

## Background

*Pseudomonas aeruginosa* is an opportunistic gram-negative pathogen that commonly infects the skin, particularly in settings such as eczematous dermatitis, intertrigo, wounds, and nail disease.<sup>1</sup> While systemic antibiotics are reserved for severe or invasive infections, topical therapy is often employed for localized disease.<sup>2</sup> However, few topical agents are specifically indicated for *P. aeruginosa*, and treatment options remain limited, especially those with broad-spectrum activity, minimal toxicity, and low resistance potential.<sup>3</sup>

Ciclopirox is a topical antifungal agent widely used for superficial mycoses. Although developed for fungal infections, emerging preclinical studies have demonstrated its antibacterial activity against a range of pathogens, including gram-negative species such as *P. aeruginosa*.<sup>4</sup> This has led to renewed interest in repurposing ciclopirox as a topical antimicrobial, particularly in dermatologic contexts where resistant or recurrent bacterial infections are increasingly common.

Despite promising in vitro data, clinical evidence for ciclopirox in *P. aeruginosa* skin infections remains sparse and fragmented, limited to isolated case reports and small-scale studies.<sup>4,5</sup> Notably, no systematic or scoping reviews have synthesized the clinical data for this indication. Given the heterogeneity in study design, treatment regimens, and reported outcomes, a scoping review is warranted to map the current clinical landscape and identify areas for future investigation.

This review aims to identify and characterize published clinical studies involving ciclopirox in the treatment of cutaneous *P. aeruginosa* infections, with attention to patient populations, formulations, infection types, therapeutic regimens, and clinical outcomes.

## Methods

### Review Protocol

This scoping review followed PRISMA-ScR guidelines and the Arksey and O'Malley framework, with refinements by Levac et al.<sup>6-8</sup>

### Search Strategy

In January 2025, PubMed and EMBASE were searched for clinical studies on ciclopirox in treating cutaneous *P. aeruginosa* infections. The PubMed strategy included terms for ciclopirox (e.g., "ciclopirox," "Loprox") and *P. aeruginosa*, combined with treatment-related keywords. The EMBASE search used equivalent Emtree terms. Searches were limited to studies published from 1980 to 2024 and applied uniformly across both databases.

### Eligibility Criteria

Included studies reported clinical outcomes of ciclopirox use for *P. aeruginosa* skin infections. Trials, observational studies, and case reports were eligible. Reviews, abstracts, in vitro/animal-only studies, and non-cutaneous infections were excluded.

### Study Selection & Data Extraction

Two reviewers (SL, SA) independently screened studies and extracted data on infection type, ciclopirox use, and outcomes. Disagreements were resolved by consensus. No formal quality appraisal performed.

