



## Evaluating the Efficacy of Therapeutic Interventions for Head Lice: A Systematic Review

Sarah Mohamadi<sup>1</sup>, Zahra Rahimi Khalifeh Kandi<sup>2</sup>, Fatemeh Sadat Izadkhah<sup>1</sup>, Fatemeh Sadat Alavi<sup>1</sup>, Zahra Hazrati-Meimaneh<sup>1,3</sup>, Bahare Izadi<sup>4</sup>, Morteza Mansourian<sup>5\*</sup>

<sup>1</sup> PhD Candidate of Health Education and Health Promotion, School of Public Health, Iran University of Medical Sciences, Tehran, Iran.

<sup>2</sup> Assistant Professor, Department of Public Health, School of Health, Qazvin University of Medical Sciences, Qazvin, Iran.

<sup>3</sup> South Tehran Health Center, Tehran University of Medical Sciences, Tehran, Iran.

<sup>4</sup> Health Promotion Research Center, Iran University of Medical Sciences, Tehran, Iran.

<sup>5</sup> Professor, Health Promotion Research Center, Iran University of Medical Sciences, Tehran, Iran.

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### Abstract

**Background:** Pediculosis remains a significant public health concern in many communities. Head lice infestations and their management continue to pose both clinical and social challenges. This systematic review aimed to evaluate the efficacy of various therapeutic interventions for head lice, focusing on their effectiveness in eradicating infestations.

**Methods:** A systematic search was conducted in databases PubMed, Web of Science, and Scopus for studies published between 2013 and 2023, using the keywords "Head lice," "Pediculus humanus capitis," "Pediculosis," and "Treatment." Randomized or controlled trials with at least minimal blinding and participants aged over six months were included. Study selection and data extraction were performed independently by two reviewers.

**Results:** A total of 21 studies involving 3,232 participants met the inclusion criteria. Treatments were classified into chemical and non-chemical categories. Among chemical treatments, permethrin, dimethicone, ivermectin, and phenothrin were the most effective. Effective non-chemical interventions included natural oils and plant-based extracts such as eucalyptus. Reported treatment success rates showed considerable variability, ranging from 20% to 100%.

**Conclusions:** Pediculosis remains highly prevalent worldwide. Although various treatment options are available, selecting the most effective and least harmful intervention based on individual and regional factors is essential for optimal management.

**Keywords:** Head lice, Pediculus humanus capitis, Systematic review, Treatment, Clinical trial.

**\*Corresponding to:** M Mansourian, **Email:** mansourian55@gmail.com

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## Introduction

Pediculosis capitis is a widespread ectoparasitic condition, particularly among children<sup>1</sup>, and remains a global health concern across both developed and developing countries<sup>2</sup>. The infestation, caused by blood-feeding lice<sup>3</sup>, affects individuals of all socioeconomic backgrounds<sup>2, 4</sup>, with higher prevalence noted in girls, especially in rural areas and among children aged 3 to 12<sup>5-7</sup>.

Although head lice are not associated with poor hygiene, body lice are often linked to poverty and homelessness<sup>8</sup>.

Transmission occurs via direct head-to-head contact or indirectly through shared items like combs, pillows, or hats<sup>8, 9</sup>.

Prevalence varies globally, ranging from 0.48%-22.4% in Europe, 0.7%-59% in Turkey, 0%-58.9% in Africa, and 3.6%-61.4% in the Americas<sup>10</sup>. An estimated 19% of schoolchildren are affected worldwide<sup>1</sup> and around 2% of adults may have pubic lice<sup>11</sup>. The overall incidence has risen significantly in the last three decades<sup>12</sup>.

Though not life-threatening, infestation can cause discomfort, psychological distress, social stigma, and school absenteeism, contributing to a financial burden on families and healthcare systems<sup>2, 4</sup>. Despite numerous available treatments, outbreaks persist<sup>13</sup>, and treatment failures due to resistance have been reported<sup>12</sup>.

While 1% permethrin is the most widely used topical agent, oral treatments may be considered when topical therapies fail<sup>4</sup>. Several pharmacologic options are available, including 1% topical permethrin (safe for children >2 months)<sup>4</sup>, oral ivermectin, wet combing, 0.5% malathion<sup>14</sup>, and newer agents such as Spinosad<sup>15</sup>. Recently, topical ivermectin has received FDA approval as an over-the-counter treatment<sup>16</sup>. Dimethicone, a silicone-based product, is commonly used in Europe<sup>17, 18</sup>, while herbal and essential oil-based remedies are also explored<sup>19-22</sup>. In some cases, adjunctive treatments like topical antibiotics or steroids may be needed<sup>23</sup>.

Considering the increasing reports of resistance to commonly used pediculicidal agents and the wide variability in both chemical and non-chemical treatment approaches worldwide, there is a clear need for a systematic evaluation of current therapeutic strategies. Therefore, this systematic review was conducted to critically assess and compare the efficacy of chemical and non-chemical interventions for head lice treatment over the past decade.

### Materials and Methods

This systematic review was conducted to evaluate the efficacy of therapeutic interventions for head lice (Pediculosis capitis). The review covered clinical studies published between January 2013 and September 2023.

