

## Supplementary Materials

### Supplementary S1: Databases and search strategies

**Supplementary Table S1. Full search strategy for articles on TTO and its components activity against ectoparasites**

| Database s          | Step | Query                                                                                                  | Item found |
|---------------------|------|--------------------------------------------------------------------------------------------------------|------------|
| PubMed              | #1   | "Tea Tree Oil"[Mesh]                                                                                   | 433        |
|                     | #2   | "Melaleuca"[Mesh]                                                                                      | 223        |
|                     | #3   | #1 OR #2                                                                                               | 582        |
|                     | #4   | "Ectoparasitic Infestations"[Mesh]                                                                     | 20,767     |
|                     | #5   | "Parasites"[Mesh]                                                                                      | 7,261      |
|                     | #6   | "Mites"[Mesh]                                                                                          | 17,014     |
|                     | #7   | "Mite Infestations"[Mesh]                                                                              | 7,053      |
|                     | #8   | "Scabies"[Mesh]                                                                                        | 3,458      |
|                     | #9   | "Blepharitis"[Mesh]                                                                                    | 1,324      |
|                     | #10  | "Pyroglyphidae"[Mesh]                                                                                  | 3,051      |
|                     | #11  | "Trombiculidae"[Mesh]                                                                                  | 632        |
|                     | #12  | "Pediculus"[Mesh]                                                                                      | 1,143      |
|                     | #13  | "Lice Infestations"[Mesh]                                                                              | 2,715      |
|                     | #14  | "Phthiraptera"[Mesh]                                                                                   | 3,050      |
|                     | #15  | "Flea Infestations"[Mesh]                                                                              | 776        |
|                     | #16  | "Siphonaptera"[Mesh]                                                                                   | 3,816      |
|                     | #17  | "Tunga"[Mesh]                                                                                          | 79         |
|                     | #18  | "Tungiasis"[Mesh]                                                                                      | 115        |
|                     | #19  | "Bedbugs"[Mesh]                                                                                        | 743        |
|                     | #20  | #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 | 46,917     |
|                     | #21  | #3 AND #20                                                                                             | <b>45</b>  |
| Embase via Scopus   | #1   | TITLE-ABS-KEY "tea tree oil"                                                                           | 1,614      |
|                     | #2   | TITLE-ABS-KEY ("melaleuca alternifolia oil")                                                           | 59         |
|                     | #3   | #1 OR #2                                                                                               | 1,624      |
|                     | #4   | TITLE-ABS-KEY (ectoparasites)                                                                          | 9,377      |
|                     | #5   | TITLE-ABS-KEY ("ectoparasitic infestations")                                                           | 2,872      |
|                     | #6   | TITLE-ABS-KEY (parasites)                                                                              | 266,246    |
|                     | #7   | TITLE-ABS-KEY (mites)                                                                                  | 47,700     |
|                     | #8   | TITLE-ABS-KEY ("mite Infestations")                                                                    | 4,236      |
|                     | #9   | TITLE-ABS-KEY (scabies)                                                                                | 7,738      |
|                     | #10  | TITLE-ABS-KEY (blepharitis)                                                                            | 3,915      |
|                     | #11  | TITLE-ABS-KEY (pyroglyphidae)                                                                          | 2,709      |
|                     | #12  | TITLE-ABS-KEY (trombiculidae)                                                                          | 991        |
|                     | #13  | TITLE-ABS-KEY (pediculus)                                                                              | 2,344      |
|                     | #14  | TITLE-ABS-KEY ("lice Infestations")                                                                    | 2,995      |
|                     | #15  | TITLE-ABS-KEY phthiraptera)                                                                            | 3,063      |
|                     | #16  | TITLE-ABS-KEY (lice)                                                                                   | 11,322     |
|                     | #17  | TITLE-ABS-KEY ("flea Infestations")                                                                    | 805        |
|                     | #18  | TITLE-ABS-KEY (siphonaptera)                                                                           | 4,211      |
|                     | #19  | TITLE-ABS-KEY (tunga)                                                                                  | 424        |
|                     | #20  | TITLE-ABS-KEY (tungiasis)                                                                              | 461        |
|                     | #21  | TITLE-ABS-KEY (fleas)                                                                                  | 10,564     |
|                     | #22  | TITLE-ABS-KEY (bedbugs)                                                                                | 978        |
|                     | #23  | #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 | 340,611    |
|                     | #24  | #3 AND #23                                                                                             | <b>151</b> |
| MEDLINE(EBS COhost) | S1   | "tea tree oil"                                                                                         | 666        |
|                     | S2   | "ectoparasitic infestations"                                                                           | 3,230      |
|                     | S3   | parasites                                                                                              | 163,268    |
|                     | S4   | mites                                                                                                  | 25,122     |
|                     | S5   | "mite infestations"                                                                                    | 10,636     |
|                     | S6   | scabies                                                                                                | 4,680      |
|                     | S7   | blepharitis                                                                                            | 2,010      |
|                     | S8   | pediculus                                                                                              | 1,359      |
|                     | S9   | "lice infestations"                                                                                    | 2,756      |
|                     | S10  | siphonaptera                                                                                           | 3,617      |

