerboard assays. Three studies used solvent-assisted extraction without residual-solvent data. No study evaluated plasma-activated *Caryocar* oil. Plausible mechanisms, untested for pequi oil, include membrane disruption by free fatty acids, inhibition of bacterial fatty-acid synthesis and altered aminoglycoside uptake; plasma activation could add lipid-derived oxidants, but this remains a hypothesis. Current evidence supports pequi oil only as a candidate antibiotic adjuvant, not as a stand-alone antibacterial. Solvent-free extraction, chemical standardisation, checkerboard/FICI testing, and comparator-controlled evaluation of plasma activation are priorities for pharmaceutical development.

Keywords: *Caryocar coriaceum*; natural products; *Staphylococcus aureus*; antimicrobial adjuvant; aminoglycosides; plasma-activated oil; residual solvents; scoping review

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1. Introduction

Antimicrobial resistance (AMR) is one of the most pressing challenges in contemporary public health. Misuse and overuse of antibiotics have accelerated the emergence and dissemination of resistant bacteria, progressively reducing therapeutic options for both common and severe infections [1,2]. In 2024, the World Health Organization (WHO) updated

its Bacterial Priority Pathogens List (BPPL), in which methicillin-resistant *Staphylococcus aureus* (MRSA) is classified in the high-priority group [3].

S. aureus is a Gram-positive bacterium associated with a broad range of infections, from skin and soft-tissue conditions to bacteraemia, pneumonia, endocarditis, and osteomyelitis [4,5]. Its capacity to form biofilms promotes adhesion to tissues and implanted devices, facilitates immune evasion, and reduces susceptibility to antimicrobials, thereby contributing to chronic and difficult-to-treat infections [6]. The growing prevalence of methicillin-resistant strains further reinforces the need for alternative or complementary therapeutic strategies [7].

In this context, plant-derived bioactive compounds have attracted increasing interest as potential antimicrobial agents or adjuvants to conventional antibiotics. The Brazilian Cerrado, one of the world's most threatened biodiversity hotspots, contains numerous species with underexplored pharmacological potential [8]. Among these, pequi oil, extracted from fruits of the genus *Caryocar* (family Caryocaraceae), has received attention for reported anti-inflammatory, antioxidant, antifungal, and antibacterial properties [9,10]. Its composition includes unsaturated fatty acids, carotenoids, and phenolic acids, and varies according to species, fruit fraction, geographic origin, extraction method, and maturation stage [9,11,12]. Two species are especially relevant: *Caryocar brasiliense* Cambess., associated with central Brazil, and *Caryocar coriaceum* Wittm., more frequently reported in north-eastern Brazil [13]. Existing syntheses include a broad review of *C. coriaceum* botany, ethnomedicinal uses, phytochemistry and biological activities [11], a systematic review of crude extracts and fractions from cashew, cajuí and pequi [14], and a June 2026 scoping review specifically covering *C. coriaceum* fixed oil, its extraction, chemistry and broad biological activities [15]. Thus, the novelty of the present work is not a first review of pequi fixed oil, but a narrowly defined evidence map of *S. aureus* outcomes, reproducibility of aminoglycoside modulation, eligibility distinctions between fruit oils and other *Caryocar* preparations, and a comparator-controlled plasma-activation research agenda.

A critical but underappreciated issue in the existing literature is the choice of oil extraction method and the reporting of residual-solvent control. Several studies have employed organic solvents, including hexane and ethyl acetate, as the primary means of fixed-oil preparation. Such approaches are not necessarily invalid for exploratory screening, but they limit direct translational interpretation unless solvent removal, residual-solvent quantification, and batch-to-batch chemical characterisation are demonstrated [16–18]. The absence of batch-level residual-solvent measurements in the particular antibacterial studies identified here is discussed separately from general oil-extraction safety and quality concerns, which have already been recognised in earlier syntheses [15].

Plasma-activated oil (PAO) produced by non-thermal atmospheric plasma (NTAP) should be understood as a post-extraction functionalisation strategy rather than as an extraction method. The safest experimental pathway is therefore solvent-free or food/pharmaceutical-compatible extraction, followed by controlled plasma activation. Cold plasma can generate reactive oxygen and nitrogen species (RONS) and lipid-derived oxidation products at relatively low bulk temperatures [19–21], which may enhance antimicrobial performance without introducing exogenous chemical reagents. This rationale is promising but remains hypothesis-generating for pequi oil because direct experimental evidence for plasma-activated *Caryocar* oil is still absent.

In lipid systems, plasma chemistry differs from aqueous plasma chemistry. Although long-lived species such as H_2O_2 and nitrogen oxides are important in water-rich systems, oils are also strongly influenced by ozone, atomic oxygen, excited species, radical initiation at unsaturated fatty-acid double bonds, lipid hydroperoxide formation, and secondary oxidation products such as aldehydes, ketones, and carboxylic acids [22–25]. These reactions

may affect carotenoids, tocopherols, phenolics, and unsaturated fatty acids, making plasma parameters and chemical characterisation essential for interpreting biological activity.

Evidence from plasma-treated lipid systems other than pequi oil is accumulating. Air-plasma-generated high-valence NOx used to activate olive oil produced antimicrobial activity against *S. aureus* [22], and plasma-activated edible oils have shown antibacterial and wound-healing effects [25,26]. Atmospheric RF plasma has also enhanced the antibacterial activity of clove oil against *E. coli*, *S. aureus*, and *S. Typhimurium* [27], and clove oil combined with encapsulated atmospheric-pressure plasma was bactericidal against *E. coli* O157:H7 and *S. aureus* [28]. Collectively, these studies support the rationale for plasma-activated oil as an antimicrobial platform, but they are contextual evidence only, and plasma-treated essential oils [27,28] differ from plasma-activated fixed oils in composition and probably in mechanism.

Plasma activation is not the only route by which the antimicrobial performance of a vegetable oil might be improved, and its choice as the focus of the research agenda requires justification. Formulation approaches, such as nanoemulsions and encapsulation, increase the dispersion of lipophilic actives in aqueous media and their contact with bacterial cells, but they do not change the chemistry of the oil itself [29]. Combination with conventional antibiotics uses a sub-inhibitory oil concentration as an adjuvant (Section 3.3.4), and enrichment of free fatty acids, for example by controlled hydrolysis, targets the fraction most likely to act on bacterial membranes [30]. Chemical ozonation converts unsaturated fatty acids into ozonides and peroxides and is the most established oxidative route, with ozonated vegetable oils already used in topical anti-infective products [31]. Non-thermal plasma shares this ozone chemistry but adds atomic oxygen, hydroxyl radicals, NOx-derived species and UV photons, and allows the reactive-species dose to be tuned electrically, at near-ambient temperature and without added reagents [22,25]. In the only plasma study that included an ozonated-oil comparator, NOx-activated olive oil was more active against *S. aureus* than ozonated oil [22]. Plasma activation was therefore chosen as the focus of the agenda because it is an oxidative strategy that is untested in pequi oil and can be tested against a matched ozonation control, not because it has been shown to outperform the alternatives.

Therefore, this scoping review aimed to: (i) map the published evidence on the antimicrobial activity of pequi oil against *S. aureus*; (ii) analyse the relationship between oil extraction methods and antimicrobial outcomes; (iii) appraise how consistently antibiotic-modifying activity has been reported, and by how many independent groups; and (iv) identify research gaps and a comparator-controlled framework for evaluating cold atmospheric plasma-mediated activation of pequi oil.

2. Materials and Methods

2.1. Review Design

This scoping review was structured using the Joanna Briggs Institute (JBI) methodological guidance and the PRISMA-ScR reporting framework [32,33]. A scoping approach was selected to characterise a small, heterogeneous research landscape, not to obtain a pooled treatment-effect estimate [34]. The review was not prospectively registered, and no protocol document is publicly archived. The research question, the Population–Concept–Context (PCC) framework and the eligibility criteria below were defined by the authors for this review. The eligibility criteria, including the *S. aureus* outcome requirement, were finalised after title-and-abstract screening had begun and were not subsequently modified during study selection. The plasma-related literature was charted separately as contextual evidence and was not included in the primary *S. aureus* oil synthesis.

2.2. Review Question

What scientific evidence is available on the antimicrobial potential of pequi oil (*Caryocar* spp.) against *Staphylococcus aureus*, and what research gaps should be addressed before controlled NTAP activation can be evaluated as a future post-extraction strategy?

2.3. PCC Framework

- Population. Pequi oil obtained from the *Caryocar brasiliense* or *Caryocar coriaceum* species.
- Concept. Antimicrobial activity of pequi oil, including direct antibacterial activity, antibiofilm effects, preformed biofilm disruption, and modulation of antibiotic activity. The relationship between extraction methods and residual-solvent control on translational relevance was also considered.
- Context. In vitro microbiological studies evaluating pequi oil against bacterial strains, with particular emphasis on *Staphylococcus aureus*. A complementary contextual mapping of NTAP applied to oils, lipid matrices, and essential-oil systems was performed to support the rationale for future plasma activation of pequi oil.