This review adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines<sup>24</sup>.



throughout all stages including study identification, screening, selection, data extraction, and synthesis. However, the review protocol was not registered in PROSPERO, which is acknowledged as a limitation due to the absence of a pre-registered methodological framework.

**Search Strategy:** A comprehensive search was carried out in three major databases: PubMed, Scopus, and Web of Science. The search included articles published in English within the specified time frame. Search terms were derived from Medical Subject Headings (MeSH), Emtree indexing, and previously published literature. The following search terms were used in various combinations: "Head Louse," "Head lice," "Pediculus human capititis," "Pediculosis," "Treatment," and "Therapy."

The electronic search was conducted between September 3 and September 7, 2023. Additionally, manual reference checks were performed on the bibliographies of included studies to maximize search sensitivity and identify any missing relevant publications.

**Study Selection:** Two independent reviewers screened titles, abstracts, and full texts to identify eligible studies. EndNote software was used to manage citations and remove duplicates. The full text of potentially relevant studies was retrieved and assessed based on predefined inclusion and exclusion criteria. All discrepancies between reviewers were resolved by consensus or through discussion with a third reviewer.

**Inclusion Criteria:** Studies were selected based on the PICO framework, Population: Humans with head lice infestation of any age, gender, or nationality, Intervention: Any form of treatment intended to reduce or eliminate head lice, Comparator: Placebo, other treatments, or no treatment (as applicable), Outcomes: Efficacy in terms of lice reduction/elimination, Additional inclusion criteria were clinical trials published in English between January 2013 and September 2023, and interventions conducted in human populations.

**Exclusion Criteria:** The exclusion criteria included studies that involved animal models or were conducted solely in *in-vitro* or laboratory settings. Additionally, articles that were not published in English, studies without access to full texts, and those with non-interventional or purely observational designs were excluded from this review.

**Data Extraction:** Data extraction was performed independently by two reviewers using a standardized Excel form. The extracted information included the study title, name of the first author, year of publication, country of study, sample size, study design, and randomization method. Detailed information about the intervention—such as type, dosage, frequency, mode of application, and duration of treatment was

also extracted, along with the main outcome measures and results. Any disagreements between the reviewers were resolved through discussion or, if necessary, by consulting a third reviewer. Studies with incomplete or missing data were excluded from the final synthesis.

**Risk of Bias Assessment:** The risk of bias in the included randomized controlled trials was independently assessed by two reviewers using the Cochrane Risk of Bias tool (RoB 2)<sup>25</sup>, which evaluates five domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Each domain was rated as having low risk, some concerns, or high risk of bias. Disagreements were resolved through discussion, or in case of persistent conflict, by consulting a third reviewer. The inter-rater agreement was evaluated using the Cohen's Kappa coefficient. The risk of bias assessment informed data interpretation and synthesis; however, no studies were excluded solely due to quality concerns.

## Results

The study selection process followed the PRISMA guidelines, as illustrated in Figure 1. During the initial search phase, a total of 7,713 records were identified. After applying publication date limits, 3,429 studies remained potentially relevant. A subsequent screening of titles and abstracts led to the exclusion of 1,075 duplicate records and 2,292 articles deemed irrelevant. A total of 21 studies met the inclusion criteria and were analyzed in the systematic review. The main characteristics of the included studies are summarized in Table 1. The studies were published between 2013 and 2023 and were conducted across various countries, including Iran, Japan, Brazil, the United Kingdom, Australia, Egypt, the United States, Germany, Indonesia, and Senegal. The majority of studies employed randomized controlled trial (RCT) designs, with variations such as double-blind, single-blind, open-label, and assessor-blinded protocols. Sample sizes ranged from 31 to 704 participants, with both pediatric and general populations included.

The interventions assessed a wide variety of pediculicides, including chemical-based treatments such as permethrin, lindane, and phenothrin, as well as non-chemical options like dimethicone, mineral oils, and essential oil formulations (e.g., eucalyptus, neem, and cinnamon). Some studies also compared mechanical methods (e.g., wet-combing) or oral treatments like ivermectin. Follow-up durations varied across studies, from a few days up to four weeks, and assessment methods generally involved clinical or visual detection of lice.

These findings highlight significant variability in treatment efficacy across chemical and non-chemical modalities, emphasizing the need for tailored approaches based on local resistance profiles and treatment accessibility.