|                                                 |     |                                                                                                                                                                                                                                                  |            |
|-------------------------------------------------|-----|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
|                                                 | S11 | "flea infestations"                                                                                                                                                                                                                              | 707        |
|                                                 | S12 | bedbugs                                                                                                                                                                                                                                          | 881        |
|                                                 | S13 | S2 OR S3 OR S4 OR S5 OR S6 S7 OR S8 OR S9 OR S10 OR S11 OR S12                                                                                                                                                                                   | 199,327    |
|                                                 | S14 | S1 AND S13                                                                                                                                                                                                                                       | <b>70</b>  |
| <b>CINAHL</b>                                   | S1  | "tea tree oil"                                                                                                                                                                                                                                   | 268        |
|                                                 | S2  | "ectoparasitic infestations" OR parasites OR mites OR "mite infestations" OR scabies OR blepharitis OR pediculus OR "lice infestations" OR siphonaptera OR "flea infestations" OR bedbugs                                                        | 9,346      |
|                                                 | S3  | "tea tree oil" AND "ectoparasitic infestations" OR parasites OR mites OR "mite infestations" OR scabies OR blepharitis OR pediculus OR "lice infestations" OR siphonaptera OR "flea infestations" OR bedbugs                                     | <b>26</b>  |
| <b>Cochran<br/>e library<br/>(CENTR<br/>AL)</b> | #1  | ("tea tree oil") AND ("ectoparasitic infestations" OR mites OR "mite infestations" OR lice OR "lice infestations" OR blepharitis OR fleas OR "flea infestations" OR bedbugs) in Title Abstract<br>Keyword - (Word variations have been searched) | <b>19</b>  |
| <b>Web of<br/>Science</b>                       | #1  | TS= ("tea tree oil")                                                                                                                                                                                                                             | 1460       |
|                                                 | #2  | TS= ("melaleuca alternifolia oil")                                                                                                                                                                                                               | 56         |
|                                                 | #3  | #2 OR #1                                                                                                                                                                                                                                         | 1470       |
|                                                 | #4  | TS= (ectoparasites)                                                                                                                                                                                                                              | 7,373      |
|                                                 | #5  | TS= ("ectoparasitic infestations")                                                                                                                                                                                                               | 40         |
|                                                 | #6  | TS= (parasites)                                                                                                                                                                                                                                  | 166,840    |
|                                                 | #7  | TS= (mites)                                                                                                                                                                                                                                      | 42,370     |
|                                                 | #8  | TS= ("mite Infestations")                                                                                                                                                                                                                        | 242        |
|                                                 | #9  | TS= (scabies)                                                                                                                                                                                                                                    | 3,360      |
|                                                 | #10 | TS= (blepharitis)                                                                                                                                                                                                                                | 1,288      |
|                                                 | #11 | TS= (pyroglyphidae)                                                                                                                                                                                                                              | 293        |
|                                                 | #12 | TS= (trombiculidae)                                                                                                                                                                                                                              | 559        |
|                                                 | #13 | TS= (pediculus)                                                                                                                                                                                                                                  | 754        |
|                                                 | #14 | TS= ("lice Infestations")                                                                                                                                                                                                                        | 212        |
|                                                 | #15 | TS= (phthiraptera)                                                                                                                                                                                                                               | 962        |
|                                                 | #16 | TS= (lice)                                                                                                                                                                                                                                       | 6,685      |
|                                                 | #17 | TS= ("flea Infestations")                                                                                                                                                                                                                        | 146        |
|                                                 | #18 | TS= (siphonaptera)                                                                                                                                                                                                                               | 1,651      |
|                                                 | #19 | TS= (tungia)                                                                                                                                                                                                                                     | 286        |
|                                                 | #20 | TS= (tungiasis)                                                                                                                                                                                                                                  | 303        |
|                                                 | #21 | TS= (fleas)                                                                                                                                                                                                                                      | 7,582      |
|                                                 | #22 | TS= (bedbugs)                                                                                                                                                                                                                                    | 405        |
|                                                 | #23 | #22 OR #21 OR #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4                                                                                                                      | 225,122    |
|                                                 | #24 | #23 AND #3                                                                                                                                                                                                                                       | 108        |
|                                                 | #25 | #23 AND #3 Refined by: [excluding] DOCUMENT TYPES: (REVIEW) I used this option                                                                                                                                                                   | <b>80</b>  |
| <b>ScienceDirect</b>                            | #1  | ("tea tree oil") AND (ectoparasites OR mites OR lice OR fleas OR bedbugs) limited to Research articles and Short communications                                                                                                                  | <b>87</b>  |
| <b>SciELO</b>                                   |     | ("tea tree oil") AND (ectoparasites OR mites OR lice OR fleas OR bedbugs)                                                                                                                                                                        | <b>1</b>   |
| <b>LILACS</b>                                   |     | ("tea tree oil") AND (ectoparasites OR mites OR lice OR fleas OR bedbugs)- 53 (52 of them from MEDLINE and 1 review) so no new article from this database                                                                                        | 0          |
| <b>ATTI</b>                                     |     | Tea tree oil                                                                                                                                                                                                                                     | 9          |
| <b>Google</b>                                   |     | Insecticidal and acaricidal activities of tea tree oil                                                                                                                                                                                           | 9          |
| <b>Total</b>                                    |     |                                                                                                                                                                                                                                                  | <b>497</b> |

\*During a complementary search on 04/04/22 12 articles were identified and included in systematic review.

**Supplementary S2: PRISMA (Preferred Reporting Items for Systematic review and Meta-Analysis)**

**Supplementary Table S2: PRISMA (Preferred Reporting Items for Systematic review and Meta-Analysis) 2009 checklist**

| Section/topic                      | #  | Checklist item                                                                                                                                                                                                                                                                                              | Reported on page # |
|------------------------------------|----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|
| <b>TITLE</b>                       |    |                                                                                                                                                                                                                                                                                                             |                    |
| Title                              | 1  | Identify the report as <b>a systematic review</b> , meta-analysis, or both.                                                                                                                                                                                                                                 | 1                  |
| <b>ABSTRACT</b>                    |    |                                                                                                                                                                                                                                                                                                             |                    |
| Structured summary                 | 2  | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2                  |
| <b>INTRODUCTION</b>                |    |                                                                                                                                                                                                                                                                                                             |                    |
| Rationale                          | 3  | Describe the rationale for the review in the context of what is already known.                                                                                                                                                                                                                              | 2–3                |
| Objectives                         | 4  | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).                                                                                                                                                  | 3                  |
| <b>METHODS</b>                     |    |                                                                                                                                                                                                                                                                                                             |                    |
| Protocol and registration          | 5  | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.                                                                                                                               | 3                  |
| Eligibility criteria               | 6  | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.                                                                                                      | 3–4                |
| Information sources                | 7  | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.                                                                                                                                  | 3–4                |
| Search                             | 8  | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.                                                                                                                                                                               | Supplementary p1–2 |
| Study selection                    | 9  | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).                                                                                                                                                   | 4                  |
| Data collection process            | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.                                                                                                                                  | 4                  |
| Data items                         | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.                                                                                                                                                                       | 4                  |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.                                                                                      | 4–5                |
| Summary measures                   | 13 | State the principal summary measures (e.g., risk ratio, difference in means).                                                                                                                                                                                                                               | Not applicable     |

|                               |    |                                                                                                                                                                                                          |                          |
|-------------------------------|----|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|
| Synthesis of results          | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$ ) for each meta-analysis.                                                | Not applicable           |
| Risk of bias across studies   | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).                                                             | Not applicable           |
| Additional analyses           | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.                                                         | Not applicable           |
| <b>RESULTS</b>                |    |                                                                                                                                                                                                          |                          |
| Study selection               | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.                                          | 5                        |
| Study characteristics         | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.                                                             | 9–34                     |
| Risk of bias within studies   | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).                                                                                                | 35 & Supplementary p7–16 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 9–34                     |
| Synthesis of results          | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency.                                                                                                  | Not applicable           |
| Risk of bias across studies   | 22 | Present results of any assessment of risk of bias across studies (see Item 15).                                                                                                                          | Not applicable           |
| Additional analysis           | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).                                                                                    | Not applicable           |
| <b>DISCUSSION</b>             |    |                                                                                                                                                                                                          |                          |
| Summary of evidence           | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).                     | 35–39                    |
| Limitations                   | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).                                            | 39                       |
| Conclusions                   | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research.                                                                                  | 39–40                    |
| <b>FUNDING</b>                |    |                                                                                                                                                                                                          |                          |
| Funding                       | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.                                                               | 40                       |