2.4. Eligibility Criteria

2.4.1. Inclusion Criteria

Studies were eligible for the primary synthesis if they (a) investigated fixed oil isolated from the pulp, internal mesocarp, or kernel of *C. brasiliense* or *C. coriaceum* fruits, rather than extracts from leaves or other plant parts; (b) measured a quantitative in vitro antibacterial, antibiofilm, or antibiotic-modifying outcome; and (c) assessed *S. aureus* in at least one microbiological assay. Supercritical CO_2 extraction itself was not an exclusion criterion when a true fruit-derived fixed oil was isolated.

2.4.2. Exclusion Criteria

Studies were excluded from the primary synthesis if they examined non-oil plant extracts, extracts from leaves or other non-fruit plant parts, multicomponent formulations without a separately tested oil arm, exclusively animal outcomes, or secondary literature. For clarity, Amaral et al. (2014) [35] tested an apolar supercritical-CO_2 extract prepared from *C. brasiliense* leaves and was excluded because it was not a fruit-derived fixed oil, despite reporting *S. aureus* inhibition. The companion cytotoxicity/phototoxicity paper [36] likewise concerned a leaf extract and did not provide an eligible fixed-oil antimicrobial assessment. Marangon et al. [37] tested chitosan/gelatin/pequi-oil emulsions and also included an oil-only arm against *S. aureus* ATCC 25923 (MIC and MBC >4000 µg/mL, i.e., no inhibition at the highest concentration tested). The emulsion effect cannot be assigned to the oil alone, and the species and fruit fraction of the commercial oil are not stated explicitly (the oil came from a community in Minas Gerais), so criterion (a) could not be verified and the record was excluded from the primary synthesis; its oil-only result is noted here for completeness. These distinctions refer to study material and design, not to the extraction solvent or to a presumption that other *Caryocar* preparations lack bioactivity. Solvent-assisted fruit-oil studies were eligible, with residual-solvent controls charted as a methodological limitation.

2.5. Complementary Contextual Eligibility Criteria for Plasma-Related Evidence

Plasma-related terms were deliberately not used as eligibility criteria for the primary synthesis. The primary question concerns the evidence base for pequi oil itself, and a plasma requirement would have reduced the eligible set to zero, because the direct *Caryocar*–plasma search found no study of plasma-activated *Caryocar* oil (Supplementary Section S4). Plasma

evidence was therefore captured by a separate complementary search and charted under the criteria below. A complementary evidence mapping was performed to identify studies involving non-thermal atmospheric plasma, plasma-activated oils, plasma-treated oils, plasma-treated lipid matrices, or combined plasma–essential-oil systems. Records were considered contextually relevant when they investigated at least one of the following aspects: plasma-induced modification of vegetable oils or lipid-rich matrices; generation or persistence of reactive oxygen and nitrogen species in oil systems; plasma-induced lipid oxidation; antimicrobial, antibiofilm, antifungal, or microbial-safety outcomes in plasma-treated lipid systems; or combined plasma–essential-oil strategies. These records were not included in the primary antimicrobial synthesis for *Caryocar* oils unless they directly evaluated pequi oil or another *Caryocar*-derived oil. Because no such study was identified, plasma-related records were retained only as contextual and mechanistic evidence to support the rationale for plasma-activated pequi oil as a future experimental strategy.

2.6. Search Strategy

Database searches were reported by a coauthor as having been carried out in PubMed (9 March 2026), Scopus (10 March 2026), Web of Science (11 March 2026), Embase (18 March 2026) and MEDLINE via the Virtual Health Library (19 March 2026), without language or publication-date restrictions; preliminary exploratory searching was conducted in February 2026. These execution dates are documented by retrospective author information (Supplementary Table S2) and have not been independently verified against dated database logs. For the primary scoping review, the search strategy combined three conceptual blocks: (1) pequi oil and *Caryocar* species; (2) antimicrobial activity and microbiological assays; and (3) in vitro microbiological outcomes. The general search equation was: ("*Caryocar brasiliense*" OR "*Caryocar coriaceum*" OR pequi OR "pequi oil" OR "pequi pulp oil") AND ("antimicrobial" OR "antibacterial" OR "*Staphylococcus aureus*" OR "anti-staphylococcal") AND ("in vitro" OR "minimum inhibitory concentration" OR "disk diffusion" OR "biofilm"). PRISMA-S-oriented search documentation is provided in Supplementary Section S4 [38]. The exact executed platform-specific strings, search histories and contemporaneous database logs were not retained; although dates were subsequently supplied by a coauthor, the general equation above cannot reproduce the original searches exactly. The use of controlled vocabulary (MeSH/Emtree), grey literature and backward citation searching in the original database process is not independently documented. To support reproduction and future updating, database-specific search strings that combine controlled vocabulary (MeSH in PubMed/MEDLINE, Emtree in Embase and DeCS in the VHL) with free-text synonyms are provided in Supplementary Table S3; they were constructed after the original searches and are not presented as the executed queries. On 14 November 2026, an additional, targeted backward-citation check was performed using the online reference lists of the four included studies (A1–A4) and two relevant reviews [11,15]. Titles and available abstracts were checked against the fruit-derived fixed-oil/*S. aureus* eligibility definition. No clearly eligible additional primary study emerged from this targeted check. This retrospective check was conducted after the March 2026 database searches and does not reconstruct the original screening records; potentially borderline records were not all assessed in full text, and the original PRISMA counts have therefore not been changed. Nascimento et al. 2026 [15] was published after these searches and was identified separately; it was used for context and was not part of the database screening.

The database providers were the National Library of Medicine (Bethesda, MD, USA) for PubMed and MEDLINE; Elsevier B.V. (Amsterdam, The Netherlands) for Scopus and Embase; Clarivate (London, UK) for Web of Science; and BIREME/PAHO/WHO (São Paulo, SP, Brazil) for the Virtual Health Library platform.

In addition to the primary search, a complementary contextual search was conducted to map evidence on non-thermal atmospheric plasma, plasma-activated oils, plasma-treated lipid matrices, and plasma–essential-oil systems. This complementary search was used only to support the mechanistic rationale for plasma activation as a future bioactivity-enhancing strategy and did not contribute records to the primary antimicrobial synthesis unless the record directly evaluated pequi oil or another *Caryocar*-derived oil. The general complementary search expressions and the selected plasma-related records retained for contextual synthesis are provided in the Supplementary Material; platform-specific executed queries, complete retrieval counts, and search dates were not retained.

2.7. Study Selection Procedure

Two reviewers independently screened titles/abstracts and full texts using a pilot eligibility calibration set, and disagreements were resolved by consensus. Records not retrievable through institutional access, interlibrary loan or author contact were classified as unavailable. Duplicates and unavailable records were counted together ($n = 24$), because separate counts were not preserved (Figure 1). Excluding unavailable records before screening may have reduced the completeness of the evidence map.

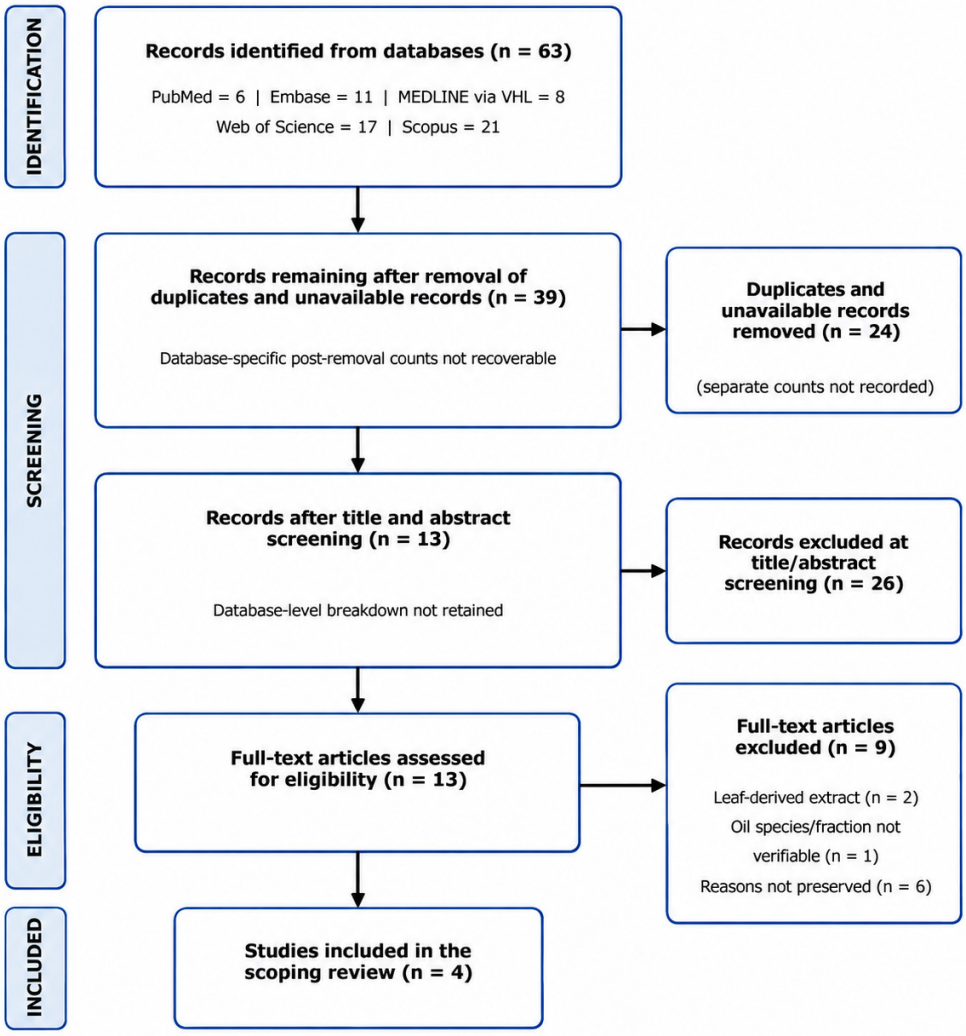

Figure 1. PRISMA-ScR flow diagram summarising the study selection process for the scoping review on the antimicrobial activity of pequi oil. A total of 63 records were identified from PubMed ($n = 6$), Embase ($n = 11$), MEDLINE via VHL ($n = 8$), Web of Science ($n = 17$), and Scopus ($n = 21$). The original database exports were not retained. After the combined removal of duplicates and unavailable

records (n = 24; separate counts were not preserved), 39 records remained for title-and-abstract screening, of which 26 were excluded. Thirteen full-text articles were assessed for eligibility, and nine were excluded, resulting in four studies included in the scoping review. Of the nine full-text exclusions, three were individually identifiable (two studies involving leaf-derived extracts and one involving oil of unverifiable species and fruit fraction). The reasons for the remaining six exclusions were not preserved. Full-text exclusions are summarised in Supplementary Table S4 where identifiable.