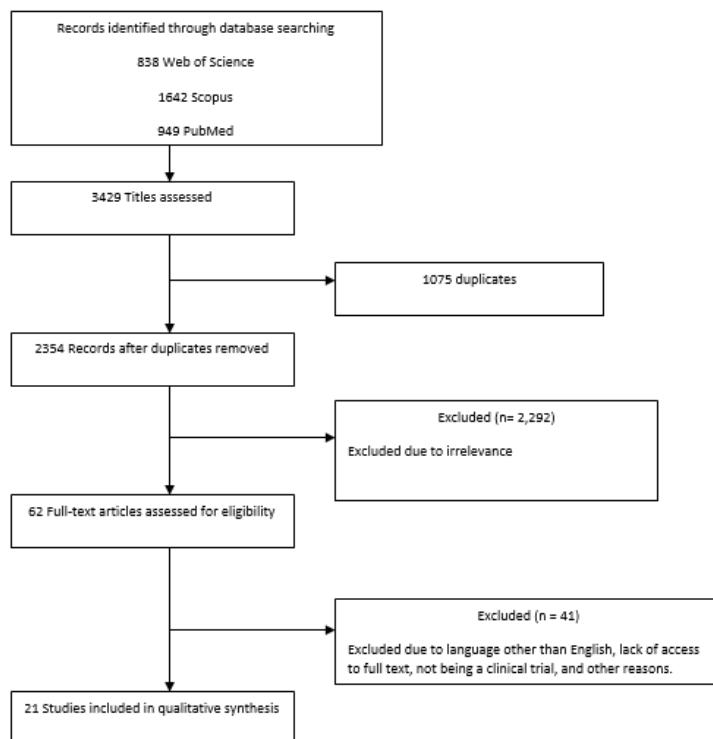


Figure 1. PRISMA flow diagram of the study selection process

Table 1. Characteristics of the studies included in the systematic review

Number	Author's name and Publication year	Location of study	Study design	sample size	Pediculicid type	Intervention	Follow-up duration	Assessment method	Outcome (Cure rate)
1	Ghalandari N <sup>26</sup> , 2023	Iran	Parallel, randomized clinical trial	154	1% Permethrin (Shampoo and Cream)	Three groups: 1. Permethrin shampoo for 10 minutes 2. Permethrin shampoo for 1 hour 3. Permethrin cream for 10 minutes. All treatments applied weekly for 3 weeks	3 weeks	Evaluation of lice presence	Fastest cure in 1-hour shampoo group: mean eradication time=1.23±0.42 weeks Significantly higher first-week cure rate in 1-hour shampoo group compared to 10-min shampoo and cream groups.
2	Yamaguchi S <sup>18</sup> , 2021	Japan	Open-label clinical trial	35	Dimethicone-containing lotion	Application of dimethicone lotion over entire scalp three times within a 7-day period	8 days (clinical assessment) + ~4 weeks (via follow-up telephone survey for recurrence)	Count of lice (adults/nymphs) and eggs	in >80% of subjects (utility rated "marginally useful" or higher)