### Supplementary S3: Studies assessing AEs

**Supplementary Table S3: A summary of studies reporting no AEs (n=12 no AEs)**

| Study                                                    | Study design                                                         | Treatment                                                                                                                                        | Treatment schedule                               | AEs                                                                                                                                                                 | Quality    |
|----------------------------------------------------------|----------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| Alver <i>et al.</i> , 2017, <sup>1</sup> Turkey          | Cohort study ( <i>Demodex</i> )                                      | TTO (10%) eyelash shampoo and TTO (4%) eyelid gel (n=28)                                                                                         | BID (Twice daily) for 1 month                    | No AEs                                                                                                                                                              | 5 (Medium) |
| Epstein <i>et al.</i> , 2020, <sup>2</sup> USA           | Randomized double-blind, placebo-controlled trial                    | Cliradex® eyelid scrubs (T4O, no concentration reported) (n=26)                                                                                  | BID for 1 month                                  | No AEs (the treatment was well tolerated and burning, or irritation symptoms reported by few patients (no specific number reported) dissipating in minutes or less) | 5 (High)   |
| Ergun <i>et al.</i> , 2020, <sup>3</sup> Turkey          | Randomized double-blind, placebo-controlled trial ( <i>Demodex</i> ) | TTO (3% w/w) plus < 5% (w/w) calendula oil, borage oil, vitamin E, vitamin B5 (n=25); TTO (3% w/w) gel (n=24)                                    | BID for 1 month                                  | No AEs                                                                                                                                                              | 4 (High)   |
| Gunnarsdóttir <i>et al.</i> , 2016, <sup>4</sup> Iceland | Case study ( <i>Demodex</i> )                                        | Tea Tree wet wipes ( <i>TTO concentration not stated</i> ) (n=2)                                                                                 | BID for 10 weeks                                 | No AEs                                                                                                                                                              | 8 (High)   |
| Karakurt and Zeytun, 2018, <sup>5</sup> Turkey           | Randomised single-blinded controlled trial ( <i>Demodex</i> )        | TTO (7.5%) eyelash shampoo (n=75)                                                                                                                | BID for 1 month                                  | No AEs                                                                                                                                                              | 2 (Low)    |
| Koo <i>et al.</i> , 2012, <sup>6</sup> South Korea       | Randomized controlled trial ( <i>Demodex</i> )                       | TTO (50%) lid scrub and TTO (10%) lid scrub (n=141)                                                                                              | TTO (50%) weekly and TTO (10%) daily for 1 month | 4.7% (5/106) reported ocular irritation but disappeared following patient's education on the proper scrubbing method                                                | 2 (Low)    |
| Mergen <i>et al.</i> , 2021, <sup>7</sup> Turkey         | Randomised double-blind, active comparator-controlled trial          | TTO (7.5%) and chamomile oil ( <i>no concentration reported</i> ) swabs applied                                                                  | BID for 2 months                                 | No AEs                                                                                                                                                              | 5 (High)   |
| Tseng S. (NCT 01647217), 2017, <sup>8</sup> USA          | Randomised controlled trial                                          | T4O (Cliradex®) lid scrub ( <i>no concentration reported</i> )                                                                                   | Once or BID for 1 month                          | No AEs                                                                                                                                                              | NA         |
| Yam <i>et al.</i> , 2014, <sup>9</sup> China             | Case series ( <i>Demodex</i> )                                       | TTO (50%) lid scrub and tea tree shampoo (0.5 ml, TTO < 10 %) lid scrub (n=16)                                                                   | TTO (50%) weekly and TTO shampoo BID for 3 weeks | No AEs                                                                                                                                                              | 10 (High)  |
| Wu <i>et al</i> 2019, <sup>10</sup> Chania               | Quasi-experimental ( <i>Demodex</i> )                                | TTO wipes ( <i>concertation not reported</i> ) and flurometholone (0.02%) eye drops (n=13); TTO wipes ( <i>concertation not reported</i> , n=13) | BID for 1 month                                  | No AEs                                                                                                                                                              | 9 (High)   |
| Whitledge 2002, <sup>11</sup> USA                        | Case study (Headlice)                                                | TTO (9%) based shampoo (7% Anise oil and 4% lemon oil, 50% SD alcohol and 28% water & 2% fragrance)                                              | One time application for 10–15 minutes           | No AEs                                                                                                                                                              | 7 (High)   |
| Wong <i>et al.</i> , 2019, <sup>12</sup> Australia       | Randomised single blinded controlled pilot trial ( <i>Demodex</i> )  | Blephadex™ Eyelid Wipes (TTO and coconut oil, <i>concentration not reported</i> ) (n=10)                                                         | Once daily for 1 month                           | No AEs                                                                                                                                                              | 3 (High)   |