2.8. Data Extraction

Study-level data were charted from the included publications using a structured set of fields covering: author(s), year, country, *Caryocar* species and fraction, oil-preparation method and solvent used (where reported), residual-solvent information, bacterial strains, microbiological assay type, antimicrobial outcomes, and key findings. Data extraction and charting were performed manually by the authors using these predefined fields, without the use of dedicated systematic-review management or automated data-extraction software. Extraction procedures were additionally classified as directly translatable (solvent-free or food/pharmaceutical-compatible) or requiring additional translational controls (solvent-assisted) for regulatory and safety interpretation. A structured methodological-quality mapping was also performed descriptively, without excluding studies, considering extraction method, chemical characterisation, residual-solvent testing, strain type, assay standardisation, controls, biofilm model, and synergy analysis. For plasma-related contextual records, the following information was charted: oil or lipid matrix, plasma source, plasma operating conditions when reported, reactive species or oxidation markers evaluated, antimicrobial or oxidative outcome, target microorganism, and relevance to the rationale for future plasma activation of pequi oil.

The methodological-quality mapping applied eight domains to each included study, each coded as reported (R), partly reported (P), not reported (NR), not applicable (NA; e.g., residual-solvent testing after solvent-free extraction), or not assessed for that study (—; e.g., biofilm/interaction tests that were not conducted): (1) extraction method, solvent and thermal history; (2) residual-solvent testing; (3) chemical characterisation of the tested batch; (4) strain identity and provenance (reference, clinical or multidrug-resistant); (5) assay standardisation, judged against Clinical and Laboratory Standards Institute (CLSI) or European Committee on Antimicrobial Susceptibility Testing (EUCAST) broth-microdilution principles, including inoculum and read-out; (6) vehicle, emulsifier and solvent controls; (7) biofilm model and read-out (biomass versus viability); and (8) interaction analysis (fixed-concentration modulation versus checkerboard fractional inhibitory concentration index, FICI, or time-kill). The eight-domain ratings were assigned and subsequently checked for internal consistency by K.J.B.C. (Karla Joelma B. Cunha). Both steps were performed by the same author; no independent second-rater methodological-quality appraisal was conducted. The domain-level ratings are given in Supplementary Table S5 and discussed alongside the methodological characteristics in Section 3.2.

2.9. Evidence Synthesis and Interpretive Conventions

Findings were synthesised narratively by outcome type. Because the included studies reported MICs in different units, concentrations were converted to μg/mL where necessary (1 mg/mL = 1000 μg/mL). The intrinsic activity of the oil was described using conventional thresholds for natural-product MICs (significant, <100 μg/mL; moderate, 100–625 μg/mL; weak, >625 μg/mL) [39,40]. These thresholds were proposed for plant extracts and pure compounds, not for whole fixed oils, which consist mainly of poorly water-soluble triacylglycerols; an apparent oil MIC therefore depends strongly on dispersion, vehicle, inoculum and read-out [41], and the categories are used here only as descriptive labels, not

as pharmacological cut-offs. Antibiotic–oil interactions were classified as MIC reduction (modulation) when the original authors compared the antibiotic MIC with and without a fixed oil concentration, and as synergy only when a fractional inhibitory concentration index (FICI ≤ 0.5) from a checkerboard assay was reported [42]. The independence of included studies was judged from author overlap in the reference list, because repeated findings from one research network carry less weight than replication by unrelated groups.

3. Results

3.1. Study Selection Results

The database searches yielded 63 records: PubMed ($n = 6$), Embase ($n = 11$), MEDLINE/VHL ($n = 8$), Web of Science ($n = 17$), and Scopus ($n = 21$). A total of 24 records were removed as duplicates or as unavailable, leaving 39 for screening. Following title-and-abstract screening, 13 full-text articles were assessed for eligibility, of which nine were excluded for not meeting the inclusion criteria. A total of four studies were included in the final synthesis (Figure 1). Three of the nine full-text exclusions can be identified: two studies tested a supercritical-CO_2 extract of *C. brasiliense* leaves rather than a fruit-derived fixed oil [35,36], and one tested an oil whose species and fruit fraction were not stated [37]. The identities and reasons for the remaining six exclusions were not preserved in the screening records and are reported as such rather than reconstructed (Table S4).

3.2. Characteristics of Included Studies

All four included studies were in vitro experimental investigations conducted in the state of Ceará, Brazil, all evaluating oil from *Caryocar coriaceum* Wittm. No included study investigated *C. brasiliense*. The studies differed in oil-preparation method, fruit fraction, bacterial strains, concentration ranges, and microbiological assays (Table 1; Supplementary Table S1). The four studies are not independent: H.D.M. Coutinho is an author of all four, J.G.M. Costa of A2–A4, and I.R.A. Menezes of A2 and A4 [43–46], so they should be read as outputs of one research network rather than as independent replication.

Three of the four studies (A1, A3, A4) employed organic-solvent-assisted extraction procedures, as reported by the original authors. For A3 (Costa et al. [44]), the source specifies Soxhlet extraction of pulp with hexane at 60 °C for 8 h; ripe fruit was collected. A1 (Almeida-Bezerra et al. [46]) also explicitly reported using ripe *C. coriaceum* fruits. Hexane and related petroleum-derived extraction solvents are subject to toxicological and regulatory concern, and residual solvents must be controlled under ICH Q3C principles when materials are intended for food, cosmetic, or biomedical translation [16,17]. These methods produce exploratory oils that may be useful for screening, but they have limited direct translational relevance unless thorough solvent elimination, residual-solvent quantification, and chemical batch characterisation are demonstrated. Only study A2 [43] used a solvent-free hydraulic pressing procedure, representing the clearest methodologically translatable study in this review.

Table 1. Methodological characteristics of the studies included in the primary scoping review. This table summarises the main methodological features of the four studies that evaluated the antimicrobial activity of pequi oil from *Caryocar* species, including the species and fruit fraction investigated, oil-preparation method, solvent use, antimicrobial assay, and bacterial strains tested. Solvent-assisted extraction was recorded as a methodological variable and was not used as an exclusion criterion.

Study	Author, Year	Species/Fruit Fraction	Oil-Preparation Method	Solvent Used	Antimicrobial Assay	Bacteria Tested
A1	Almeida-Bezerra et al., 2025 [46]	*C. coriaceum*/internal mesocarp	Solvent-assisted extraction	n-Hexane	Broth microdilution; biofilm inhibition; preformed biofilm disruption	*S. mutans*, *E. faecalis*, *S. aureus* (ATCC 25923), *P. aeruginosa*

Table 1. *Cont.*

Study	Author, Year	Species/Fruit Fraction	Oil-Preparation Method	Solvent Used	Antimicrobial Assay	Bacteria Tested
A2	Pereira et al., 2020 [43]	*C. coriaceum*/pulp and kernel	Hydraulic pressing/solvent-free extraction	Not applicable	Broth microdilution; antibiotic modulation	*S. aureus*, *B. cereus*, *E. coli*, *P. aeruginosa*, *K. pneumoniae*, MDR strains
A3	Costa et al., 2011 [44]	*C. coriaceum*/pulp	Soxhlet extraction (hexane, 60 °C, 8 h)	Hexane	Agar-disc diffusion	*S. flexneri*, *S. choleraesuis*, *S. aureus* (ATCC 12692), *E. coli*, *P. aeruginosa*, *K. pneumoniae*, *S. pneumoniae*
A4	Saraiva et al., 2011 [45]	*C. coriaceum*/pulp	Soxhlet extraction (3 h), rotary evaporation at 70 ± 2 °C	Ethyl acetate	Broth microdilution; antibiotic modulation	*E. coli*, *S. aureus*, *P. aeruginosa*, *P. vulgaris*, MDR strains

Structured Methodological-Quality Mapping

A structured methodological-quality mapping (Table 2) was added to clarify how each included study supports, or limits, translational interpretation. This mapping was descriptive and was not used to exclude studies, in keeping with the scoping-review objective.

