Natural Resources for Human Health
eISSN: 2583-1194

Original Research

Received 25 May 2026
Revised 26 June 2026
Accepted 21 July 2026

Natural Resources for Human Health 2026, Vol. 6 (10s): 859–868

KEYWORDS:
skin inflammation, inflamed skin, Lumbricus rubellus, treatment

The Role of Lumbricus Rubellus Extract on Inflamed Skin: A Systematic Review

Andi Widya Sumpala, Farida Tabri, Widya Widita, Andi Hardianty

Department of Dermatology, Venereology, and Aesthetics, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia
Corresponding Author*: Andi Widya Sumpala, MD. Department of Dermatology, Venereology, and Aesthetics, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia, 90245. Perintis Kemerdekaan Street, Km. 10, Tamalanrea Indah. 90245, Makassar, South Sulawesi.
Email: sumpalaw@gmail.com

ABSTRACT: This systematic review seeks to consolidate both preclinical and clinical data on the effectiveness, mechanisms, and safety of Lumbricus rubellus extract as a possible treatment for inflamed skin or inflammatory skin diseases. The review followed PRISMA guidelines. An extensive search was performed across PubMed, ScienceDirect, ProQuest, Google Scholar, Cochrane, and DOAJ for studies published over the last decade, utilizing Boolean combinations of Lumbricus rubellus AND (skin inflammation OR acne OR dermatitis OR urticaria OR psoriasis). The risk of bias was evaluated using Cochrane RoB, ROBINS-I, or the SYRCLE tool as suitable, and the findings were narratively synthesized. Five studies from Indonesia, including randomized controlled trials, quasi-experimental, and in vivo studies, assessed the impact of Lumbricus rubellus extract on inflammatory skin conditions. The findings indicated reductions in IL-31, IL-5, IgE, eosinophils, and Staphylococcus aureus colonization, along with increases in IL-10 and FOXP3, suggesting immunomodulatory effects. These changes correlated with improvements in SCORAD scores, though the extent varied and some results were not consistently significant. When used alongside standard therapies, additional benefits were observed. Preclinical studies also showed a decrease in paw edema. Reported side effects were mild, primarily nausea and gastrointestinal discomfort, with no serious incidents noted. Lumbricus rubellus extract shows promise as an adjunctive treatment for inflammatory skin conditions due to its immunomodulatory, anti-inflammatory, and antibacterial properties.

1. INTRODUCTION

The skin is the body's largest organ, enveloping the entire outer surface. Its structure consists of a complex network that functions as the first line of defense against pathogens, ultraviolet (UV) radiation, chemicals, and physical damage.[1] The skin functions not only as a physical barrier against external threats but also as a complex immune organ composed of various effector cells and molecules. Numerous cell types play a role in maintaining the skin's immune defense.[2] Skin inflammation is a common dermatological condition that arises when the immune system responds to various stimuli, resulting in symptoms such as redness, swelling, itching, and discomfort. This condition may be triggered by multiple factors, including infections, allergic reactions, irritants, autoimmune processes, and genetic susceptibility. Frequent causes include bacterial or fungal infections, contact dermatitis due to exposure to irritants or allergens, as well as conditions like psoriasis, eczema, and reactions to insect bites. Therefore, a clear understanding of its underlying mechanisms is essential for appropriate treatment and management.[3]

Inflammation is an essential defense mechanism that supports survival by helping the body eliminate harmful agents or causes of disease.[4] In some cases, pharmacological treatment is required to control this response. Commonly, inflammation is treated using non-steroidal anti-inflammatory drugs (NSAIDs); however, their use is often associated with side effects affecting the gastrointestinal tract, liver, and kidneys. Long-term consumption of NSAIDs can further increase the risk of serious complications, particularly in the digestive and excretory systems.[5,6] Considering these risks, there is increasing interest in developing alternative therapies from natural sources that are more accessible and have fewer side effects, especially those with anti-inflammatory potential used in traditional medicine, one of which is *Lumbricus rubellus*.[6]

For centuries, earthworms and other natural remedies have been widely used in traditional Chinese, Arabic, and Indian medicine to treat inflammatory and blood-related disorders. In Bali, powdered red earthworms have also been traditionally utilized for inflammation-related conditions, although scientific validation is still limited. Previous research indicates that ethanolic extracts of red earthworms sourced from organic farmland in Bali are rich in polyphenols and possess strong antioxidant activity, suggesting their potential role as anti-inflammatory agents.[6] Earthworm (*Lumbricus sp.*) extract also possesses antibacterial activity that can inhibit the growth of pathogenic microorganisms, including both Gram-positive and Gram-negative bacteria. The antibacterial activity of *Lumbricus sp.* extract may indirectly contribute to anti-inflammatory effects by reducing pathogenic microbial load, thereby decreasing immune activation and subsequent inflammatory responses.[7]