**Supplementary Table S4: A summary of studies reporting no AEs (n=10)**

| Study                                                    | Study design                                                                                         | Treatment                                                                                     | Treatment schedule                                                                                                                    | AEs                                                                                                                                                                                                                                                                                      | Quality  |
|----------------------------------------------------------|------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|
| Ebneyamin <i>et al.</i> , 2019, <sup>13</sup> Iran       | Randomized double-blind, placebo-controlled trial (demodex) (n=35 in both groups) ( <i>Demodex</i> ) | Permethrin (2.5%) with TTO (100%) gel (n=17)                                                  | BID for 3 months                                                                                                                      | No allergic reactions, and no major AEs observed but skin dryness (n=21, 60.0% moderate and 37.1% mild), burning and stinging (n=7, 20%), erosion (n=7, 20%) and erythema (n=3, 8.6%)                                                                                                    | 5 (High) |
| Liu and Gong, 2021, <sup>14</sup> China                  | Randomized controlled trial                                                                          | TTO eye care patch ( <i>no concertation reported</i> ) (n=25)                                 | Every night for 3 months                                                                                                              | 16% (4/25, slight to moderate irritation with conjunctival congestion)                                                                                                                                                                                                                   | 3 (High) |
| Maher 2018, <sup>15</sup> United Arab Emirates           | Quasi-experimental ( <i>Demodex</i> )                                                                | TTO (0.02%) eyelid (Naviblef™) scrub foam (n=20)                                              | BID for 1 month                                                                                                                       | 1 (contact dermatitis) in Test Vs 1 (eye irritation) in Control                                                                                                                                                                                                                          | 9 (High) |
| Zulkarnain <i>et al.</i> , 2019, <sup>16</sup> Indonesia | Randomized double blind controlled trial (Scabies)                                                   | TTO (5%) cream (n=24); TTO (5%) cream and permethrin (5%) cream (n=24); Permethrin (5%) cream | <i>No report on frequency of administration</i>                                                                                       | Minor irritation: <i>Week 1</i> : 0/24 in TTO group Vs 1/24 in Combination group Vs 1/24 in the permethrin group ( $P=0.624$ ); <i>Week 2</i> : 6/24 in TTO group Vs 10/24 in Combination group Vs 2/24 in the permethrin group ( $P=0.07$ )                                             | 3 (High) |
| Gao <i>et al.</i> , 2005, <sup>17</sup> USA              | Cohort study ( <i>Demodex</i> )                                                                      | TTO (50%) lid scrub and tea tree shampoo (0.5 ml, TTO < 10 %) lid scrub (n=9)                 | TTO (50%) lid scrub weekly (three-time application) and tea tree (0.5 ml) shampoo daily (two time) for 1 month followed by once daily | TTO (50%) generated irritation in some patients ( <i>no data is reported</i> )                                                                                                                                                                                                           | 9 (High) |
| Gao <i>et al.</i> , 2007, <sup>18</sup> USA              | Case series ( <i>Demodex</i> )                                                                       | TTO (50%) lid scrub and Tea Tree (0.5 ml, TTO < 10 %) shampoo lid scrub (n=11)                | TTO (50%) lid scrub weekly (three-time application) and tea tree (0.5 ml) shampoo daily (two time) BID for 1 month                    | TTO (50%) office lid scrub caused mild irritation in 3 and moderate irritation in 6 participants                                                                                                                                                                                         | 8 (High) |
| Gao <i>et al.</i> , 2012, <sup>19</sup> USA              | Cohort study ( <i>Demodex</i> )                                                                      | TTO (5%) ointment (n=24)                                                                      | BID for 1 month                                                                                                                       | Mild ocular irritation in 2 participants                                                                                                                                                                                                                                                 | 7 (High) |
| Barker and Altman, 2010, <sup>20</sup> Australia         | Randomised assessor-blind controlled trial (Headlice)                                                | TTO (10% w/v) / Lavender oil (LO, 1% w/v) lotion (n=43)                                       | Three times on Days 1, 7 & 14                                                                                                         | 25 individuals with mild (n=22) and moderate (n=3) AEs (n=13 or 30.2% with stinging, n= 8 or 18.6% with flaky scalp/dry scalp and n=4 or 9.3% with erythema among these, n=3 moderate AEs (n=1, stinging of the eyes; n=1, stinging of the neck; and n=1, skin erythema) in TTO/LO group | 5 (High) |
| Barker and Altman, 2011, <sup>21</sup> Australia         | <i>Ex vivo</i> Randomised assessor-blind controlled trial (Headlice)                                 | TTO (10% w/v) / LO (1% w/v) lotion (n=31)                                                     | Once on Days 1                                                                                                                        | 4 (12.9%) individuals with mild AEs (n=3 stinging and n=1 redness) in TTO/LO group                                                                                                                                                                                                       | 5 (High) |
| Messaoud <i>et al.</i> , 2019, <sup>22</sup> Tunisia     | Randomized open level-controlled trial ( <i>Demodex</i> )                                            | Sterile wipe (T4O [ 2.5%] + hyaluronic acid [0.2%, moisturizing agent]) (n=24)                | Once daily and BID for 29 days                                                                                                        | 1/24 (moderate burning sensation after application which resolved after 3s) in Test group I Vs 2/24 (visual acuity) in Test group II                                                                                                                                                     | 2 (Low)  |

### Supplementary S3: Quality assessments

#### Supplementary S3.1: Jadad Quality assessment for RCT

The methodological quality of included studies was assessed using the instrument developed by Jadad *et al.* (1996).<sup>23</sup> The scale awards one to five points to a RCT as presented in Supplementary table 4.

#### Supplementary Table S5: Criteria for quality assessment components of Jadad scale.

| No                 | Items                                                                                                                                               | Answers       | Scoring  |
|--------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|---------------|----------|
| 1.                 | Was the study described as randomized and method of randomization was sated?                                                                        | Yes           | +1       |
|                    |                                                                                                                                                     | No            | 0        |
| 2.                 | Was the method to generate the sequence of randomisation was described and it was appropriate?                                                      | Yes           | +1       |
|                    |                                                                                                                                                     | Not described | 0        |
|                    |                                                                                                                                                     | Inappropriate | -1       |
| 3.                 | Was the study described as double-blinding (participant and outcome assessor)?                                                                      | Yes           | +1       |
|                    |                                                                                                                                                     | No            | 0        |
| 4.                 | Was there adequate description of the method of masking (eg, identical placebo)?                                                                    | Yes           | +1       |
|                    |                                                                                                                                                     | No            | 0        |
|                    |                                                                                                                                                     | Inappropriate | -1       |
| 5.                 | Was there a description of withdrawals and dropouts for each group and If there were no withdrawals, is there a statement indicating no withdrawal? | Yes           | +1       |
|                    |                                                                                                                                                     | No            | 0        |
| <b>Total score</b> |                                                                                                                                                     |               | <b>5</b> |