Table 2. Structured methodological-quality mapping of included studies. This table summarises extraction method, residual-solvent control, chemical characterisation, microbiological design, and translational interpretation. It is descriptive and was not used as a risk-of-bias tool or exclusion criterion.

Study	Extraction and Residual-Solvent Control	Chemical Characterisation	Microbiological Design	Translational Interpretation
A1 [46]	Solvent-assisted n-hexane extraction; residual-solvent quantification not clearly reported.	GC–MS fatty-acid composition reported (eight fatty acids); stability and residual-solvent data insufficient.	Broth microdilution and crystal-violet biofilm assays; DMSO used to prepare oil; chlorhexidine as biofilm reference. Labelled dosing solutions differ from final in-well concentrations.	Exploratory antibiofilm evidence; limited direct translation without residue and viable-biofilm validation.
A2 [43]	Discontinuous hydraulic pressing, solvent-free (500 g, about 2 h; yields 11.1% pulp, 26.8% kernel).	Fatty-acid profiles reported for pulp and kernel oils.	Broth MIC and antibiotic MIC-modulation assays with standard and MDR strains. A BHI-plus-inoculum control and drug-alone comparison are described, but a separate oil-dispersion vehicle-matched control is not specified in the accessible report.	Best extraction basis for translational follow-up; synergy requires mechanistic confirmation.
A3 [44]	Soxhlet extraction with hexane at 60 °C for 8 h; residual-solvent quantification not clearly reported.	Chemical and residue characterisation limited for translational interpretation.	Agar-disc diffusion; no broth MIC directly comparable with the other studies. *S. aureus* ATCC 12692 was used; Tween 80 and distilled water were designated negative controls in the original agar-disc diffusion assay.	Direct activity reported, but not directly comparable with MIC-based studies.
A4 [45]	Soxhlet extraction with ethyl acetate; lower regulatory concern than hexane, but residue data not clearly reported.	Fixed oil evaluated; batch composition and stability data limited.	Broth MIC and aminoglycoside MIC-modulation assays. The authors report testing DMSO below 10% without antibacterial or modulatory activity; exact final well DMSO levels and treatment-specific matching remain unclear.	Strongest antibiotic-modifying signal, but needs solvent-free replication and FICI/checkerboard confirmation.

3.3. Synthesis by Outcome Type

3.3.1. Direct Antibacterial Activity Against Planktonic Cells

Direct antibacterial activity of pequi oil alone was variable and assay-dependent. Costa et al. [44] reported inhibition zones in an agar diffusion assay; such results cannot be equated with broth MICs. Saraiva et al. [45] reported an oil MIC of 512 for both *S. aureus* strains tested (ATCC 12692 and the resistant isolate SA358). The values are printed as mg/mL, but the same article describes a 10 mg/mL stock solution, so the unit is internally inconsistent; µg/mL is the more plausible reading and is used here, as in Pereira et al. [43], who cite the Saraiva value as µg/mL. The publisher-hosted abstract of Saraiva et al. [45] explicitly

reports an oil MIC of 512 µg/mL, whereas the article body contains an inconsistent unit. No formal erratum was identified in the bibliographic verification. The value is therefore presented with the original-body-unit caveat; no conclusion depends on resolving the discrepancy. Pereira et al. [43] described MIC values of at least 1024 µg/mL for most of the tested standard and resistant strains; the only lower value in that article (812.75 µg/mL, pulp oil) was for *E. coli* ATCC 10536, not *S. aureus*, and a 2026 review that lists ≥813 µg/mL for this study appears to have misattributed it. Almeida-Bezerra et al. [46] reported a planktonic MIC >1024 µg/mL in its Methods but >512 µg/mL in its Discussion, where the latter value is attributed to a cited study (its ref. [31], Pereira et al.); the article does not reconcile these cut-offs. Accordingly, the A1 result is presented as a censored value with inconsistent reporting, rather than as a precise MIC. The 10 and 100 mg/mL solutions in its antibiofilm protocol were not interchangeable with the planktonic MIC.

3.3.2. Inhibition of Biofilm Formation

Only Almeida-Bezerra et al. [46] investigated *S. aureus* biofilm formation using crystal-violet biomass measurements. The results presented in that study indicate that treatments with the fixed oil of *C. coriaceum* (FOCC), at nominal concentrations of 10 and 100 mg/mL, reduced stained biofilm biomass by approximately 55% and 60%, respectively; the authors described the overall inhibition as approximately 60%. These are nominal test-solution concentrations, whereas the Methods report the addition of 20 µL test material to a 200 µL assay well; the final in-well exposure therefore requires careful definition by the authors of the primary study. The report inconsistently labels 10 mg/mL as an MIC while also reporting a planktonic MIC >1024 µg/mL. Crystal-violet biomass changes do not establish bactericidal activity or viable-biofilm eradication. Crystal-violet staining quantifies total attached biomass, cells and matrix together, whose proportions change across the stages of the biofilm life cycle [47], and it does not distinguish live from dead cells; viable counts, metabolic-activity assays or microscopy would be required to support any claim of biofilm killing or eradication [48].

3.3.3. Disruption of Preformed Biofilms

The same study [46] evaluated disruption of established biofilm biomass. The results reported by Almeida-Bezerra et al. [46] indicate approximately 50% and 35% reductions in *S. aureus* biofilm biomass at nominal FOCC treatment-solution concentrations of 10 and 100 mg/mL, respectively, suggesting a non-monotonic response rather than a demonstrated concentration-dependent effect. These approximate values were read from the published figure; no raw numerical dataset was available. Reductions in total stained biomass cannot be interpreted as killing of sessile organisms, and the study did not establish a minimum biofilm eradication concentration (MBEC) or quantify surviving colony-forming units.

3.3.4. Modulation of Antibiotic Activity

Two studies from an overlapping research network investigated antibiotic modulation. Saraiva et al. [45] documented an oil MIC of 512 (same unit caveat as above) against the reference and resistant *S. aureus* strains. Aminoglycosides were then tested with and without a sub-inhibitory oil concentration of 32, one-sixteenth of the MIC (MIC/16), in the same unit. The authors summarise the aminoglycoside MIC reductions as 50–99.8% across strains. Pereira et al. [43] also described reductions in aminoglycoside MICs for *S. aureus*, but not *E. coli*, with pulp and almond oils at a sub-inhibitory oil concentration of 128 µg/mL (MIC/8), using amikacin and gentamicin. Both should be classified as antibiotic-modifying signals, not conclusively as pharmacological synergy, because checkerboard fractional inhibitory concentration indices (FICIs) or validated time-kill interaction metrics were not

reported [42]. The direct antibacterial, antibiofilm, and antibiotic-modifying outcomes are summarized in Table 3.

Table 3. Summary of antimicrobial outcomes against *Staphylococcus aureus*. This table synthesises the main antimicrobial findings reported for *Staphylococcus aureus* across the included studies, organised by outcome type: direct antibacterial activity against planktonic cells, inhibition of biofilm formation, disruption of preformed biofilms, and modulation of antibiotic activity. Because the included studies used different assays, concentration units, and experimental conditions, the findings should be interpreted descriptively rather than quantitatively compared.

Study	Direct Planktonic Activity	Biofilm Formation Inhibition	Preformed Biofilm Disruption	Antibiotic Modulation	Interpretation
A1 [46]	Planktonic MIC inconsistently reported: >1024 µg/mL (Methods) versus >512 µg/mL (Discussion, attributed to a cited study); the original does not reconcile these values.	Approximately 55–60% lower crystal-violet biomass for nominal 10 and 100 mg/mL solutions (Figure 2); final well concentration should be distinguished from dosing solution.	Approximately 50% (10 mg/mL) and 35% (100 mg/mL) decrease in stained *S. aureus* biomass (Figure 3); not a viable-cell eradication assay.	Not assessed	Exploratory antibiofilm signal; based on a single biomass-oriented study, not proof of sessile-cell killing.
A2 [43]	Weak isolated activity; MIC ≥ 1024 µg/mL	Not assessed	Not assessed	Positive modulation of amikacin and gentamicin (oil at 128 µg/mL, MIC/8)	Supports resistance-modifying potential
A3 [44]	Variable inhibition by agar diffusion	Not assessed	Not assessed	Not assessed	Direct activity reported, but not directly comparable with MIC-based studies
A4 [45]	MIC 512 for both *S. aureus* strains (publisher-hosted abstract: 512 µg/mL; article-body units inconsistent)	Not assessed	Not assessed	Reported 50–99.8% reductions in aminoglycoside MICs; oil at 32 (MIC/16, same unit as the MIC); no FICI.	Strongest evidence for antibiotic-modifying activity; requires solvent-free replication and formal synergy metrics.

3.4. Complementary Search: Plasma-Activated Oil Systems

To contextualise the rationale for PAO, a complementary search was carried out and the retained studies were mapped separately from the primary pequi-oil evidence. The record counts and dates of this selective narrative search were not retained. Records were retained when they reported plasma treatment of a vegetable oil, essential oil, oil constituent or lipid-containing matrix together with at least one antimicrobial, antibiofilm or lipid-oxidation outcome; reviews and studies of plasma-activated water without a lipid phase were not retained. Retention was purposive: the aim was to cover each mechanistic category relevant to a pequi-oil experiment, not to be exhaustive, so the 22 records illustrate the range of the evidence rather than form a systematic sample of it. The contextual set comprised 22 selected publications (Table S6). No eligible study investigated plasma activation of pequi oil or of any other *Caryocar*-derived oil. The 22 records are heterogeneous: five evaluated plasma-activated edible or natural oils directly [22,25,26,49,50], nine combined plasma with essential oils or their constituents [27,51–58], four characterised plasma-induced lipid oxidation in oils or lipids [59–62], and four addressed lipid-containing powders, packaging films, or plasma-polymerised coatings [63–66].