Despite these promising biological activities, most existing studies on *Lumbricus rubellus* are limited to in vitro experiments, animal models, or specific only on one condition such as atopic dermatitis. Moreover, there is still a lack of comprehensive synthesis of available research evaluating its effectiveness and mechanisms in inflammatory skin conditions. Therefore, a systematic review is needed to critically evaluate and summarize the current evidence regarding the role of *Lumbricus rubellus* extract in skin inflammation.

2. METHODS

2.1 Search strategy

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was performed across multiple electronic databases, including PubMed, ScienceDirect, ProQuest, Google Scholar, Cochrane Library, and DOAJ, focusing on studies published within the last ten years (2016-2026).

The search aimed to identify studies evaluating the effects of Lumbricus rubellus extract on inflammatory dermatoses, including atopic dermatitis, eczema, psoriasis, acne vulgaris, urticaria, and other inflammatory skin conditions. Boolean operators were applied using the following search strategy: ("Lumbricus rubellus" OR earthworm extract) AND ("inflammatory dermatoses" OR "skin inflammation" OR "cutaneous inflammation" OR "inflammatory skin disease" OR "atopic dermatitis" OR eczema OR dermatitis OR psoriasis OR acne OR "acne vulgaris" OR urticaria). Additionally, the reference lists of included studies and relevant review articles were manually screened to identify further eligible studies.

2.2 Data extraction

The inclusion criteria were designed to capture studies investigating the effects of Lumbricus rubellus extract on inflamed skin or inflammatory skin disease, either dermatitis, psoriasis, acne, etc. Eligible studies included preclinical studies (in vivo and in vitro), bacterial culture studies, clinical trials, and observational studies involving human subjects, including randomized controlled trials (RCTs) and cohort studies with comparative designs. Studies were included if they reported at least one of the following outcomes: reduction in clinical signs of skin inflammation (e.g., erythema, edema, pruritus), modulation of inflammatory biomarkers (such as TNF-α, IL-1β, IL-4, IL-6, IL-10, or IL-31), or improvement in skin barrier function.

Studies were excluded if they were not related to inflammatory skin conditions, reported only pharmacokinetic data without relevant biological or clinical outcomes, or were categorized as case reports, review articles, conference abstracts, editorials, or unpublished manuscripts. Studies lacking measurable inflammatory or clinical outcomes were also excluded to ensure the reliability of the findings.

Data extraction was conducted independently by four reviewers. Extracted data included study characteristics (author, year, sample size), study design (preclinical or clinical), intervention details (dosage, duration), and outcomes (clinical manifestations, cytokine levels, skin barrier parameters). Any discrepancies were resolved through discussion with a fifth reviewer.

2.3 Risk of bias assessment

Risk of bias in the included studies was evaluated using appropriate tools according to study design, including the Cochrane Risk of Bias (ROB) tool for randomized controlled trials (RCTs), the ROBINS-I tool for non-randomized clinical studies, and SYRCLE-tool for in vivo studies. This assessment was conducted independently by two reviewers, with any disagreements resolved through consultation with a third reviewer.

2.4 Data synthesis and analysis

For data synthesis and analysis, findings from the included studies were integrated using a narrative approach. The outcomes of interest were summarized qualitatively, supported by descriptive statistics where applicable. Clinical outcomes, such as reductions in inflammatory symptoms, improvements in skin barrier function, or improvements in inflammatory markers were collected and compared across studies. The results were then categorized based on the reported effects of Lumbricus rubellus extract on skin inflammation. The synthesis process was carried out by two reviewers and subsequently reviewed by additional authors to ensure accuracy and consistency.

3. RESULTS AND DISCUSSION

3.1 Data Searching

During the identification stage, records were retrieved from several electronic databases, including ScienceDirect, PubMed, ProQuest, Google Scholar, Cochrane Library, and DOAJ, yielding a total of 538 potentially relevant articles (Figure 1). After removing duplicate entries, 416 records were used to be screened. Subsequently, 29 full-text articles were sought for retrieval, of which 26 met the predefined eligibility criteria after assessment. Twenty one studies were excluded due to irrelevant outcomes, resulting in a final inclusion of five studies for qualitative analysis.