#### Supplementary Table S6: Quality assessment results of the included studies using Jadad scale.

|     | Author(s), Year                                   | Randomisation<br>0–2 points | Blinding<br>0–2<br>points | Withdrawals<br>0–1 point | Total<br>0–5<br>points |
|-----|---------------------------------------------------|-----------------------------|---------------------------|--------------------------|------------------------|
| 1.  | Barker and Altman, 2010 <sup>20</sup>             | 2                           | 2                         | 1                        | 5                      |
| 2.  | Barker and Altman, 2011 <sup>21</sup>             | 2                           | 2                         | 1                        | 5                      |
| 3.  | Ebneyamin <i>et al.</i> , 2019 <sup>13</sup>      | 2                           | 2                         | 1                        | 5                      |
| 4.  | Epstein <i>et al.</i> , 2020 <sup>2</sup>         | 2                           | 2                         | 1                        | 5                      |
| 5.  | Ergun <i>et al.</i> , 2020 <sup>3</sup>           | 1                           | 2                         | 1                        | 4                      |
| 6.  | Karakurt and Zeytun, 2018, <sup>5</sup>           | 1                           | 0                         | 1                        | 2                      |
| 7.  | Koo <i>et al.</i> , 2012 <sup>6</sup>             | 1                           | 0                         | 1                        | 2                      |
| 8.  | Liu and Gong, 2021 <sup>14</sup>                  | 2                           | 0                         | 1                        | 3                      |
| 9.  | Mergen <i>et al.</i> , 2021 <sup>7</sup>          | 2                           | 2                         | 1                        | 5                      |
| 10. | Messaoud <i>et al.</i> , 2019 <sup>22</sup>       | 1                           | 0                         | 1                        | 2                      |
| 11. | Mohammadpour <i>et al.</i> , 2020 <sup>24</sup> I | 2                           | 1                         | 1                        | 4                      |
| 12. | Murphy <i>et al.</i> , 2018 <sup>25</sup>         | 1                           | 0                         | 1                        | 2                      |
| 13. | Tseng S. (NCT 01647217), 2017, <sup>8</sup> USA   | -                           | -                         | -                        | NA                     |
| 14. | Wang <i>et al.</i> , 2020 <sup>26</sup>           | 2                           | 0                         | 1                        | 3                      |
| 15. | Wong <i>et al.</i> , 2019 <sup>12</sup>           | 2                           | 0                         | 1                        | 3                      |
| 16. | Zhang <i>et al.</i> , 2019 <sup>27</sup>          | 1                           | 0                         | 1                        | 2                      |
| 17. | Zulkarnain <i>et al.</i> , 2019 <sup>16</sup>     | 1                           | 1                         | 1                        | 3                      |

NB: Tseng S. (NCT 01647217) is only available in registry record and could not evaluate the Jadad score.

**Supplementary S3.2: JBI quality assessment for quasi-experimental studies**

**Supplementary Table S7: Criteria for JBI Quality assessment for quasi-experimental studies**

| No | Criteria                                                                                                                                 |
|----|------------------------------------------------------------------------------------------------------------------------------------------|
| 1. | Is it clear in the study what is the ‘cause’ and what is the ‘effect’ (i.e. there is no confusion about which variable comes first)?     |
| 2. | Were the participants included in any comparisons similar?                                                                               |
| 3. | Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest? |
| 4. | Was there a control group?                                                                                                               |
| 5. | Were there multiple measurements of the outcome both pre and post the intervention/exposure?                                             |
| 6. | Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?        |
| 7. | Were the outcomes of participants included in any comparisons measured in the same way?                                                  |
| 8. | Were outcomes measured in a reliable way?                                                                                                |
| 9. | Was appropriate statistical analysis used?                                                                                               |

**Supplementary Table S8: Quality assessment results of the quasi-experimental studies using JBI tool**

|    | Author(s), Year                          | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | Q |
|----|------------------------------------------|---|---|---|---|---|---|---|---|---|---|
| 1. | Maher 2018 <sup>15</sup>                 | Y | Y | Y | Y | Y | Y | Y | N | Y | H |
| 2. | Wu <i>et al</i> 2019 <sup>10</sup>       | Y | Y | Y | Y | Y | Y | Y | Y | Y | H |
| 3. | Lu <i>et al.</i> , 2021 <sup>28</sup>    | Y | Y | Y | Y | Y | Y | Y | Y | Y | H |
| 4. | Zhong <i>et al.</i> , 2021 <sup>29</sup> | Y | Y | Y | Y | Y | Y | Y | Y | Y | H |

Abbreviations: H: High; L: Low; M: Medium; Q: quality

Responses are reported as: Y: Yes; N: No; U: Unclear; NA: Not applicable

**Supplementary S3.3: JBI Quality assessment for cohort studies**

**Supplementary Table S9: Criteria for JBI Quality assessment for cohort studies**

| No  | Criteria                                                                                                   |
|-----|------------------------------------------------------------------------------------------------------------|
| 1.  | Were the two groups similar and recruited from the same population?                                        |
| 2.  | Were the exposures measured similarly to assign people to both exposed and unexposed groups?               |
| 3.  | Was the exposure measured in a valid and reliable way?                                                     |
| 4.  | Were confounding factors identified?                                                                       |
| 5.  | Were strategies to deal with confounding factors stated?                                                   |
| 6.  | Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)? |
| 7.  | Were the outcomes measured in a valid and reliable way?                                                    |
| 8.  | Was the follow up time reported and sufficient to be long enough for outcomes to occur?                    |
| 9.  | Was follow up complete, and if not, were the reasons to loss to follow up described and explored?          |
| 10. | Were strategies to address incomplete follow up utilized?                                                  |
| 11. | Was appropriate statistical analysis used?                                                                 |

**Supplementary Table S10: Quality assessment results of the cohort studies using JBI tool**

|    | Author(s), Year                                    | 1  | 2  | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | Q |
|----|----------------------------------------------------|----|----|---|---|---|---|---|---|---|----|----|---|
| 1. | Alver <i>et al.</i> , 2017 <sup>1</sup>            | NA | NA | Y | U | U | Y | Y | Y | N | N  | Y  | M |
| 2. | Gao <i>et al.</i> , 2005 <sup>17</sup>             | Y  | Y  | Y | U | U | Y | Y | Y | Y | Y  | Y  | H |
| 3. | Gao <i>et al.</i> , 2012 <sup>19</sup>             | NA | NA | Y | U | U | Y | Y | Y | Y | Y  | Y  | H |
| 4. | Hirsch-Hoffmann <i>et al.</i> , 2015 <sup>30</sup> | NA | NA | Y | U | U | Y | N | Y | N | N  | N  | L |
| 5. | Jacobi <i>et al.</i> , 2021 <sup>31</sup>          | NA | NA | Y | Y | Y | Y | Y | Y | Y | Y  | Y  | H |
| 6. | Kim <i>et al.</i> , 2011 <sup>32</sup>             | NA | NA | Y | U | U | Y | Y | Y | Y | Y  | Y  | H |

|     |                                           |    |    |   |   |   |   |   |   |   |   |   |   |   |
|-----|-------------------------------------------|----|----|---|---|---|---|---|---|---|---|---|---|---|
| 7.  | Kojima <i>et al.</i> , 2011 <sup>33</sup> | NA | NA | Y | U | U | Y | Y | Y | Y | Y | Y | Y | H |
| 8.  | Liang <i>et al.</i> , 2018 <sup>34</sup>  | NA | NA | Y | Y | Y | Y | Y | Y | N | Y | Y | H |   |
| 9.  | McCage <i>et al.</i> 2002 <sup>35</sup>   | NA | NA | Y | U | U | Y | Y | Y | Y | Y | N | M |   |
| 10. | Nicholls <i>et al.</i> 2016 <sup>36</sup> | NA | NA | Y | Y | N | Y | N | Y | Y | N | N | M |   |