Overall, these studies provide mechanistic and experimental context for plasma-treated lipid systems, including increases in peroxide value, carboxylic acids, and reactive oxygen or nitrogen species associated with the lipid matrix. In the direct PAO studies, plasma-activated oils showed enhanced antibacterial activity against *S. aureus*, MRSA, and Gram-negative bacteria compared with untreated controls [22,25,26,50]; the NOx-activated olive oil study [22] is notable for including ozonated-oil and plasma-activated-water comparators.

Because these records concern other matrices, they were classified as contextual evidence and were not included in the primary antimicrobial synthesis for *C. coriaceum* or *C. brasiliense* oils; they support the research agenda in Section 4.3.

4. Discussion

This scoping review mapped evidence on the antimicrobial activity of pequi oil with emphasis on *S. aureus*. Although only four studies met the inclusion criteria, the review reveals a sparse, geographically and institutionally concentrated, and methodologically heterogeneous evidence base. The most important translational issue is not simply whether pequi oil is active, but whether its preparation, chemical characterisation, and microbiological testing are sufficiently standardised to support meaningful comparison and future application.

4.1. Heterogeneity of Antimicrobial Outcomes

The central point of comparison between the four selected articles is methodological heterogeneity. Costa et al. [44] employed agar-disc diffusion and expressed results as percentage concentrations and inhibition halo diameters, while Saraiva et al. [45] and Pereira et al. [43] used broth microdilution in association with aminoglycosides. Almeida-Bezerra et al. [46], in addition to microdilution, performed crystal violet assays for biofilm formation and preformed biofilm disruption. Thus, the different approaches cannot be directly compared, since MIC values are reported in different units across the studies (A1: planktonic MIC in μg/mL but biofilm test solutions in mg/mL; A2: μg/mL; A4: printed as mg/mL, apparently in error; A3: diffusion halos). This disparity is further aggravated by differences in fruit fraction, extraction solvent, bacterial inoculum, and control design. Expressed in common units, intrinsic MICs for *S. aureus* were ≥1024 μg/mL in A2 and 512 μg/mL in A4, whereas the biofilm assays in A1 used oil test solutions labelled 10 and 100 mg/mL (10,000–100,000 μg/mL). Because 20 μL of test material was added to a 200 μL well, the in-well concentration would be about tenfold lower if the solutions were not otherwise diluted (≈1–10 mg/mL), which is still far above the planktonic MICs and difficult to reconcile with pharmaceutical use of the oil as an antibacterial.

Assay-level factors may also contribute to the variability. Fixed oils are immiscible with broth and need an emulsifier or co-solvent (typically DMSO or polysorbate); the vehicle itself can affect growth, inoculum dispersion, turbidity-based read-outs, and the partitioning of hydrophilic antibiotics such as aminoglycosides. Table 2 distinguishes reported controls from incomplete reporting: A4 tested DMSO at concentrations below 10% and reported no antibacterial or modulatory activity in that vehicle control, although final well-level DMSO concentrations are not stated; A2 reported a BHI/inoculum control but did not clearly describe a matched oil-dispersion vehicle control in the accessible experimental methods. Emulsifier concentration, inoculum preparation and read-out could not be verified consistently across all primary-study methods. These effects matter for oils: the identity and final concentration of the solvent or emulsifier can change the apparent MIC of lipophilic natural products, and agar-diffusion assays are particularly unsuitable because non-polar constituents diffuse poorly in the aqueous agar matrix [41]. In oil–aminoglycoside combinations, an emulsifier may also alter the free fraction of the hydrophilic antibiotic or the permeability of the bacterial membrane independently of the oil. Valid comparisons therefore require vehicle-only, vehicle-plus-antibiotic and oil-plus-vehicle arms at identical final concentrations; these controls were not fully documented in the included studies (Table 2).

In addition to assay variation, the fruit fraction used for oil preparation introduces compositional differences that may affect biological performance. Pereira et al. [43] documented

different fatty-acid profiles between pulp oil (oleic acid 72.41%, palmitic acid 27.59%) and almond oil (oleic acid 48.09%, palmitic acid 46.27%) for the same species. Unsaturated fatty acids may contribute to antimicrobial or antibiotic-modifying activity in lipid matrices, but this relationship remains inferential for pequi oil. Because oils consist mainly of triacylglycerols, the free fatty acid content (acid value) rather than total composition may be what matters. Free fatty acids can disrupt bacterial membranes and inhibit enoyl-ACP reductase (FabI) in *S. aureus* [67,68]; these mechanisms are plausible for the oleic- and palmitic-rich fraction of pequi oil but have not been tested for it. Aminoglycoside uptake also depends on the proton-motive force [69], so membrane-active lipids could in principle either facilitate or hinder uptake, and the direction of the effect is an empirical question.

Fruit maturity is a further, incompletely documented source of variability. In *C. brasiliense*, fruit development from anthesis to maturity took about 12 weeks (84 days) in a cerrado population, with β-carotene, soluble solids and vitamin C reaching their maxima at the end of this period [70]; off-season fruits from southern Minas Gerais took 117 days from anthesis to abscission [71]. Pulp from fruits collected after natural fall contained more pigments (total carotenoids and β-carotene), lipids and proteins than pulp from fruits picked from the tree [72]. Comparable developmental data for *C. coriaceum* were not located. Almeida-Bezerra et al. (A1) [46] and Costa et al. (A3) [44] explicitly described using ripe *C. coriaceum* fruits; Pereira et al. (A2) [43] and Saraiva et al. (A4) [45] did not clearly report fruit maturity in the charted methods. Neither A1 nor A3 provided a quantitative maturity index, and none of the four studies compared maturity stages or established an effect of maturity on antimicrobial activity. Because maturity changes lipid yield and the content of carotenoids and other minor constituents that may contribute to, or quench, bioactivity, these variables should be recorded and standardised in future antimicrobial studies of pequi oil.

Figure 2 summarises the antimicrobial mechanisms that are plausible for pequi oil and separates them by level of evidence. For the untreated oil, the candidate mechanisms are those established for long-chain free fatty acids in other systems: insertion into the cytoplasmic membrane with permeabilisation, leakage and dissipation of the proton-motive force; inhibition of the enoyl-acyl carrier protein reductase FabI by unsaturated fatty acids; and an indirect effect on aminoglycoside uptake, which depends on the proton-motive force [30,67–69]. The only effects actually observed in the included studies are the reduction in aminoglycoside MICs (A2, A4) and the reduction in crystal-violet biomass (A1), and neither study tested a mechanism. For plasma-activated oil, the proposed mechanisms are oxidative (lipid peroxidation in the bacterial membrane and oxidation of protein thiols and nucleic acids by ozonides, hydroperoxides, aldehydes and NOx-derived species carried by the oil [22,25]) and remain hypotheses for pequi oil (Section 4.3).

The strongest recurring observation is a reduction in aminoglycoside MICs in the presence of the oil, documented by A2 and A4. In A4, gentamicin, kanamycin, amikacin, and neomycin were tested alone and in combination with *C. coriaceum* oil, and MIC reductions of 50% to 99.8% were observed, suggesting a resistance-modifying or antibiotic-enhancing role rather than only direct bactericidal activity. A2 reported a similar effect for amikacin and gentamicin with both pulp and kernel oils. Two cautions apply. First, A2 and A4 share authors, so they are better read as two experiments from one network than as independent replication. Second, modulation was expressed as percentage MIC reduction, not as FICI, and the oil was used at a fixed sub-inhibitory concentration (MIC/16 in A4; Section 3.3.4), so a dose–response relationship was not examined. Extraction method and chemical composition also cannot be separated without a controlled comparison, so the effect should be attributed cautiously to oil composition until solvent-free, chemically standardised preparations are tested by independent groups.