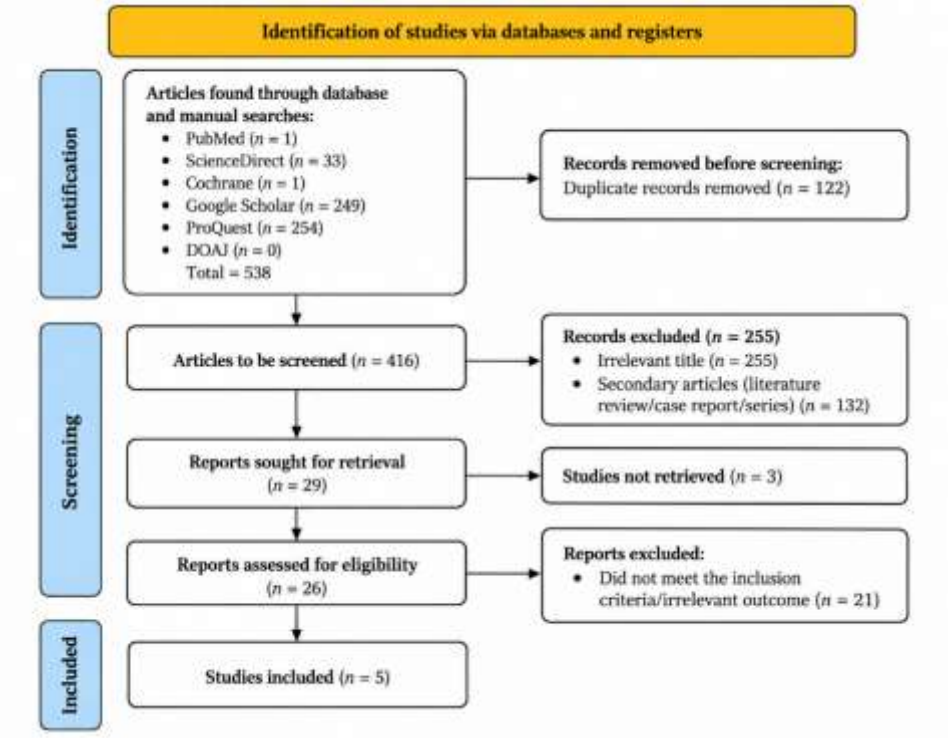

Figure 1. PRISMA flow diagram

3.2 Study Characteristics

A total of five studies were included, all of which investigated the effects of Lumbricus rubellus extract in various formulations and dosages for inflammatory skin conditions (Table 1). The included studies were conducted in Indonesia and utilized a variety of methodological designs, including randomized controlled trials, quasi-experimental studies, true experimental designs, and

in vivo animal studies. The study populations comprised both human subjects, primarily patients with atopic dermatitis across pediatric and adult age groups, and animal models, particularly male Wistar rats with induced inflammation. Sample sizes ranged from small to moderate, typically involving 30 participants or experimental subjects per study. Across all studies, Lumbricus rubellus extract was consistently used as the primary intervention. It was administered either as a monotherapy or in combination with conventional treatments such as topical corticosteroids (e.g., fluocinolone acetonide), emollients (e.g., vaseline), or compared with standard anti-inflammatory drugs like diclofenac sodium. These combinations suggest a potential synergistic effect when used alongside standard therapies.

In terms of formulation and route of administration, the extract was predominantly given in oral capsule form in clinical studies, while animal studies employed oral gavage. Dosages varied considerably, ranging from 250 mg twice daily in children to higher age-adjusted doses up to 2000 mg/day in adults. In animal models, doses ranged from 50 to 100 mg/kg body weight. However, inconsistencies and limited reporting regarding dosage details across studies make it difficult to establish a clear dose–response relationship. The duration of treatment varied between studies, ranging from 14 to 30 days in clinical settings and up to two weeks in animal studies. Outcomes measured included clinical severity scores such as SCORAD, levels of inflammatory and immunological markers (including IL-4, IL-5, IL-10, IL-31, IgE, eosinophils, and FOXP3), bacterial colonization (particularly Staphylococcus aureus), and, in preclinical models, reduction in paw edema as an indicator of inflammation. Overall, baseline severity of inflammatory skin conditions in human studies was generally mild to moderate. Across the included studies, administration of Lumbricus rubellus extract was associated with improvements in clinical and immunological parameters of inflammation, although the extent of these effects varied depending on study design, population, and intervention protocol.