Abbreviations: H: High; L: Low; M: Medium; Q: quality

Responses are reported as: Y: Yes; N: No; U: Unclear; NA: Not applicable

### Supplementary S3.4: JBI Quality assessment for case series studies

#### Supplementary Table S11: Criteria for JBI Quality assessment for cohort studies

| No  | Criteria                                                                                                      |
|-----|---------------------------------------------------------------------------------------------------------------|
| 1.  | Were there clear criteria for inclusion in the case series?                                                   |
| 2.  | Was the condition measured in a standard, reliable way for all participants included in the case series?      |
| 3.  | Were valid methods used for identification of the condition for all participants included in the case series? |
| 4.  | Did the case series have consecutive inclusion of participants?                                               |
| 5.  | Did the case series have complete inclusion of participants?                                                  |
| 6.  | Was there clear reporting of the demographics of the participants in the study?                               |
| 7.  | Was there clear reporting of clinical information of the participants?                                        |
| 8.  | Were the outcomes or follow up results of cases clearly reported?                                             |
| 9.  | Was there clear reporting of the presenting site(s)/clinic(s) demographic information?                        |
| 10. | Was statistical analysis appropriate?                                                                         |

**Supplementary Table S12: Quality assessment results of the case series studies using JBI tool**

|    | <b>Author(s), Year</b>                       | <b>1</b> | <b>2</b> | <b>3</b> | <b>4</b> | <b>5</b> | <b>6</b> | <b>7</b> | <b>8</b> | <b>9</b> | <b>10</b> | <b>Q</b> |
|----|----------------------------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|-----------|----------|
| 1. | Evren Kemer <i>et al</i> 2020 <sup>37</sup>  | Y        | Y        | Y        | N        | N        | Y        | Y        | Y        | Y        | Y         | H        |
| 2. | Gao <i>et al.</i> , 2007 <sup>18</sup>       | Y        | Y        | Y        | U        | U        | Y        | Y        | Y        | Y        | Y         | H        |
| 3. | Kheirkhah <i>et al.</i> , 2007 <sup>38</sup> | Y        | Y        | Y        | U        | U        | Y        | Y        | Y        | Y        | U         | H        |
| 4. | Liang <i>et al.</i> , 2010 <sup>39</sup>     | Y        | Y        | Y        | U        | U        | Y        | Y        | N        | Y        | U         | M        |
| 5. | Patel <i>et al.</i> 2020 <sup>40</sup>       | Y        | Y        | Y        | U        | U        | Y        | Y        | U        | Y        | U         | M        |
| 6. | Yam <i>et al.</i> , 2014 <sup>9</sup>        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y         | H        |

Abbreviations: H: High; L: Low; M: Medium; Q: quality

Responses are reported as: Y: Yes; N: No; U: Unclear; NA: Not applicable

**Supplementary S3.5: JBI Quality assessment for case studies**

**Supplementary Table S13: Criteria for JBI Quality assessment for cohort studies**

| <b>No</b> | <b>Criteria</b>                                                                      |
|-----------|--------------------------------------------------------------------------------------|
| 1.        | Were patient's demographic characteristics clearly described?                        |
| 2.        | Was the patient's history clearly described and presented as a timeline?             |
| 3.        | Was the current clinical condition of the patient on presentation clearly described? |
| 4.        | Were diagnostic tests or assessment methods and the results clearly described?       |
| 5.        | Was the intervention(s) or treatment procedure(s) clearly described?                 |
| 6.        | Was the post-intervention clinical condition clearly described?                      |
| 7.        | Were adverse events (harms) or unanticipated events identified and described?        |
| 8.        | Does the case report provide takeaway lessons?                                       |

**Supplementary Table S14: Quality assessment results of the case studies using JBI tool**

|    | <b>Author(s), Year</b>                          | <b>1</b> | <b>2</b> | <b>3</b> | <b>4</b> | <b>5</b> | <b>6</b> | <b>7</b> | <b>8</b> | <b>Q</b> |
|----|-------------------------------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| 1. | Currie <i>et al.</i> , 2004 <sup>41</sup>       | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | H        |
| 2. | Galea <i>et al.</i> , 2014 <sup>42</sup>        | Y        | Y        | Y        | Y        | Y        | Y        | N        | Y        | H        |
| 3. | Gunnarsdóttir <i>et al.</i> , 2016 <sup>4</sup> | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | H        |
| 4. | Huo <i>et al.</i> , 2021 <sup>43</sup>          | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | H        |
| 5. | Novelo 2015 <sup>44</sup>                       | N        | N        | Y        | N        | N        | Y        | N        | Y        | L        |
| 6. | Tighe <i>et al.</i> , 2013 <sup>45</sup>        | Y        | N        | Y        | Y        | Y        | Y        | N        | Y        | M        |
| 7. | Walton <i>et al.</i> , 2004 <sup>46</sup>       | Y        | Y        | N        | Y        | Y        | Y        | N        | Y        | M        |
| 8. | Whitledge 2002 <sup>11</sup>                    | Y        | Y        | Y        | N        | Y        | Y        | Y        | Y        | H        |
| 9. | Yin <i>et al.</i> , 2021 <sup>47</sup>          | Y        | Y        | Y        | Y        | N        | Y        | N        | Y        | M        |