3	Kassiri, H <sup>27</sup> , 2020	Iran	Observer-blinded randomized controlled trial	444	1% Permethrin shampoo, 1% Lindane shampoo, 4% Dimethicone lotion, and Placebo Intervention	- Permethrin & Dimethicone: 2 applications, 1 week apart - Lindane: Single application	15 days total (assessments on Day 2, Day 8, and Day 15)	Clinical examination for live lice presence	Day 2: Permethrin: 56.8%, Lindane: 31.5%, Dimethicone: 51.4%, Placebo: 10.8% Day 8: Permethrin: 69.4%, Lindane: 73%, Dimethicone: 60.4% Day 15: Permethrin: 90.1%, Lindane: 86.5%, Dimethicone: 94.6% Permethrin: 79.5% lice-free Dimethicone: 83% lice-free Ivermectin: 90.6% lice-free Statistical Significance: significant (P-value>0.05) Novel lotion: 21/22 cured (95.5%) Permethrin: 9/23 cured (39.1%) Statistical significance: P-value<0.0001 After first treatment: 7/31 lice-free (22.6%) At study end (Day 16): 12/31 lice-free (38.7%)
4	Hamedanian L <sup>28</sup> , 2021	Iran	Randomized, controlled, single-blinded comparative trial	179	1% Permethrin shampoo (WHO gold standard), 4% Dimethicone lotion, Ivermectin lotion	Single application from each product	30 days total; assessments on Day 14 and Day 30	Clinical examination for presence of adult lice or live nits	Dimethicone: 83% lice-free Ivermectin: 90.6% lice-free Statistical Significance: significant (P-value>0.05) Novel lotion: 21/22 cured (95.5%) Permethrin: 9/23 cured (39.1%) Statistical significance: P-value<0.0001 After first treatment: 7/31 lice-free (22.6%) At study end (Day 16): 12/31 lice-free (38.7%)
5	Cardoso, J.H.L <sup>29</sup> , 2020	Brazil	Double-blind, randomized, controlled, superiority trial	45	Novel lotion (semi-crystalline polymers + plant extracts), and 1% Permethrin lotion	single application of either lotion for 15 minutes	10 days	clinical cure defined via presence/absence of lice	Permethrin: 9/23 cured (39.1%) Statistical significance: P-value<0.0001 After first treatment: 7/31 lice-free (22.6%) At study end (Day 16): 12/31 lice-free (38.7%)
6	Burgess I.F <sup>30</sup> , 2020	England	Open-label clinical study	31	1% fractionated coconut oil shampoo	Two applications — Day 0 and Day 8	16 days total; assessments on Day 1, Day 8, and Day 16	Detection comb (manual examination for lice)	After 1 week: Permethrin 66%, Wet combing 63% (P-value=0.740) After 2 weeks: Permethrin 94%, Wet combing 89% (P-value=0.507)
7	Sungkar S <sup>31</sup> , 2019	Indonesia	Randomized Controlled Trial	121	Permethrin lotion, Wet combing with conditioner (non-chemical comparator)	Permethrin group: Lotion applied to wet hair for 10 minutes, followed by lice removal with fine-toothed comb and shampoo wash Wet-combing group: Same procedure, but using conditioner instead of permethrin	14 days (re-evaluation on Day 14)	Direct head examination for presence of lice	Permethrin: 81%, 74%, 70%, 63% on days 2, 6, 9, 14 Dimethicone: 83%, 92%, 100%, 100% on days 2, 6, 9, 14 d-Phenothrin: 96%, 88%, 96%, 92% on days 2, 6, 9, 14 Significant differences on days 9 (P-value=0.008) and 14 (P-value=0.003) 88.2% (test product) vs. 2.9% (reference) after first treatment; cure rate significantly above pre-defined 70% threshold 92.9% absolute reduction in hatch rate (100% unhatched eggs in abametapir group vs. 64% in control); statistically significant (P-value<.0001)
8	Kalari H <sup>32</sup> , 2019	Iran	Randomized controlled, assessor-blinded trial (3-arm parallel design)	77	Group 1: 1% Permethrin (pyrethroid-based) Group 2: 0.2% d-Phenothrin (Parasidose, pyrethroid-based) Group 3: 4% Dimethicone (non-chemical)	Two applications (one week apart) of each product	14 days (re-inspection on days 2, 6, 9, 14)	Visual inspection with plastic detection comb	Permethrin: 81%, 74%, 70%, 63% on days 2, 6, 9, 14 Dimethicone: 83%, 92%, 100%, 100% on days 2, 6, 9, 14 d-Phenothrin: 96%, 88%, 96%, 92% on days 2, 6, 9, 14 Significant differences on days 9 (P-value=0.008) and 14 (P-value=0.003) 88.2% (test product) vs. 2.9% (reference) after first treatment; cure rate significantly above pre-defined 70% threshold 92.9% absolute reduction in hatch rate (100% unhatched eggs in abametapir group vs. 64% in control); statistically significant (P-value<.0001)
9	Eertmans F <sup>33</sup> , 2019	Florida, USA	Randomized, controlled, investigator-blinded, bicentric study	70	Aqueous dispersion of novel silylated polyol (test product) vs. pyrethrum-based pediculicide (reference)	Two applications on Day 0 and Day 7, per usage instructions	10 days (until study end)	Clinical evaluation for lice presence	Permethrin: 81%, 74%, 70%, 63% on days 2, 6, 9, 14 Dimethicone: 83%, 92%, 100%, 100% on days 2, 6, 9, 14 d-Phenothrin: 96%, 88%, 96%, 92% on days 2, 6, 9, 14 Significant differences on days 9 (P-value=0.008) and 14 (P-value=0.003) 88.2% (test product) vs. 2.9% (reference) after first treatment; cure rate significantly above pre-defined 70% threshold 92.9% absolute reduction in hatch rate (100% unhatched eggs in abametapir group vs. 64% in control); statistically significant (P-value<.0001)
10	Bowles V.M. <sup>34</sup> , 2019	Australia	Randomized, double-blind, phase 2 clinical trial.	50	Abametapir lotion, 0.74%	Single application of abametapir lotion applied to scalp and hair for 10 minutes	14 days (incubation period for egg hatch observation) additional clinical assessments on Day 1 and Day 7	Microscopic examination of viable eggs collected before and after treatment	Permethrin: 81%, 74%, 70%, 63% on days 2, 6, 9, 14 Dimethicone: 83%, 92%, 100%, 100% on days 2, 6, 9, 14 d-Phenothrin: 96%, 88%, 96%, 92% on days 2, 6, 9, 14 Significant differences on days 9 (P-value=0.008) and 14 (P-value=0.003) 88.2% (test product) vs. 2.9% (reference) after first treatment; cure rate significantly above pre-defined 70% threshold 92.9% absolute reduction in hatch rate (100% unhatched eggs in abametapir group vs. 64% in control); statistically significant (P-value<.0001)