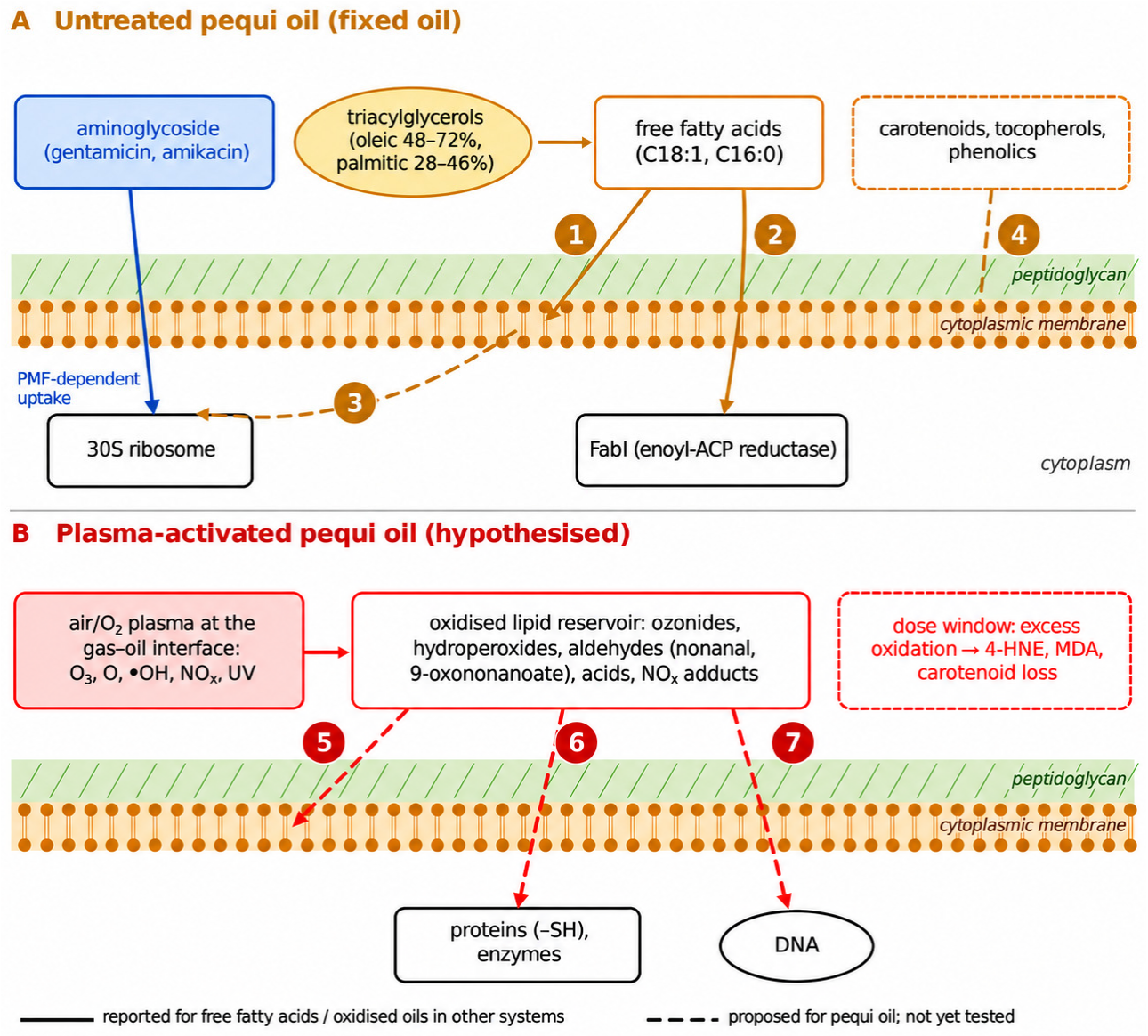

Figure 2. Candidate antimicrobial mechanisms of pequi oil against *S. aureus*, coded by level of evidence. (**A**) Untreated oil: (1) membrane insertion of free fatty acids released from triacylglycerols, causing permeabilisation and proton-motive-force (PMF) dissipation; (2) inhibition of the enoyl-acyl carrier protein reductase FabI by unsaturated fatty acids; (3) modulation of PMF-dependent aminoglycoside uptake, the only mechanism linked to an observed outcome (aminoglycoside MIC reduction in A2 and A4); (4) possible contribution of carotenoids, tocopherols and phenolics. (**B**) Plasma-activated oil (hypothesised): plasma-generated O_3, O, •OH and NO_x convert the oil into a reservoir of ozonides, hydroperoxides, aldehydes and carboxylic acids that could cause (5) membrane lipid peroxidation, (6) protein thiol oxidation and (7) DNA damage; excess oxidation would also form cytotoxic aldehydes (4-hydroxy-2-nonenal, 4-HNE; malondialdehyde, MDA) and consume carotenoids. Solid arrows, mechanisms reported for free fatty acids or oxidised oils in other systems [30,67,68]; dashed arrows, mechanisms proposed for pequi oil but not tested. The biofilm-biomass reduction reported in A1 has no established mechanism and is not drawn. The scheme is a hypothesis map and does not represent new data.

4.2. The Extraction Method Problem: Residual Solvents and Translational Viability

Three of the four included studies (A1, A3, A4) employed organic-solvent-assisted extraction as the primary means of oil recovery. Hexane (A1 and A3) is widely used in vegetable-oil extraction but is an ICH Q3C Class 2 residual solvent, with a permitted daily exposure of 2.9 mg/day (concentration limit 290 ppm) that requires strict control in products

intended for human exposure [17]. A4 used Soxhlet extraction with ethyl acetate for 3 h followed by rotary evaporation at 70 ± 2 °C; ethyl acetate is an ICH Q3C Class 3 solvent (generally acceptable up to 50 mg/day without justification) of lower regulatory concern, but residual-solvent testing was still not clearly reported. Thus, the main issue is not that solvent-assisted studies are unusable, but that their direct biomedical or antimicrobial translation is limited unless solvent removal, residual-solvent quantification, and batch chemical characterisation are demonstrated.

Solvent-assisted protocols may introduce additional translational variables through solvent exposure, thermal treatment, concentration and solvent removal. Almeida-Bezerra et al. [46] reported that n-hexane extraction proceeded for 72 h at room temperature, followed by rotary evaporation; the paper did not describe 72 h of solvent removal. Costa et al. [44] reported Soxhlet extraction of ripe-fruit pulp using hexane at 60 °C for 8 h, as shown in Tables 1 and 2 and Supplementary Table S5. These reported conditions do not establish the absence of residual solvent after extraction. Without gas-chromatographic residual-solvent quantification, neither extraction history nor the evaporation step alone establishes that residual solvent is absent.

Only study A2 used a solvent-free procedure (hydraulic pressing) [43]. Aminoglycoside MIC reductions were reported both for this oil and for the ethyl-acetate-extracted oil of A4, which argues against residual solvent as the sole explanation of the effect, although it does not exclude a contribution. With a single solvent-free study, differences in fruit fraction, batch and assay, and no study comparing extraction routes on the same fruit lot, the included evidence cannot show that solvent-free extraction is associated with stronger, or weaker, antimicrobial activity. The case for hydraulic pressing or supercritical CO_2 extraction as starting points for translational work rests instead on safety and regulatory grounds. NTAP should then be considered as a controlled post-extraction functionalisation step, not as a replacement for safe oil extraction.

Taken together, these observations support three conclusions that go beyond the residual-solvent question. First, the extraction route is a compositional variable as well as a safety variable: solvent polarity, temperature and duration change oil yield and the recovery of carotenoids, tocopherols and other minor lipophilic constituents, and cold pressing, hexane extraction and supercritical CO_2 extraction of the same seed material give oils that differ in yield and minor-component profile [73,74]. Extraction is therefore a potential confounder of bioactivity, not only a regulatory concern. Second, in the present evidence base, extraction method is confounded with fruit fraction, research group, assay and publication year, so no study-level comparison can isolate its effect. Third, for pharmaceutical development, every oil batch tested for antimicrobial activity should be described by a minimum dataset, so that biological results can be linked to a defined material: extraction method with temperature and time, residual solvent by headspace gas chromatography against ICH Q3C limits where solvents are used, acid value, peroxide value, fatty-acid profile and total carotenoid content.

4.3. Plasma Activation as an Unexplored Post-Extraction Strategy

The absence of direct evidence for plasma-activated pequi oil defines a research gap rather than evidence of efficacy. NTAP should therefore be considered, at this stage, as a post-extraction functionalisation strategy to be tested using solvent-free or otherwise food/pharmaceutical-compatible pequi oil. In this framework, plasma would be used to modify the lipid matrix and determine whether antimicrobial or antibiotic-modifying activity can be altered under controlled conditions; it should not be assumed to overcome extraction-related safety limitations.

Plasma-lipid chemistry should also be distinguished from the better-known chemistry of plasma-activated water [75,76]. In oils, antimicrobial activity may be influenced by ozone,

atomic oxygen, excited species, gas-phase NOx, humidity, oil thickness, gas–liquid interfacial area, and temperature rise during treatment. These variables determine radical initiation at unsaturated fatty-acid double bonds, propagation of lipid peroxidation, formation of lipid hydroperoxides, and generation of secondary oxidation products such as aldehydes, ketones, and carboxylic acids [59–61]. For pequi oil, the following points are inferences from its composition rather than observations: in oleate-rich oils such as pequi oil, a single C=C bond per chain and only minor polyunsaturated fractions make radical-chain autoxidation comparatively slow, so ozone addition across the double bond (ozonolysis) is expected to be an important plasma-driven pathway alongside radical attack at the allylic positions (Equations (1)–(4)). The relative weight of these pathways in pequi oil, and the fate of its carotenoids and phenolics under plasma exposure, have not been measured.