Abbreviations: H: High; L: Low; M: Medium; Q: quality

Responses are reported as: Y: Yes; N: No; U: Unclear; NA: Not applicable

**Supplementary S3.6: ToxRTool assessment for in vitro studies**

**Supplementary Table S15: Criteria considered for ToxRTool reliability assessment for in vitro studies**

| No | Criteria                                                                                                                                       |
|----|------------------------------------------------------------------------------------------------------------------------------------------------|
| 1. | <b>Was the test substance identified?</b>                                                                                                      |
| 2. | Is the purity of the substance given?                                                                                                          |
| 3. | Is information on the source/origin of the substance given?                                                                                    |
| 4. | Is all information on the nature and/or physico-chemical properties of the test item given, which you deem indispensable for judging the data? |
| 5. | Is the test system described?                                                                                                                  |
| 6. | Is information given on the source/origin of the test system?                                                                                  |
| 7. | Is necessary information on test system properties, and on conditions of cultivation and maintenance given?                                    |

|     |                                                                                            |
|-----|--------------------------------------------------------------------------------------------|
| 8.  | Is the method of administration given?                                                     |
| 9.  | Are doses administered or concentrations in application media given?                       |
| 10. | Are frequency and duration of exposure as well as time-points of observations explained?   |
| 11. | Were negative controls included (give also point, if not necessary)?                       |
| 12. | Were positive controls included (give also point, if not necessary)?                       |
| 13. | Is the number of replicates (or complete repetitions of experiment) given?                 |
| 14. | Are the study endpoint(s) and their method(s) of determination clearly described?          |
| 15. | Is the description of the study results for all endpoints investigated                     |
| 16. | Are the statistical methods for data analysis given and applied in a transparent manner?   |
| 17. | Is the study design chosen appropriate for obtaining the substance-specific data aimed at? |
| 18. | Are the quantitative study results reliable?                                               |

**Supplementary Table S16: Quality assessment results of the in vitro studies using ToxRTool**

|    | Author(s), Year                           | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | Q  |
|----|-------------------------------------------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|
| 1. | Bulut and Tanriverdi, 2021 <sup>48</sup>  | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y  | Y  | Y  | N  | Y  | Y  | Y  | Y  | Y  | R  |
| 2. | Cheung <i>et al.</i> , 2018 <sup>49</sup> | Y | Y | Y | Y | Y | Y | N | Y | Y | Y  | Y  | Y  | Y  | Y  | Y  | Y  | Y  | Y  | R  |
| 3. | Frame <i>et al.</i> , 2018 <sup>50</sup>  | Y | Y | Y | Y | Y | Y | N | Y | Y | Y  | Y  | Y  | Y  | Y  | Y  | Y  | Y  | Y  | R  |
| 4. | Gao <i>et al.</i> , 2005 <sup>17</sup>    | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y  | Y  | Y  | Y  | Y  | N  | N  | Y  | Y  | R  |
| 5. | Kabat 2019 <sup>51</sup>                  | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y  | Y  | Y  | Y  | Y  | Y  | Y  | Y  | Y  | R  |
| 6. | Oseka and Sedzikowska, 2014 <sup>52</sup> | Y | N | N | N | Y | Y | Y | Y | Y | Y  | Y  | Y  | N  | Y  | Y  | N  | N  | N  | NA |
| 7. | Tighe <i>et al.</i> , 2013 <sup>45</sup>  | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y  | Y  | Y  | Y  | Y  | Y  | Y  | N  | Y  | R  |
| 8. | Yurekli and Botsali, 2021 <sup>53</sup>   | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y  | Y  | Y  | Y  | Y  | Y  | N  | Y  | Y  | R  |
| 9. | Fang <i>et al</i> 2016 <sup>54</sup>      | Y | Y | N | Y | Y | Y | Y | Y | Y | Y  | Y  | Y  | Y  | Y  | Y  | Y  | Y  | Y  | R  |

|     | <b>Author(s), Year</b>                        | <b>1</b> | <b>2</b> | <b>3</b> | <b>4</b> | <b>5</b> | <b>6</b> | <b>7</b> | <b>8</b> | <b>9</b> | <b>10</b> | <b>11</b> | <b>12</b> | <b>13</b> | <b>14</b> | <b>15</b> | <b>16</b> | <b>17</b> | <b>18</b> | <b>Q</b> |     |
|-----|-----------------------------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|----------|-----|
| 10. | Walton <i>et al.</i> , 2000 <sup>55</sup>     | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y         | Y         | Y         | Y         | Y         | Y         | Y         | Y         | Y         | Y        | R   |
| 11. | Walton <i>et al.</i> , 2004 <sup>46</sup>     | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y         | Y         | Y         | Y         | Y         | Y         | Y         | Y         | Y         | Y        | R   |
| 12. | Hill <i>et al.</i> , 2001 <sup>56</sup>       | Y        | Y        | N        | Y        | Y        | N        | N        | Y        | Y        | Y         | N         | Y         | N         | N         | Y         | N         | N         | N         | N        | NA  |
| 13. | McDonald and Tovey, 1993 <sup>57</sup>        | Y        | Y        | Y        | Y        | Y        | N        | N        | Y        | Y        | Y         | Y         | Y         | Y         | N         | Y         | Y         | Y         | Y         | Y        | R   |
| 14. | Priestley <i>et al.</i> , 1998 <sup>58</sup>  | Y        | N        | N        | Y        | Y        | N        | Y        | Y        | Y        | Y         | Y         | Y         | Y         | Y         | Y         | N         | Y         | Y         | Y        | R   |
| 15. | Rim and Jee, 2006 <sup>59</sup>               | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y         | Y         | Y         | Y         | N         | Y         | N         | N         | N         | N        | NR  |
| 16. | Williamson <i>et al.</i> , 2007 <sup>60</sup> | Y        | N        | N        | Y        | Y        | Y        | Y        | Y        | Y        | Y         | Y         | Y         | Y         | Y         | Y         | N         | Y         | Y         | Y        | R   |
| 17. | Yang <i>et al.</i> , 2013 <sup>61</sup>       | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y         | Y         | Y         | Y         | Y         | N         | N         | Y         | Y         | Y        | R   |
| 18. | Akkad <i>et al.</i> , 2016 <sup>62</sup>      | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y         | Y         | Y         | Y         | Y         | Y         | N         | Y         | Y         | Y        | R   |
| 19. | Candy <i>et al.</i> , 2018 <sup>63</sup>      | Y        | Y        | Y        | Y        | Y        | Y        | N        | Y        | Y        | Y         | Y         | Y         | Y         | N         | N         | Y         | Y         | Y         | Y        | R   |
| 20. | De Wolff, 2008, <sup>64</sup>                 | Y        | N        | N        | Y        | Y        | Y        | Y        | Y        | Y        | Y         | Y         | Y         | N         | Y         | Y         | N         | Y         | Y         | Y        | RwR |
| 21. | Di Campli <i>et al.</i> , 2012 <sup>65</sup>  | Y        | Y        | Y        | Y        | Y        | Y        | N        | Y        | Y        | Y         | Y         | Y         | Y         | Y         | Y         | N         | Y         | Y         | Y        | R   |
| 22. | Downs <i>et al.</i> , 2000 <sup>66</sup>      | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y         | Y         | Y         | N         | N         | N         | N         | Y         | Y         | Y        | RwR |
| 23. | Heukelbach <i>et al.</i> , 2008 <sup>67</sup> | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y        | Y         | Y         | Y         | Y         | Y         | Y         | Y         | Y         | Y         | Y        | R   |
| 24. | McCage <i>et al.</i> 2002 <sup>35</sup>       | Y        | N        | N        | N        | Y        | Y        | Y        | Y        | Y        | Y         | N         | Y         | N         | Y         | N         | N         | Y         | N         | N        | NR  |
| 25. | Priestley <i>et al.</i> , 2006 <sup>68</sup>  | Y        | Y        | Y        | Y        | Y        | Y        | N        | Y        | Y        | Y         | Y         | Y         | Y         | N         | N         | N         | Y         | Y         | Y        | RwR |