11	Greive KA <sup>35</sup> , 2018	Australia	Multi center, randomized, assessor-blind, parallel-group trial (Trial 1); single-blind, open-label trial (Trial 2)	male and female primary school children (up to Year 7) with confirmed active head lice (live lice only)	MOOV Head Lice Solution containing 11% eucalyptus oil + 1% Leptospermum petersonii Banlice Mousse with 1.65 mg/g pyrethrins + 16.5 mg/g piperonyl butoxide (P/PB mousse)	A topical head lice treatment (MOOV Head Lice Solution) containing 11% w/w eucalyptus oil and 1% w/w Leptospermum petersonii, applied on days 0, 7, and 14, following manufacturer's instructions.	EO/LP (Trial 1): assessed on day 21 P/PB (Trial 1): assessed on day 14 Trial 2 (EO/LP): assessment at 30 minutes post-treatment	visual inspection	Trial 1 (per-protocol): <ul style="list-style-type: none"><li>EO/LP: 83% cure rate</li><li>P/PB: 36% cure rate</li></ul> Statistical significance: p < 0.0001 Trial 2: <ul style="list-style-type: none"><li>EO/LP: 100% pediculicidal effect (no lice showed signs of life at 30 minutes)</li></ul> Abametapir Lotion: <ul style="list-style-type: none"><li>Study 1: 81.1% of index subjects louse-free at post-baseline visits (P-value=0.001)</li><li>Study 2: 81.8% of index subjects louse-free at post-baseline visits (P-value&lt;0.001)</li></ul> Vehicle Lotion: <ul style="list-style-type: none"><li>study 1: 50.9% of index subjects louse-free at post-baseline visits</li><li>Study 2: 47.2% of index subjects louse-free at post-baseline visits</li></ul> Exploratory Endpoint (Day 14): <ul style="list-style-type: none"><li>Study 1: 88.2% abametapir group louse-free (P-value&lt;0.001)</li><li>Study 2: 81.0% abametapir group louse-free (P-value&lt;0.001)</li></ul> Licener® group (Test): <ul style="list-style-type: none"><li>100% cure rate after single treatment (60/60)</li><li>100% cure rate after two treatments (58/58)</li></ul> Statistically superior to reference group in combined success rate (p=0.024)
12	Bowles V.M <sup>36</sup> , 2018	Multiple centers	Randomized, double-blind, multicenter, vehicle-controlled clinical trial	704	Abametapir lotion (0.74%) vs. Vehicle lotion	Single application of abametapir lotion or vehicle lotion to dry hair for 10 minutes, then rinsed with water. No nit combing was permitted for 14 days before and after treatment.	Day 1, Day 7, Day 14 post-treatment	Lice count by trained evaluators for presence of live lice.	Study 1: 81.1% of index subjects louse-free at post-baseline visits (P-value=0.001) Study 2: 81.8% of index subjects louse-free at post-baseline visits (P-value<0.001) Vehicle Lotion: study 1: 50.9% of index subjects louse-free at post-baseline visits Study 2: 47.2% of index subjects louse-free at post-baseline visits Exploratory Endpoint (Day 14): <ul style="list-style-type: none"><li>Study 1: 88.2% abametapir group louse-free (P-value&lt;0.001)</li><li>Study 2: 81.0% abametapir group louse-free (P-value&lt;0.001)</li></ul> Licener® group (Test): <ul style="list-style-type: none"><li>100% cure rate after single treatment (60/60)</li><li>100% cure rate after two treatments (58/58)</li></ul> Statistically superior to reference group in combined success rate (p=0.024) Jacutin® group (Reference): <ul style="list-style-type: none"><li>94.74% cure rate after single treatment (54/57)</li><li>96.30% cure rate after two treatments (52/54)</li></ul> Eucalyptus: Highest efficacy; significant nit mortality vs. permethrin (p=0.009) Cinnamon vs. Permethyl: Similar efficacy (p=0.139) Eucalyptus vs. Cinnamon: Eucalyptus significantly more effective (p=0.06)
13	Semmler M <sup>37</sup> , 2017	Egypt	Randomized, investigator-blinded, controlled clinical trial	119	Licener® shampoo (Neem extract, silicone-free), Jacutin® Pedicul Fluid (Dimethicone-based)	Single treatment with either product on Day 1 and Day 9	Before treatment, 1-2 hours after treatment, Days 5 and 13 post-treatment	Lice count by combing	Study 1: 81.1% of index subjects louse-free at post-baseline visits (P-value=0.001) Study 2: 81.8% of index subjects louse-free at post-baseline visits (P-value<0.001) Vehicle Lotion: study 1: 50.9% of index subjects louse-free at post-baseline visits Study 2: 47.2% of index subjects louse-free at post-baseline visits Exploratory Endpoint (Day 14): <ul style="list-style-type: none"><li>Study 1: 88.2% abametapir group louse-free (P-value&lt;0.001)</li><li>Study 2: 81.0% abametapir group louse-free (P-value&lt;0.001)</li></ul> Licener® group (Test): <ul style="list-style-type: none"><li>100% cure rate after single treatment (60/60)</li><li>100% cure rate after two treatments (58/58)</li></ul> Statistically superior to reference group in combined success rate (p=0.024) Jacutin® group (Reference): <ul style="list-style-type: none"><li>94.74% cure rate after single treatment (54/57)</li><li>96.30% cure rate after two treatments (52/54)</li></ul> Eucalyptus: Highest efficacy; significant nit mortality vs. permethrin (p=0.009) Cinnamon vs. Permethyl: Similar efficacy (p=0.139) Eucalyptus vs. Cinnamon: Eucalyptus significantly more effective (p=0.06)
14	Ghavami M.B <sup>38</sup> , 2017	Iran	Single-blind clinical trial	95	Eucalyptus oil shampoo, Cinnamon oil shampoo, 1% Permethrin shampoo	34, 31 and 30 subjects in three groups, receiving eucalyptus, cinnamon and permethrin treatment respectively	Pre-treatment, Day 3, and Day 7 post-treatment	Clinical exam, lab incubation of nits	Study 1: 81.1% of index subjects louse-free at post-baseline visits (P-value=0.001) Study 2: 81.8% of index subjects louse-free at post-baseline visits (P-value<0.001) Vehicle Lotion: study 1: 50.9% of index subjects louse-free at post-baseline visits Study 2: 47.2% of index subjects louse-free at post-baseline visits Exploratory Endpoint (Day 14): <ul style="list-style-type: none"><li>Study 1: 88.2% abametapir group louse-free (P-value&lt;0.001)</li><li>Study 2: 81.0% abametapir group louse-free (P-value&lt;0.001)</li></ul> Licener® group (Test): <ul style="list-style-type: none"><li>100% cure rate after single treatment (60/60)</li><li>100% cure rate after two treatments (58/58)</li></ul> Statistically superior to reference group in combined success rate (p=0.024) Jacutin® group (Reference): <ul style="list-style-type: none"><li>94.74% cure rate after single treatment (54/57)</li><li>96.30% cure rate after two treatments (52/54)</li></ul> Eucalyptus: Highest efficacy; significant nit mortality vs. permethrin (p=0.009) Cinnamon vs. Permethyl: Similar efficacy (p=0.139) Eucalyptus vs. Cinnamon: Eucalyptus significantly more effective (p=0.06)