3.3 Efficacy of Lumbricus rubellus Extract in Skin Inflammation

Several studies demonstrated that *Lumbricus rubellus* extract contributes to the reduction of inflammatory biomarkers and improvement of clinical outcomes in inflammatory skin conditions. Notably, significant decreases in *Staphylococcus aureus* colonization and IL-31 levels were observed, alongside reductions in SCORAD scores, indicating improvement in disease severity. Additional immunological effects included increased IL-10 levels and decreased IgE and eosinophil counts, suggesting a shift toward improved immune regulation. Furthermore, increases in FOXP3 expression and reductions in IL-5 levels were reported, supporting the extract's role in modulating Th2-driven inflammation.

In terms of clinical outcomes, most studies reported improvements in atopic dermatitis severity, primarily assessed using the SCORAD index. Greater reductions and a higher proportion of patients achieving significant improvement were generally observed in groups receiving *Lumbricus rubellus* extract compared to controls. However, in some studies, clinical improvement was reported qualitatively without standardized scoring, limiting objective comparison. Other studies showed modest reductions in SCORAD over short durations, with all patients remaining within the mild disease category. Additionally, when used in combination with standard treatments such as emollients, *Lumbricus rubellus* extract provided additional, statistically significant improvements compared to conventional therapy alone, supporting its role as an adjunctive treatment.

Preclinical evidence further supports these findings, as demonstrated by reduced paw edema in animal models, indicating anti-inflammatory activity. However, this model reflects general inflammation rather than specific skin inflammation.

Despite generally positive findings, the assessment of clinical outcomes was often limited, with reliance mainly on SCORAD and a lack of broader dermatological endpoints. In some cases, statistical significance was not consistently achieved across all parameters, indicating variability in treatment effects.

Regarding safety, no serious adverse events were reported. Mild side effects, such as gastrointestinal discomfort, were observed in some studies, suggesting that the extract is relatively well tolerated. Overall, the available evidence indicates that *Lumbricus rubellus* extract has potential as an adjunctive therapy for inflammatory skin conditions, particularly through its combined immunomodulatory and anti-inflammatory effects. However, the current evidence remains limited and heterogeneous, highlighting the need for further well-designed studies to confirm its efficacy and clinical relevance.

3.4 Risk of bias

Overall, the risk of bias assessment demonstrated that most domains were predominantly classified as low risk, particularly in areas such as selection of participants, missing outcome data, and selective reporting, indicating generally sound methodological quality among the included studies. However, several domains showed a considerable proportion of unclear risk, especially in

classification of interventions, deviations from intended interventions, and measurement of outcomes, suggesting limitations in reporting transparency (Figure 2). Similarly, in the second assessment, domains such as random group allocation, baseline similarity, random outcome assessment, selective reporting, and attrition bias were largely rated as low risk. In contrast, blinding-related domains, including blinding of group allocation, interventions, and outcome assessment, as well as other bias, were frequently categorized as unclear, reflecting insufficient methodological detail (Figure 3). Importantly, no domains were identified as high risk of bias. This indicates that although certain aspects of study design and reporting were not clearly described, the overall quality of the included studies remains acceptable with relatively low risk of significant bias.