These chemical reactions may be associated with bioactive performance, but the dose window must be controlled. Moderate oxidative functionalisation may increase antimicrobial potential, whereas excessive oxidation may degrade carotenoids, tocopherols, and other bioactive compounds or generate undesirable lipid-oxidation by-products. For this reason, future studies on plasma-activated pequi oil should report gas composition, humidity, plasma source, discharge power or energy density, treatment time, oil volume and layer thickness, gas–liquid interfacial area, temperature rise, peroxide value, anisidine value, acid value, TBARS/MDA, volatile oxidation products by GC-MS, FTIR/Raman markers, and fatty-acid profile before and after activation. Excessive oxidation is a safety issue as well as a loss of efficacy. Secondary oxidation products include reactive aldehydes such as 4-hydroxy-2-nonenal, malondialdehyde and 2-alkenals (in pequi oil mainly from its minor polyunsaturated fraction), which are cytotoxic and genotoxic and react with proteins and nucleic acids [77]; ozonated oils intended for topical use are characterised by peroxide value for similar reasons [31]. Highly oxidised oil may also become rancid and lose its carotenoids, the constituents responsible for much of the antioxidant value of pequi oil. Any plasma-activation study should therefore pre-specify an upper oxidation limit (for example, a maximum peroxide or anisidine value), measure cytotoxicity in relevant human cells (keratinocytes or fibroblasts for topical use) in parallel with antimicrobial endpoints, and follow both activity and oxidation markers during storage.

PAO derived from olive oil, sunflower oil, copaiba oil, and other lipid systems has demonstrated enhanced antimicrobial activity compared with untreated controls, including activity against *S. aureus*, MRSA, *E. coli*, and *P. aeruginosa* [22,25–27,49,50]. Nevertheless, these studies are contextual evidence only. The plasma–essential-oil studies are a weaker analogue still. Essential oils are volatile mixtures of terpenoids and phenylpropanoids, such as eugenol, thymol and carvacrol, that are antimicrobial in their own right at low concentrations; in those studies, plasma enhanced an agent that was already active, often in the vapour phase or on food surfaces. Fixed oils such as pequi oil are non-volatile triacylglycerol matrices with weak intrinsic activity, so any effect of plasma would come mainly from converting the matrix into a reservoir of oxidised species. The two systems differ in composition, mechanism and route of application, and results from one cannot be transferred to the other [27,29]. Composition matters: pequi pulp oil is oleic-dominated (72.4% oleic and 27.6% palmitic acid in A2 [43]), so NOx-activated olive oil [22] is the closest compositional analogue, whereas perilla seed oil [49], rich in α-linolenic acid, is not. They support the plausibility of plasma activation but do not demonstrate that pequi oil will respond in the same way. A rigorous experimental design should compare untreated pequi oil, ozonated pequi oil, plasma-activated pequi oil, and plasma-activated water/oil emulsions to determine whether any enhancement is plasma-specific or reflects generic oxidation.

Given that pequi oil is dominated by oleic and palmitic acids and also contains carotenoids and phenolic constituents, controlled plasma activation is a rational, experimentally testable strategy to determine whether the antimicrobial properties of *C. coriaceum* oil can be modified. The aminoglycoside-modifying activity documented in A2 and A4 is especially relevant: future studies should determine whether plasma treatment changes the effective MIC of aminoglycosides against *S. aureus* or MRSA and whether any interaction is synergistic, additive, antagonistic, or absent using formal checkerboard/FICI and time-kill approaches. Figure 3 outlines a comparator-controlled design that separates plasma-specific effects from generic oxidation.

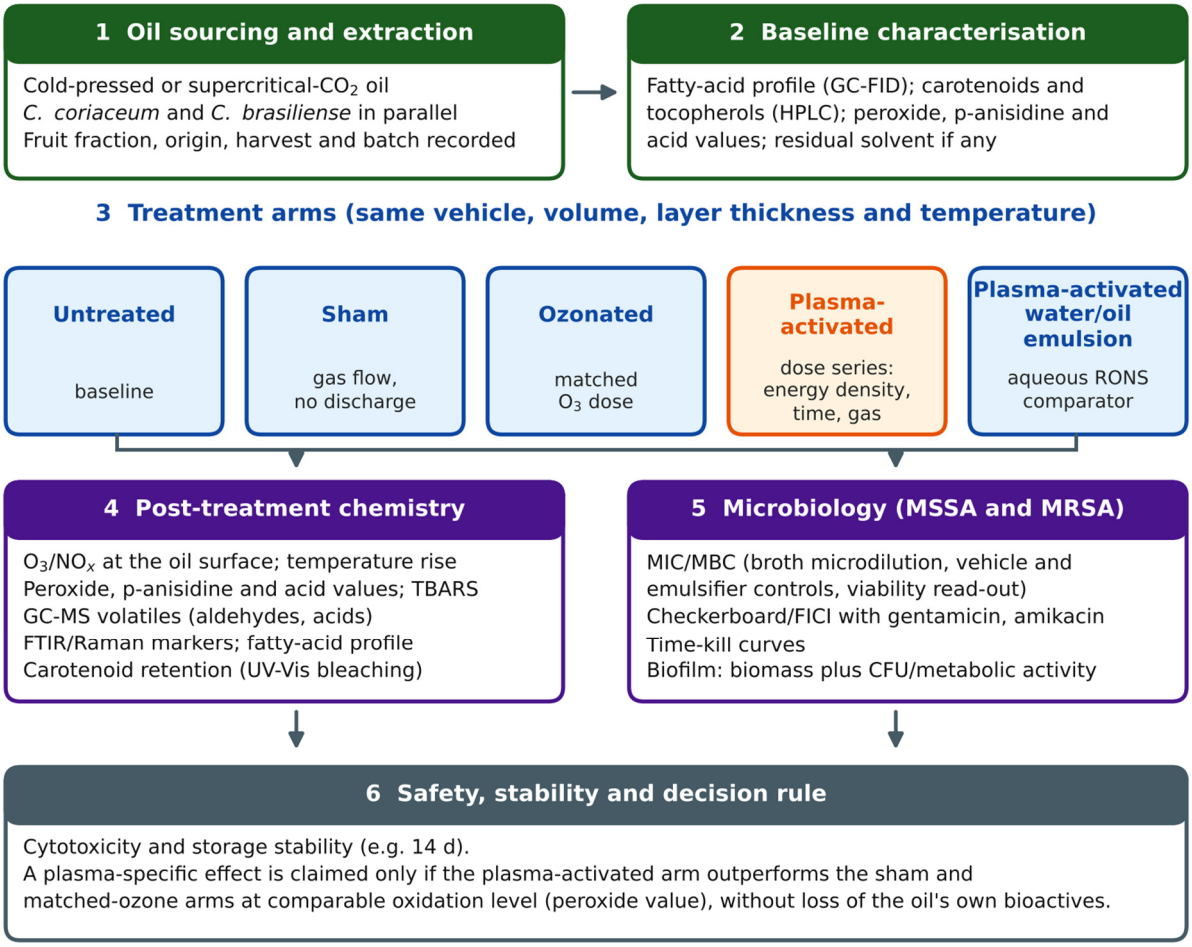

Figure 3. Proposed comparator-controlled framework for testing plasma-activated pequi oil. Cold-pressed or supercritical-CO_2 oil from both *Caryocar* species is characterised at baseline (steps 1–2) and divided into untreated, sham-gas, matched-ozone, plasma-activated, and plasma-activated water/oil-emulsion arms (step 3). Chemical (step 4) and microbiological (step 5) read-outs follow in MSSA and MRSA, with safety and stability testing and a decision rule that credits a plasma-specific effect only if the plasma-activated arm outperforms the sham and ozone arms at comparable oxidation level (step 6). The scheme is a proposal and does not represent published data.

To make the framework in Figure 3 operational, plasma treatment must be standardised and reported as a dose. We recommend reporting the energy delivered per unit oil volume (J/mL), calculated from the measured discharge power (voltage–current or Lissajous analysis) and treatment time, together with feed-gas composition, flow and humidity, electrode-to-oil gap, oil volume, layer thickness and interfacial area, and the oil temperature during treatment; ozone and NOx concentrations above the oil should be measured, for example by ultraviolet or infrared absorption. The sham arm should use the same reactor,

gas flow, geometry, duration and temperature without discharge, to account for evaporation, mixing and oxygenation caused by the gas flow alone. The ozonated arm should receive ozone from a separate generator at the ozone exposure (concentration × time) measured in the plasma arm and, in a second series, should be matched to the peroxide value of the plasma-activated oil. If the plasma-activated oil remains more active than ozonated oil at matched peroxide value, the difference can be attributed to plasma-specific species such as NOx-derived products, short-lived radicals and UV; if not, the effect is better explained by generic oxidation. Several independent oil batches, replicate treatments and blinded microbiological read-outs are needed to support either conclusion.

Initiation:

$$\mathrm{R{-}H + X\bullet \rightarrow R\bullet + XH} \quad (1)$$

(X• represents a hydrogen-abstracting radical, such as •OH; H abstraction is illustrated at an allylic carbon of an unsaturated fatty-acid chain.)

Propagation:

$$\mathrm{R\bullet + O_2 \rightarrow ROO\bullet} \quad (2)$$

(peroxyl radical)

$$\mathrm{ROO\bullet + R{-}H \rightarrow ROOH + R\bullet}$$

(lipid hydroperoxide + new radical)

Chain branching:

$$\mathrm{ROOH \rightarrow RO\bullet + \bullet OH} \quad (3)$$

$$\mathrm{RO\bullet \rightarrow} \text{ aldehydes, ketones, short-chain carboxylic acids}$$

Ozonolysis of the C=C bond:

$$\mathrm{R{-}CH{=}CH{-}R' + O_3 \rightarrow} \text{ primary ozonide} \rightarrow \quad (4)$$

$$\text{Criegee intermediate + aldehyde} \rightarrow$$

$$\text{ozonides, aldehydes, and carboxylic acids}$$

(for oleate: nonanal and 9-oxononanoate, then nonanoic and azelaic acids).