15	Wolf L. <sup>39</sup> , 2016	Germany	Randomized, controlled, investigator-blinded trial	107	Mineral oil-based shampoo (physical mode of action) Pyrethroid-based solution (Goldgeist Forte)	Two applications (Day 0 and Day 7) according to product instructions	Up to Day 10 (assessments at 1h, 24h post first use, pre/post second use, Day 10)	Visual scalp examination for lice	Mineral oil shampoo: 96.1% (Day 10, corrected for re-infestation) Pyrethroid solution: 94% (Day 10) Lice-free until end of study: Mineral oil 78%, Control 60% Permethrin: 71.8% (Day 2), 64.1% (Day 6), 89.7% (Day 9), 89.7% (Day 14)
16	Moemenbellah L. <sup>40</sup> , 2016	Iran	Community-based comparative trial	82	Lindane shampoo 1% Permethrin shampoo 1%	Application of shampoo treatment after screening with plastic lice-detection combs in schools	Days 2, 6, 9, and 14	Detection comb inspection	Lindane: 92.5% (Day 2), 92.5% (Day 6), 97.5% (Day 9), 95.0% (Day 14) (P-value=0.017 and P-value=0.002)
17	Leulmi H. <sup>41</sup> , 2016	Senegal	Community-based comparative trial	440	Oral ivermectin (400 µg/kg, 2 doses) 0.23% d-phenothrin shampoo	Ivermectin arm: Two oral doses, 7 days apart. 1-4 tablets per dose depending on weight. Shampoo arm: Shampoo applied to wet hair, massaged until foam, left 3-5 minutes, rinsed. Process repeated twice. After shampooing, fine-toothed combing used to remove dead nit	Ivermectin group: Days 2, 3, 4, 5, 6 (post first dose), then Day 7 second dose, and efficacy assessed at Days 8 and 15. Shampoo group: Assessments on Days 3 and 15 post-treatment.	Scalp inspection for lice presence	Ivermectin: 77.4% (41/53) Shampoo: 32.3% (42/130) (P-value<10 <sup>-7</sup> )
18	Burgess I.F. <sup>42</sup> , 2014	United Kingdom	RCT, assessor-blind, controlled	278	0.5% phenothrin mousse, 0.2% phenothrin lotion, mechanical removal (wet-combing with conditioner)	Mousse: 30 min application, once Lotion: 2 hr application, once Wet combing: 4 sessions over 12 days (All followed by shampoo washing)	day 14 post-treatment (for insecticides); up to Day 14 after final combing (for mechanical group)	Absence of lice (visual inspection)	Phenothrin mousse: 20.0% (21/105) Phenothrin lotion: 21.5% (23/107) Wet-combing: 19.1% (12/63) (No statistically significant difference) 0.5% ivermectin: 73.7% lice eradication at day 15. All ivermectin groups significantly more effective than placebo, P ≤ 0.003. ITT worst-case: Tocopheryl acetate: 56.5% (13/23) vs. Permethrin: 22.7% (5/22) (P-value=0.033) Adjusted for re-infestation: Tocopheryl acetate: 73.9% vs. Permethrin: 22.7% (P-value=0.001)
19	Meinking T. L. <sup>43</sup> , 2013	USA	RCT, double-blind	78 (aged 2–62)	Topical ivermectin lotion (0.15%, 0.25%, 0.5%) vs. placebo	Single 10-minute application of ivermectin lotion (various concentrations)	Day 1 (2h & 6h), Days 2, 8 (±1), and 15 (+2)	Scalp and hair examination by trained observers	Dimethicone: 69.8% (ITT), 77.1% (per-protocol) Permethrin: 14.9% (ITT), 15.6% (per-protocol)
20	Burgess I.F. <sup>44</sup> , 2013	United of Kingdom	RCT, assessor-blind	45 individuals (randomized) (23: tocopheryl acetate, 22: permethrin)	20% tocopheryl acetate spray vs. 1% permethrin creme rinse	Tocopheryl acetate: applied to dry hair for 20 minutes (2 applications, 7 days apart) Permethrin: applied for 10 minutes to towel-dried hair (2 applications, 7 days apart)	Days 1, 6, 9, and 14 after first treatment	Dry detection combing	Dimethicone: 69.8% (ITT), 77.1% (per-protocol) Permethrin: 14.9% (ITT), 15.6% (per-protocol)
21	Burgess I.F. <sup>45</sup> , 2013	United of Kingdom	RCT, open-label, parallel group	80 per-protocol	4% dimethicone liquid gel vs. 1% permethrin creme rinse	Dimethicone: single 15-min application Permethrin: two 10-min applications, 7 days apart	Days 1, 6, 9, and 14 post-treatment	Dry detection combing using "PDC" comb; lice stages recorded if present	Dimethicone: 69.8% (ITT), 77.1% (per-protocol) Permethrin: 14.9% (ITT), 15.6% (per-protocol)