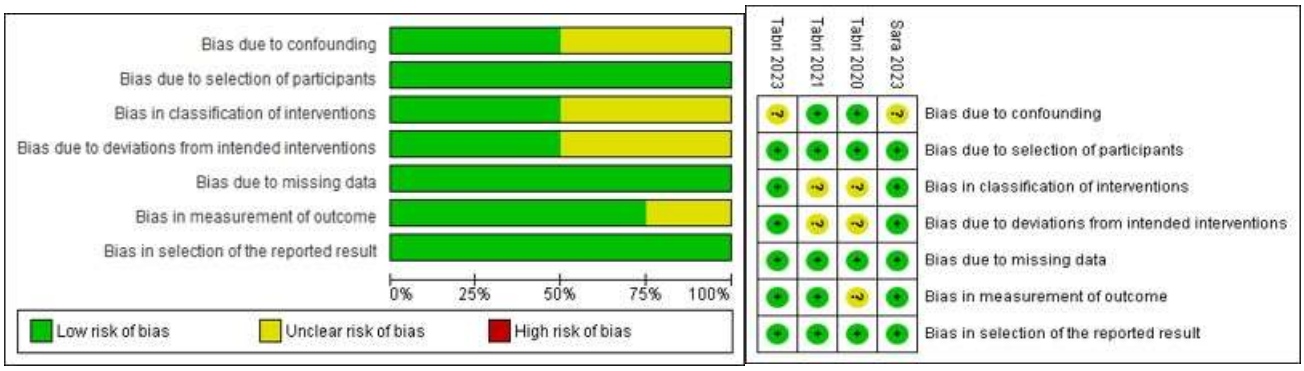

Figure 2. Risk of Bias using ROBINS-I tool

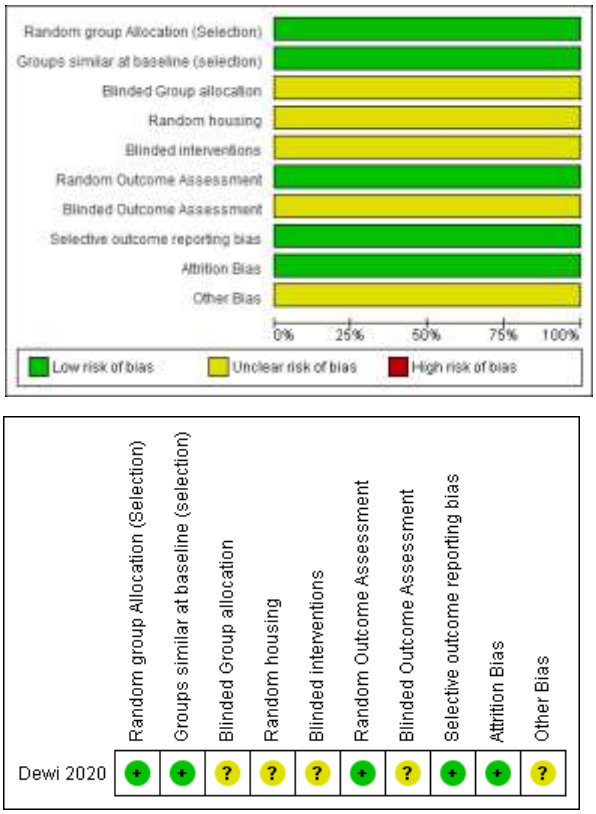

Figure 3. Risk of bias assessment using SYRCLE-tool

3.5 Discussion

Inflammatory skin diseases occur across all age groups, genders, and ethnicities and are among the most common reasons for dermatology consultations.[12] Earthworms have been utilized for medicinal purposes since as early as 1340 AD. In traditional Oriental medicine, they are recognized for their anti-inflammatory, analgesic, and antipyretic properties. Additionally, earthworms have been reported to exhibit anticancer potential, partly by inhibiting excessive glucose uptake.[13–15] For the

management of inflammation, commonly used first-line therapies include topical calcineurin inhibitors such as pimecrolimus and tacrolimus, topical corticosteroids like dexamethasone, as well as non-steroidal anti-inflammatory drugs (NSAIDs). However, prolonged use of these agents may result in significant adverse effects, including immunosuppression, organ dysfunction, and suppression of the hypothalamic–pituitary–adrenal axis. Therefore, there is a growing need to develop safer and more effective therapeutic alternatives, one of which is earthworm.[16]

The findings from the included studies demonstrate that *Lumbricus rubellus* extract exhibits notable immunomodulatory and anti-inflammatory properties, which may contribute to its therapeutic potential in inflammatory skin conditions. Several studies consistently reported modulation of key immune markers associated with inflammation. For instance, the extract was shown to significantly reduce *Staphylococcus aureus* colonization and IL-31 levels, a cytokine closely associated with pruritus in atopic dermatitis. This reduction is clinically relevant, as *S. aureus* colonization is known to exacerbate skin inflammation and barrier dysfunction.[8,17,18]

In addition to reducing pro-inflammatory mediators, *Lumbricus rubellus* extract was also associated with increased levels of IL-10 and FOXP3, alongside decreased levels of IL-5, IgE, and eosinophils. These findings indicate a shift toward enhanced regulatory T cell (Treg) activity and suppression of Th2-dominant immune responses, which are central to the pathogenesis of atopic dermatitis. The increase in IL-10 and FOXP3 suggests improved immune regulation, while the reduction in IL-5, IgE, and eosinophils reflects decreased allergic inflammation.[7,9,11,19]