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only

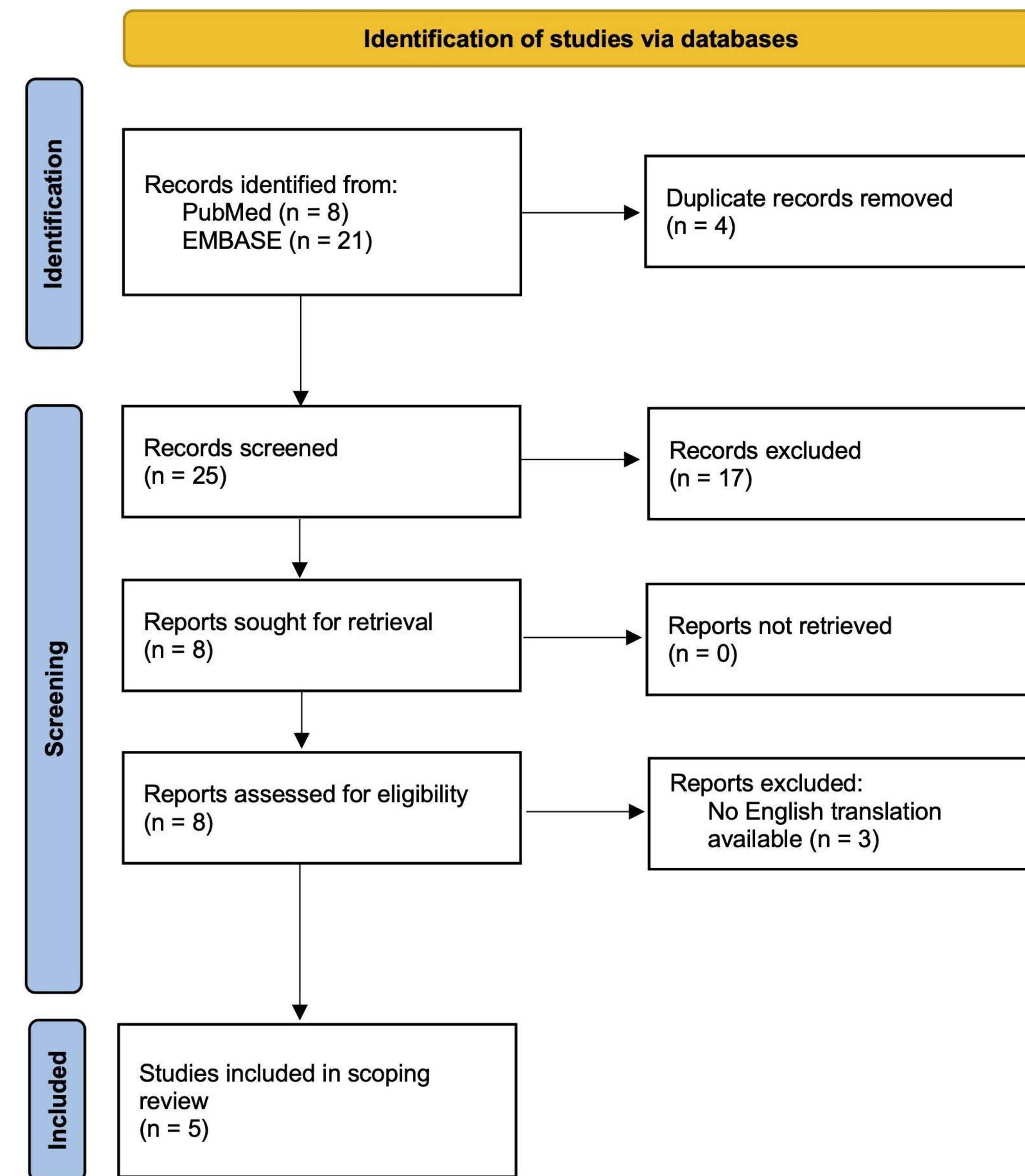


Figure 1. PRISMA-ScR flow diagram of study selection.

Study (Author, Year)	Study Design	Infection Type	Ciclopirox Formulation	Co-treatments	Outcome Summary
del Palacio et al. (2002)	Prospective randomized controlled trial	Otomycosis	Ciclopirox olamine 1% cream or 1% solution	Daily mechanical suction of debris	Reduction in gram-negative bacteria, including <i>P. aeruginosa</i> ; 50% cure rate with cream, 25% with solution; both better tolerated than boric acid
Foti et al. (2001)	Case report	Interdigital tinea pedis (with secondary <i>P. aeruginosa</i> infection)	Ciclopirox olamine 1% cream	Terbinafine, econazole	Initial improvement noted; allergic contact dermatitis confirmed by patch testing; secondary bacterial infection complicated by <i>P. aeruginosa</i>
Thomas et al. (2005)	Case report	Cellulitis	Ciclopirox topical suspension	Oral levofloxacin, acetic acid compresses	Complete healing within 4 weeks of combined treatment
Romaszkiewicz et al. (2018)	Case series (reported in letter)	Mixed bacterial/fungal nail infection ( <i>P. aeruginosa</i> and <i>Candida albicans</i> )	Topical ciclopirox	Oral fluconazole, topical ciprofloxacin (eye drops)	Marked clinical and dermoscopic improvement within 1 month; near-complete resolution after 3 months
Gish et al. (2019)	Case report	Green nail syndrome (presumed <i>P. aeruginosa</i> )	Ciclopirox lacquer	None	No clinical improvement observed; progressive green discoloration

Figure 2. Summary of Clinical Studies Reporting Use of Ciclopirox for Cutaneous *P. aeruginosa* Infections.

## Results

A total of 29 records were identified. After removing 4 duplicates, 25 titles and abstracts were screened. Seventeen studies were excluded (6 unrelated to cutaneous *P. aeruginosa*, 11 review articles). Of 8 full-text articles reviewed, 5 met inclusion criteria: 1 randomized controlled trial, 3 case reports, and 1 case series. Infections reported included otomycosis, interdigital tinea pedis, cellulitis, and nail infections. Ciclopirox was applied topically in various formulations, either as monotherapy or alongside other treatments. Clinical outcomes were mixed, ranging from complete resolution to partial improvement, treatment failure, or hypersensitivity reactions.

## Discussion & Conclusion

This scoping review identified five clinical studies examining ciclopirox in the treatment of cutaneous *Pseudomonas aeruginosa* infections, including one randomized controlled trial and four case-based reports.<sup>9-13</sup> While primarily developed as an antifungal, ciclopirox has demonstrated in vitro activity against several Gram-negative bacteria, including *P. aeruginosa*.<sup>4,5</sup> Its proposed antibacterial mechanism involves iron chelation, which disrupts microbial metabolism, along with possible interference in lipopolysaccharide biosynthesis and other cellular processes.<sup>4,5,14</sup>

In vitro studies show that ciclopirox inhibits the growth of *P. aeruginosa*, though higher concentrations may be required compared to other bacteria, likely due to *P. aeruginosa*'s intrinsic resistance mechanisms such as efflux pumps and low membrane permeability.<sup>15,16</sup> These findings suggest that while ciclopirox has antibacterial potential, its clinical efficacy may be limited by microbial resistance traits, highlighting the importance of validating in vitro activity in clinical contexts.

Clinically, ciclopirox was used topically in varied formulations, often alongside other agents. In the single trial, it reduced *P. aeruginosa* presence in otomycosis cases, despite the primary target being fungi.<sup>9</sup> Case reports described partial or complete resolution of mixed infections when used with systemic or topical antimicrobials, though outcomes were inconsistent.<sup>10,11</sup> Some reports noted treatment failure or hypersensitivity reactions, particularly in patients with comorbidities.<sup>12,13</sup>

Overall, while early evidence suggests ciclopirox may serve as a useful adjunct in mixed infections, its standalone role in treating cutaneous *P. aeruginosa* remains unclear. Clinical studies are limited in number and design, and optimal treatment parameters have not been established. Further research is needed to determine its therapeutic value, especially amid rising concerns over antimicrobial resistance.

## References