## Discussion

This study provides a comprehensive overview of clinical trials investigating the therapeutic efficacy of various treatments for head lice (*Pediculus humanus capitis*). In total, 21 studies were included, encompassing a broad range of chemical and non-chemical interventions. These trials

collectively illustrate the evolving landscape of pediculosis management and the ongoing need to optimize treatment strategies. The included trials can be categorized into chemical and non-chemical approaches, each offering distinct advantages and limitations.

## Chemical Methods



**Permethrin:** Permethrin 1% remains the most widely recommended first-line pediculicide by the American Academy of Pediatrics, largely due to its established efficacy and safety profile. Acting on voltage-gated sodium channels, permethrin induces neuronal hyperexcitation and eventual death of lice<sup>46</sup>. While effective as a pediculicide, permethrin is not ovicidal, necessitating nit combing and often a second application after 7–10 days if live lice persist<sup>47</sup>.

Clinical experience has revealed considerable variability in cure rates, which are influenced by proper application, treatment adherence, and regional resistance patterns<sup>26, 31, 40, 48–50</sup>. For instance, Ghalandari et al.<sup>26</sup> found that a 1-hour permethrin shampoo regimen significantly reduced both infestation duration and pruritus, highlighting the importance of optimizing treatment protocols. Furthermore, combining permethrin with mechanical methods such as wet-combing may enhance overall treatment success<sup>31</sup>. Despite its widespread use, emerging global resistance to pyrethroids underscores the need for ongoing surveillance and the development of alternative strategies<sup>51–53</sup>. Such trends highlight the importance of monitoring resistance and tailoring treatment protocols accordingly.

**Phenothrin:** Phenothrin, a synthetic permethrin derivative, has emerged as a viable alternative, particularly in regions experiencing rising permethrin resistance<sup>32, 42, 46</sup>. This shift highlights the growing need for alternative treatments in lice management, especially in regions where permethrin resistance is becoming a significant concern. Comparative studies suggest that different formulations, such as mousse versus lotion, exhibit similar overall efficacy, though the mousse formulation may be associated with higher reinestation rates<sup>42</sup>. These findings indicate that treatment outcomes are influenced not only by the active ingredient but also by formulation, application technique, and patient adherence.

**Ivermectin:** Ivermectin, available in both oral and topical forms, has gained attention as an effective alternative for challenging or resistant head lice infestations<sup>54</sup>. Oral ivermectin has shown excellent efficacy and a favorable safety profile, making it suitable for children and for community-based mass treatments<sup>55, 56</sup>. In comparative studies, oral ivermectin has often outperformed conventional topical agents, while topical ivermectin lotions have demonstrated promising single-application efficacy<sup>57</sup>. Notably, ivermectin has shown potential in reducing infestations in underserved populations, emphasizing its practical utility in public health interventions<sup>58</sup>. This is particularly significant in regions with limited access to healthcare, where oral ivermectin offers a practical and efficient solution for large-scale treatment.

However, the potential development of resistance remains a limitation that warrants cautious use and continuous monitoring<sup>41</sup>.

**Dimethicone:** Dimethicone 4% lotion represents a paradigm shift in lice management, functioning via a physical mechanism that suffocates and dehydrates lice rather than relying on neurotoxicity<sup>59</sup>. Dimethicone is a colorless, odorless, hydrophobic fluid that is applied to the entire length of the hair and scalp<sup>60</sup>. Clinical trials have consistently demonstrated its rapid action, high efficacy, and low reinestation rates,

including effectiveness against pyrethroid-resistant lice<sup>18, 27, 32, 45</sup>.

Dimethicone's safety profile makes it particularly suitable for pediatric patients, and its convenience and efficacy have been confirmed across diverse geographic and clinical settings<sup>37</sup>. For example, in Fars Province, Iran, dimethicone achieved a 100% cure rate by day 14, outperforming pyrethroid-based treatments<sup>32</sup>. This makes it an attractive option for younger patients, where safety is a primary concern. Its rapid action further underscores its utility as an effective pediculicide. These data suggest that dimethicone may serve as a cornerstone for resistance-free, safe, and effective head lice management.