Clinical outcomes across the studies further support these immunological findings. Improvements in disease severity, as measured by SCORAD, were consistently observed in both intervention and control groups; however, the groups receiving *Lumbricus rubellus* extract generally demonstrated greater reductions. In one study, more than 35% improvement in SCORAD was achieved in a higher proportion of patients receiving the extract, although statistical significance was not always reached. Other studies reported modest but consistent reductions in SCORAD scores over short treatment durations, particularly in patients with mild atopic dermatitis.[7,8,11] Moreover, *Lumbricus rubellus* extract appears to have potential as an adjunctive therapy. When combined with standard treatments such as emollients (e.g., vaseline), the extract provided additional, statistically significant improvements in disease severity compared to conventional therapy alone. This suggests that its role may be more appropriate as a complementary treatment rather than a standalone therapy.[11]

Research has demonstrated that the administration of natural products like earthworm can improve and sustain anti-inflammatory and antioxidant activities, as well as support hematological parameters and serum biochemical profiles in animals.[20] One in vivo study using a carrageenan-induced paw edema model demonstrated a significant reduction in edema volume following administration of the extract, indicating its ability to suppress acute inflammatory responses. Although this model does not specifically represent skin inflammation, it provides supporting evidence for the extract's general anti-inflammatory activity.[6]

Despite these promising findings, several limitations should be acknowledged. Many of the included studies were conducted with small sample sizes and relatively short follow-up periods, which may limit the generalizability of the results. In addition, some studies did not utilize standardized clinical scoring systems, thereby reducing the overall strength and comparability of the evidence. The inconsistency in statistical significance across outcomes also indicates variability in treatment effects. Importantly, the available evidence is largely limited to atopic dermatitis, with a lack of studies investigating other types of inflammatory skin diseases. This narrow focus restricts the broader applicability of the findings to skin inflammation as a whole.

Overall, the current evidence suggests that *Lumbricus rubellus* extract has potential therapeutic benefits in inflammatory skin conditions through its combined antibacterial, immunomodulatory, and anti-inflammatory effects. However, further well-designed clinical trials with larger sample sizes, standardized outcome measures, and longer follow-up durations are needed to confirm its efficacy and establish its role in clinical practice.

4. CONCLUSION

Lumbricus rubellus extract demonstrates potential as an adjunctive therapeutic agent in inflammatory skin conditions through its immunomodulatory, anti-inflammatory, and antibacterial properties. These effects are reflected in the modulation of immune responses, including the reduction of pro-inflammatory cytokines (such as IL-4, IL-5, and IL-31), IgE levels, and microbial colonization, alongside the enhancement of regulatory markers such as IL-10 and FOXP3. Collectively, these mechanisms contribute to the improvement of clinical manifestations of skin inflammation. However, current evidence remains largely

limited to atopic dermatitis, with minimal data available on other inflammatory skin diseases. Therefore, further research is required, particularly other skin inflammation condition, to better establish the efficacy and clinical applicability of *Lumbricus rubellus* extract as a safe and consistent adjunctive therapy for inflammatory skin conditions.

ACKNOWLEDGEMENTS

None.

AUTHOR CONTRIBUTIONS

Andi Widya Sumpala contributed to the literature search, data extraction, data synthesis, interpretation, and manuscript drafting. **Farida Tabri, Widya Widita,** and **Andi Hardianty** contributed to data extraction, risk-of-bias assessment, interpretation, and critical revision. All authors approved the final manuscript.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICS STATEMENT

An ethics statement is not applicable.

REFERENCES

[1] Yousef H, Alhajj M, Fakoya AO, Sharma S. Anatomy, Skin (Integument), Epidermis. StatPearls. 2024 Jun 8. PubMed PMID: 29262154.

[2] Tampa M, Neagu M, Caruntu C, Constantin C, Georgescu S. Skin Inflammation—A Cornerstone in Dermatological Conditions. J Pers Med. 2022 Aug 25;12(9):1370. doi:10.3390/jpm12091370

[3] Tanzil K. Complex Mechanisms of Skin Inflammation and Treatment Strategies. 2023. doi:10.35248/2684-1436.23.8.216

[4] L. Kiss A. Inflammation in Focus: The Beginning and the End. Pathology and Oncology Research. 2022 Jan 4;27. doi:10.3389/pore.2021.1610136

[5] Ghlichloo I, Gerriets V. Nonsteroidal Anti-Inflammatory Drugs (NSAIDs). First Aid Perioperative Ultrasound: Acute Pain Manual for Surgical Procedures. 2023 May 1;127–38. doi:10.1007/978-3-031-21291-8_8 PubMed PMID: 31613522.