Termination occurs by radical–radical recombination; 4-HNE and MDA arise mainly from polyunsaturated chains and are expected to be minor in oleate-rich oils.

4.4. Geographic and Research-Network Concentration, and Species Representativeness

All four studies meeting the stated primary-synthesis definition evaluated fixed oil from fruits of *C. coriaceum*, and their authorship overlaps; this evidence does not represent four fully independent research groups. The search did retrieve *C. brasiliense* publications, but these are not direct counterexamples to the included-study claim: Amaral et al. [35] investigated supercritical-CO_2 extracts obtained from leaves and the companion paper [36] focused on leaf-extract cytotoxicity and phototoxicity; Marangon et al. [37] evaluated chitosan/gelatin emulsions containing pequi oil and also tested the oil alone against *S. aureus* ATCC 25923 (MIC and MBC >4000 µg/mL), but because the species and fruit fraction of that oil are not stated explicitly, the record is borderline. The statement that no included study examined *C. brasiliense* fruit fixed oil therefore depends on that eligibility decision, and it does not mean that no antimicrobial evidence exists for *C. brasiliense*. A robust future

comparison should use fruit-derived oils from both species, chemically standardised and assayed by independent laboratories.

4.5. Limitations of This Review

The primary limitations of this scoping review are the small number of included studies, exclusively in vitro evidence, methodological heterogeneity, and overlapping author groups within one Brazilian state. The review was not prospectively registered; the eligibility criteria were finalised after screening began, and the available documentation does not establish whether earlier records were reassessed. Incomplete search and selection records limit full reproducibility: duplicate and unavailable records were counted together, and the reasons for six full-text exclusions could not be documented individually. The March 2026 searches were not systematically updated, so relevant studies may have been missed. No formal risk-of-bias assessment was conducted; the eight-domain quality mapping (Section 2.8; Table S5) is descriptive rather than a validated risk-of-bias evaluation. The complementary plasma literature mapping is contextual, not systematic. Fruit maturity was reported for A1 and A3 but not clearly for A2 and A4, and none of the included studies compared maturity stages.

4.6. Research Agenda

The findings of this review support a structured agenda for future research (Table 4). Priorities include: (i) replication of key findings using solvent-free extraction methods; (ii) inter-species comparison of *C. brasiliense* and *C. coriaceum*; (iii) independent replication and mechanistic investigation of aminoglycoside interactions using checkerboard/FICI and time-kill assays; (iv) controlled evaluation of plasma-activated pequi oil as an untested post-extraction strategy; (v) comparison of untreated oil, ozonated oil, plasma-activated oil, and plasma-activated water/oil emulsions; and (vi) integrated chemical, microbiological, and safety characterisation before translational claims are made. Figure 3 summarises a comparator-controlled design that covers items (iv)–(vi).

Table 4. Proposed research agenda based on gaps identified in this scoping review. This table summarises the main methodological and translational gaps identified in the current evidence base and proposes future experimental approaches to advance the investigation of pequi oil as an antimicrobial and resistance-modifying natural product. Particular emphasis is placed on solvent-free extraction, inter-species comparison, mechanistic validation of aminoglycoside synergism, comparator designs for plasma specificity, and experimental evaluation of plasma-activated pequi oil.

Research Gap	Proposed Approach	Rationale	Priority
Lack of studies combining solvent-free extraction, full chemical characterisation, and standardised antimicrobial testing	Replicate key findings using cold-pressed or supercritical CO_2-extracted pequi oil, with complete chemical characterisation	Improves comparability, regulatory relevance, and translational interpretation	High
No included study tested *C. brasiliense* fruit-derived fixed oil against *S. aureus* (leaf extracts and oil-containing composites excluded by scope)	Parallel evaluation of *C. brasiliense* and *C. coriaceum* under identical experimental conditions	Chemical composition may differ between species, limiting generalisability	High
Mechanism of aminoglycoside modulation remains unclear; no FICI data	Membrane permeability assays, efflux-pump assays, and checkerboard/FICI analysis	Mechanistic validation is required to support resistance-modifying claims	High
Aminoglycoside modulation reported by a single research network, without FICI	Independent replication with checkerboard/FICI and time-kill assays, with vehicle and emulsifier controls	Separates true synergy from assay artefacts of hydrophobic oils	High
No study has evaluated plasma-activated pequi oil	NTAP treatment of solvent-free pequi oil, followed by RONS quantification, peroxide index, fatty-acid profile, MIC and biofilm assays	PAO may enhance antimicrobial and resistance-modifying properties	High

Table 4. *Cont.*

Research Gap	Proposed Approach	Rationale	Priority
Limited MRSA and mature biofilm data	Evaluate untreated and plasma-activated pequi oil against MRSA planktonic cells and biofilms	MRSA biofilms are clinically relevant targets	Medium
No ex vivo or in vivo validation	*Galleria mellonella* or murine infection models after in vitro validation	Bridges exploratory findings toward translational evidence	Future
Unclear whether antimicrobial enhancement is plasma-specific or generic oxidation	Compare untreated pequi oil, ozonated pequi oil, plasma-activated pequi oil, and plasma-activated water/oil emulsions	Discriminates plasma-specific effects from nonspecific oxidative chemistry	High
Safety and stability of oxidised or plasma-treated pequi oil unknown	Cytotoxicity, storage stability (e.g., 14 d), and carotenoid retention after activation	Excess oxidation may generate undesirable by-products and erode native bioactives	Medium

5. Conclusions

The available evidence suggests that pequi oil, particularly from *Caryocar coriaceum*, may exhibit antimicrobial and antibiotic-modifying properties relevant to *Staphylococcus aureus*. However, the evidence base is very limited: four in vitro studies, all on *C. coriaceum* from one Brazilian state and all sharing at least one author, so the findings have not been replicated by an independent group, and the studies are methodologically heterogeneous. A major translational barrier is the frequent use of solvent-assisted extraction without clearly reported residual-solvent quantification and batch chemical characterisation. This limitation does not invalidate exploratory antimicrobial screening, but it prevents direct clinical or biomedical interpretation unless additional controls are performed.

The most consistent finding is the reduction in aminoglycoside MICs in the presence of the oil, reported in two studies from overlapping research groups; it constitutes the strongest basis for further investigation but requires independent replication with checkerboard/FICI and time-kill testing. Biofilm inhibition results are promising but remain limited to a single study and should be regarded as preliminary until viable sessile-cell assays, MRSA biofilm models, and mechanistic antibiofilm analyses are performed.

Future research should prioritise solvent-free or food/pharmaceutical-compatible extraction, systematic chemical characterisation, residual-solvent control when applicable, and standardised microbiological protocols. Plasma activation remains an untested post-extraction strategy for pequi oil and should be evaluated through controlled comparative experiments that relate plasma dose and lipid-phase chemistry to antimicrobial and antibiotic-modifying outcomes. Such studies should establish efficacy, safety, and chemical stability before plasma-activated pequi oil is advanced as a translational antimicrobial platform.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/jpbi3040030/s1. Table S1 (characteristics of the four studies included in the primary synthesis); Table S2 (documentation of the primary database searches and complementary plasma/lipid search, including retrospectively reported search dates and reporting limitations); Table S3 (database-specific search strategies reconstructed for reproducibility and future updates, rather than the originally executed queries); Table S4 (available information on full-text exclusions and unavailable records); Table S5 (eight-domain methodological-quality assessments of the four included studies); Table S6 (22 plasma-related studies retained as contextual evidence); and Table S7 (PRISMA-ScR checklist). No supplementary figures are included. Main-text and supplementary citations refer to the same numerically ordered reference list. Additional database-labelled publications are cited here [78–92] and listed in Supplementary Section S2 for search traceability; none was included in the four-study primary synthesis.

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Abbreviations

The following abbreviations are used in this manuscript:

4-HNE	4-hydroxy-2-nonenal
AMR	antimicrobial resistance
BPPL	Bacterial Priority Pathogens List
CFU	colony-forming unit
CLSI	Clinical and Laboratory Standards Institute
DeCS	Health Sciences Descriptors
DMSO	dimethyl sulfoxide
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FabI	enoyl-acyl carrier protein reductase
FICI	fractional inhibitory concentration index
FOCC	fixed oil of *Caryocar coriaceum*
FTIR	Fourier-transform infrared spectroscopy
GC–MS	gas chromatography–mass spectrometry
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
JBI	Joanna Briggs Institute
MBC	minimum bactericidal concentration
MBEC	minimum biofilm eradication concentration
MDA	malondialdehyde

MDR	multidrug-resistant
MeSH	Medical Subject Headings
MIC	minimum inhibitory concentration
MRSA	methicillin-resistant *Staphylococcus aureus*
MSSA	methicillin-susceptible *Staphylococcus aureus*
NTAP	non-thermal atmospheric plasma
PAO	plasma-activated oil
PCC	Population–Concept–Context
PMF	proton-motive force
PRISMA-S	PRISMA extension for reporting literature searches
PRISMA-ScR	Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews
RONS	reactive oxygen and nitrogen species
TBARS	thiobarbituric acid reactive substances
VHL	Virtual Health Library

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