**Abametapir:** Abametapir 0.74% (Xeglyze) is the first topical, single-use pediculicide with demonstrated direct ovicidal and larvicidal activity. Unlike many traditional treatments that primarily target live lice, abametapir is effective across multiple stages of the louse life cycle. In July 2020, the U.S. Food and Drug Administration (FDA) approved abametapir for the treatment of head lice in patients six months of age and older<sup>61</sup>.

Clinical studies indicate that a single application can maintain lice-free status through day 14, reducing the need for repeated treatments and combing<sup>34, 36</sup>. These findings support abametapir's potential as a convenient, single-application alternative to multi-dose regimens, also the ovicidal property positions abametapir as a promising solution to reduce reinestation rates and eliminate the need for combing or repeated treatments.

**Tocopherol Acetate:** Tocopherol acetate 20% spray has been shown to possess superior pediculicidal activity compared to 1% permethrin<sup>44</sup>, suggesting a promising alternative for settings where conventional neurotoxic treatments are less effective or resistance is prevalent.

Overall, chemical pediculicides remain fundamental to lice management, but increasing resistance and limited ovicidal activity highlighting the need for integrated approaches that combine efficacy, safety, and resistance management.

### Non-chemical treatments

With increasing resistance to conventional neurotoxic pediculicides and safety concerns in pediatric use, non-chemical and physically acting interventions have gained growing attention. These approaches emphasize safety, ease of use, and resistance-free mechanisms, often achieving comparable or superior outcomes to chemical treatments.

Cardoso et al. developed a novel lotion combining *Protium heptaphyllum* extract with semi-crystalline polymers, which demonstrated higher efficacy and ovicidal activity than 1% permethrin, effectively preventing egg hatching<sup>29</sup>. In contrast, a 1% fractionated coconut oil shampoo achieved only partial success, with 38.7% of participants lice-free at follow-up, highlighting the limited standalone potential of lipid-based products<sup>30</sup>.

New physically acting formulations, such as silylated polyol dispersions, have shown promising results, achieving an 88.2% recovery rate and outperforming dimethicone while improving user compliance<sup>33</sup>. Essential oil-based preparations



have also shown strong potential. For instance, a natural product containing eucalyptus oil and *Leptospermum petersonii* showed 100% pediculicidal efficacy after a single use, surpassing a conventional pyrethrin-based control<sup>35</sup>. Similarly, neem extract shampoo outperformed a dimethicone formulation, confirming its ovicidal properties and clinical usefulness<sup>37</sup>.

However, results across plant-based products vary. Ghavami et al. found that eucalyptus oil shampoo showed the highest efficacy, while cinnamon oil and permethrin formulations had similar, lower effects<sup>38</sup>. This outcome suggests that not all essential oils are equally effective, and emphasizes the importance of evidence-based selection when considering natural therapies.

Mineral oil-based products have also emerged as sustainable options. A German trial found consistently higher cure rates with a mineral oil shampoo than with a conventional pediculicide, attributed to its physical suffocation mechanism, which prevents resistance development<sup>39</sup>. This reinforces the appeal of mineral oil-based formulations as sustainable, resistance-free pediculicides, especially in regions facing treatment failures with conventional agents.

Overall, non-chemical and physical-mode treatments offer effective, safe, and resistance-free alternatives for head lice management. Their favorable safety profiles and suitability for children make them particularly valuable for large-scale or recurrent infestations, supporting their inclusion in future integrated treatment guidelines. Collectively, non-chemical options broaden the therapeutic landscape and complement chemical pediculicides in integrated management programs.

**Conclusion:** Despite advances in pediculicide formulations and evolving treatment strategies, head lice infestation remains a persistent global public health concern. Outbreaks continue to occur globally, indicating that current control measures have limited long-term impact. Evidence from multiple studies demonstrates that both chemical and non-chemical treatment approaches exhibit variable levels of efficacy, often influenced by factors such as resistance patterns, product formulation, and adherence to treatment protocols. Therefore, treatment strategies should be evidence-based and individualized, taking into account the patient's age, clinical condition, previous treatment history, and local resistance data. Future research should focus on resistance monitoring, combination therapies, and the long-term safety of emerging formulations.

**Limitation:** This review has some limitations that should be acknowledged. First, the restriction to English-language publications may have introduced language bias, potentially excluding relevant studies published in other languages. Second, publication bias is a concern, as studies with non-significant or negative results are less likely to be published and may therefore be underrepresented. Third, the absence of a meta-analytic component limits the ability to quantitatively synthesize findings across studies. Finally, the review was not registered in PROSPERO, which may affect its transparency, methodological rigor, and reproducibility.

## Ethical Considerations

This study was approved by the Research and Ethics Council of Iran University of Medical Sciences (Code: IR.IUMS.REC.1397.772).

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## Conflict of Interest

The authors declare that there is no conflict of interest.

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