[6] Dewi NWS, Mahendra AN. The in-vivo anti-inflammatory effect of red earthworm (Lumbricus rubellus) ethanolic extract from organic farmland in Bali, Indonesia. Bali Medical Journal. 2020 Oct 13;9(3):652–5. doi:10.15562/bmj.v9i3.1788

[7] Tabri F, Bayasari PS, Nurdin RSC, Anwar AI, Adriani A, Ilyas F. The Effectiveness of Lumbricus rubellus Extract Toward Interleukin-10 and Immunoglobulin E and Atopic Dermatitis Scoring Index (SCORAD). Open Access Maced J Med Sci. 2021 Nov 10;9(B):1428–34. doi:10.3889/oamjms.2021.7196

[8] Sara M, Ilyas F, Hasballah K, Nurjannah N, Mudatsir M. The Effects of Lumbricus rubellus Extract on Staphylococcus aureus Colonization and IL-31 Levels in Children with Atopic Dermatitis. Medicina (B Aires). 2023 Nov 15;59(11):2007. doi:10.3390/medicina59112007

[9] Tabri F, Bayasari PS, Camelia RS, Anwar AI, Adriani A, Ilyas. F. THE EFFECT OF LUMBRICUS RUBELLUS EXTRACTS ON IL-4, IL-10, IgE, AND EOSINOFIL LEVELS IN ATOPIC DERMATITIS PATIENT. Systematic Reviews in Pharmacy. 2020;11(10):1039–65. doi:10.31838/SRP.2020.10.153

[10] Tabri F, Bayasari PS, Nurdin RSC, Anwar AI, Adriani A, Ilyas F. The Effectiveness of Lumbricus rubellus Extract Toward Interleukin-10 and Immunoglobulin E and Atopic Dermatitis Scoring Index (SCORAD). Open Access Maced J Med Sci. 2021 Nov 10;9(B):1428–34. doi:10.3889/oamjms.2021.7196

[11] Tabri F, Djawad K, Wahab S, Madjid A, Azhari T, Rezki N, et al. Effect of Lumbricus rubellus Extract on FOXP3, Interleukin-5 and Bacteria Inhibitory on the Skin of Atopic Dermatitis Corresponding author: 1*. Vol. 63. 2023;63(10).

[12] Hessler-Waning M, Heinecke G. Diagnosis and Management of Common Inflammatory Skin Diseases in Older Adults. Clin Geriatr Med. 2024 Feb;40(1):11–23. doi:10.1016/j.cger.2023.09.007

[13] Mathur A, Verma SK, Singh SK, Prakash A, Prasad GBKS, Dua VK. ANTI-INFLAMMATORY ACTIVITY OF EARTHWORM EXTRACTS. Int J Pharm Sci Res. 2011;2(2):278–81.

[14] Hardiana I, Wahyudin E, Aswad M, Agustina R. Integrative Analysis of the Pharmacological Activities of Lumbricus rubellus: Evidence from Preclinical and Clinical Research. Borneo Journal of Pharmacy. 2025 Nov 30;8(4):313–25. doi:10.33084/bjop.v8i4.8741

[15] Zhu Z, Deng X, Xie W, Li H, Li Y, Deng Z. Pharmacological effects of bioactive agents in earthworm extract: A comprehensive review. Animal Model Exp Med. 2024 Oct 3;7(5):653–72. doi:10.1002/ame2.12465

[16] Sung YY, Yuk HJ, Kim SH, Kim DS. Effects of Earthworm (Pheretima communisima) extract on atopic dermatitis: An in vitro and in vivo study. Heliyon. 2025 Jan;11(1):e41140. doi:10.1016/j.heliyon.2024.e41140

[17] Nakatsuji T, Chen TH, Two AM, Chun KA, Narala S, Geha RS, et al. Staphylococcus aureus Exploits Epidermal Barrier Defects in Atopic Dermatitis to Trigger Cytokine Expression. Journal of Investigative Dermatology. 2016 Nov;136(11):2192–200. doi:10.1016/j.jid.2016.05.127

[18] Özdemir E, Öksüz L. Effect of Staphylococcus aureus colonization and immune defects on the pathogenesis of atopic dermatitis. Arch Microbiol. 2024 Oct 20;206(10):410. doi:10.1007/s00203-024-04134-w

[19] Ng THS, Britton GJ, Hill E V., Verhagen J, Burton BR, Wraith DC. Regulation of Adaptive Immunity; The Role of Interleukin-10. Front Immunol. 2013;4. doi:10.3389/fimmu.2013.00129

[20] BALAMURUGAN M, PARTHASARATHI K, COOPER EL, RANGANATHAN LS.

[21] Earthworm paste (Lampito mauritii, Kinberg) alters inflammatory, oxidative, haematological and serum biochemical indices of inflamed rat. Eur Rev Med Pharmacol Sci. 2017;11:77–90.

Table 1. Study Characteristics

Author, year	Country	Study design	Sample size (n)	Age (years)	Study subjects	Intervention	Control	*Lumbricus* formulation	*Lumbricus* dosage	Duration	Outcome measured
Sara, 2023[8]	Indonesia	Randomized controlled trial	Intervention: 20; Control: 20	Intervention: 10.75 ± 2.17; Control: 11.1 ± 2.26	Childhood atopic dermatitis patients	Topical fluocinolone acetonide 0.025% combined with *Lumbricus rubellus* extract (Vermint®)	Topical fluocinolone acetonide 0.025% and placebo	Oral capsule	250 mg twice daily for 14 days	14 days	*Staphylococcus aureus* colonization, IL-31 levels, and SCORAD index
Tabri, 2020[9]	Indonesia	Quasi-experimental	Intervention: 15; Control: 15	5 to >64	Patients with mild atopic dermatitis	*Lumbricus rubellus* extract	Not reported	Not reported	Not stated; given for 2 weeks	30 days	IL-4, IL-10, IgE, and eosinophil levels

Tabri, 2021[10]	Indonesia	Quasi-experimental	Intervention: 15; Control: 15	5–44	Patients with atopic dermatitis	*Lumbricus rubellus* extract	Not reported	Not reported	Children 1–3 years: 2 × 250 mg; children >3–12 years: 2 × 500 mg; adults: 2 × 1000 mg for 7 days	15 days	IL-10, IgE, and SCORAD index
Tabri, 2023[11]	Indonesia	True experimental study with pre-test and post-test control group design	Intervention: 15; Control: 15	0–45	Mild atopic dermatitis patients	Topical vaseline and *Lumbricus rubellus* capsule extract	Topical vaseline	Oral capsule	Adult dose: 2000 grams/day; children: thermic formula (children's body weight in kg × maximum adult dose)/70	30 days	Serum FOXP3, IL-5 levels, and bacterial inhibition
Dewi, 2020[6]	Indonesia	In vivo	Control: 10; Intervention: 20	–	Male Wistar rats with skin inflammation-induced paw edema	Red earthworm ethanolic extract	Non-steroidal anti-inflammatory drug (NSAID), diclofenac sodium 9 mg/kgBW	Oral gavage	50–100 mg/kg BW	2 weeks	Rat paw edema (reduction in edema volume)

Table 2. Outcomes of Included Studies

Author, year	Adverse effects	Main findings	Clinical outcomes
Sara, 2023[8]	Not reported	Significant reductions in *Staphylococcus aureus* colonization ($p = 0.001$) and IL-31 levels ($p = 0.013$). A >35% improvement in SCORAD was observed, although not statistically significant ($p = 0.057$).	Both groups showed improved atopic dermatitis severity. The *L. rubellus* group had a greater SCORAD reduction and a higher proportion of patients achieving >35% improvement.
Tabri, 2020[9]	Nausea and intestinal disorders	Significant differences between groups were observed on day 8 but not day 15. IL-10 increased, while IgE and eosinophil levels decreased.	Clinical improvement was reported qualitatively in mild atopic dermatitis; no standardized severity score was used.
Tabri, 2021[10]	Intestinal disorders	IgE levels differed significantly between groups at earlier time points but not by day 15. Overall, *L. rubellus* extract was associated with reduced SCORAD.	Both groups showed slight SCORAD reductions over 15 days, with marginally greater improvement in the *L. rubellus* group; all patients remained in the mild category.
Tabri, 2023[11]	Not reported	Increased FOXP3 expression ($p < 0.001$) and decreased IL-5 levels ($p < 0.001$) were observed.	Both groups improved over four weeks; *L. rubellus* extract combined with vaseline produced an additional statistically significant reduction in SCORAD compared with vaseline alone.
Dewi, 2020[6]	Not reported	Ethanolic *L. rubellus* extract demonstrated anti-inflammatory activity by reducing paw edema compared with the negative control. Significant differences were observed in several treatment groups ($p < 0.05$).	Reduction in paw edema indicated anti-inflammatory activity in the animal model.