|     | Author(s), Year                               | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | Q   |
|-----|-----------------------------------------------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|-----|
| 26. | Veal 1996 <sup>69</sup>                       | Y | Y | Y | Y | Y | N | Y | Y | Y | Y  | Y  | Y  | Y  | N  | Y  | N  | Y  | Y  | R   |
| 27. | Williamson <i>et al.</i> , 2007 <sup>60</sup> | Y | N | N | Y | Y | N | N | Y | Y | Y  | Y  | Y  | Y  | Y  | Y  | N  | Y  | Y  | RwR |
| 28. | Yang <i>et al.</i> , 2004 <sup>70</sup>       | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y  | Y  | Y  | Y  | N  | Y  | N  | Y  | Y  | R   |
| 29. | De Wolff, 2008 <sup>64</sup>                  | Y | N | N | Y | Y | Y | Y | Y | Y | Y  | Y  | Y  | Y  | N  | Y  | N  | Y  | Y  | RwR |
| 30. | Nair and Sasi, 2017 <sup>71</sup>             | Y | N | N | Y | Y | N | N | Y | Y | Y  | N  | Y  | Y  | N  | Y  | N  | Y  | Y  | NR  |

Abbreviations: R: Reliable without restrictions; RwR: Reliable with restrictions; NR: not reliable; NA: Not assignable

Responses are reported as: Y: Yes; N: No

### Supplementary S3.7: ToxRTool assessment for in vivo studies

Supplementary Table S17: Criteria considered for ToxRTool reliability assessment for *in vivo* studies

| No  | Criteria                                                                                                                                       |
|-----|------------------------------------------------------------------------------------------------------------------------------------------------|
| 1.  | Was the test substance identified?                                                                                                             |
| 2.  | Is the purity of the substance given?                                                                                                          |
| 3.  | Is information on the source/origin of the substance given?                                                                                    |
| 4.  | Is all information on the nature and/or physico-chemical properties of the test item given, which you deem indispensable for judging the data? |
| 5.  | Is the species given?                                                                                                                          |
| 6.  | Is the sex of the test organism given?                                                                                                         |
| 7.  | Is information given on the strain of test animals plus, if considered necessary to judge the study, other specifications?                     |
| 8.  | Is age or body weight of the test organisms at the start of the study given?                                                                   |
| 9.  | For repeated dose toxicity studies only (give point for other study types): Is information given on the housing or feeding conditions?         |
| 10. | Is the administration route given?                                                                                                             |
| 11. | Are doses administered or concentrations in application media given?                                                                           |
| 12. | Are frequency and duration of exposure as well as time-points of observations explained?                                                       |
| 13. | Were negative and positive controls included (give point also, when absent but not required)?                                                  |
| 14. | Is the number of animals per group given?                                                                                                      |
| 15. | Are sufficient details of the administration scheme given to judge the study?                                                                  |

|     |                                                                                                                                                                                                                                   |
|-----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 16. | For inhalation studies and repeated dose toxicity studies only (give point for other study types): Were achieved concentrations analytically verified or was stability of the test substance otherwise ensured or made plausible? |
| 17. | Are the study endpoint(s) and their method(s) of determination clearly described?                                                                                                                                                 |
| 18. | Is the description of the study results for all endpoints investigated transparent and complete?                                                                                                                                  |
| 19. | Are the statistical methods applied for data analysis given and applied in a transparent manner?                                                                                                                                  |
| 20. | Is the study design chosen appropriate for obtaining the substance-specific data aimed at?                                                                                                                                        |
| 21. | Are the quantitative study results reliable?                                                                                                                                                                                      |

**Supplementary Table S18: Quality assessment results of the in vivo studies using ToxRTool**

|    | Author(s), Year                | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | Q   |
|----|--------------------------------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|-----|
| 1. | Fitzjarrell 1995 <sup>72</sup> | Y | Y | N | Y | Y | Y | Y | N | Y | Y  | Y  | Y  | Y  | N  | N  | Y  | N  | N  | N  | Y  | Y  | NR  |
| 2. | Novelo, 2015 <sup>44</sup>     | Y | Y | N | Y | Y | N | Y | Y | Y | Y  | Y  | Y  | Y  | Y  | Y  | Y  | Y  | N  | N  | Y  | Y  | RwR |

Abbreviations: R: Reliable without restrictions; RwR: Reliable with restrictions; NR: Not reliable

Responses are reported as: Y: Yes; N: No

## Supplementary S4: Study characteristics of the excluded studies

### Supplementary S4.1: Excluded studies

#### Supplementary Table S19: Studies excluded after full text review (n=21)

| No                                       | Author, year                                       | Title                                                                                                                                                               | Reason for exclusion                                                                                                                                       |
|------------------------------------------|----------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Excluded during the first search</b>  |                                                    |                                                                                                                                                                     |                                                                                                                                                            |
| 1.                                       | Chen <i>et al.</i> , 2019 <sup>73</sup>            | Acaricidal activity of plant-derived essential oil components against <i>Psoroptes ovis</i> in vitro and in vivo                                                    | Veterinary ectoparasites                                                                                                                                   |
| 2.                                       | Ebneyamin <i>et al.</i> , 2019 <sup>74</sup>       | The efficacy and safety of permethrin 2.5% with tea tree oil gel on rosacea treatment: A double-blind, controlled clinical trial                                    | Duplicate                                                                                                                                                  |
| 3.                                       | Ellse <i>et al.</i> , 2013 <sup>75</sup>           | Control of the chewing louse <i>Bovicola (Werneckiella) ocellatus</i> in donkeys, using essential oils                                                              | Veterinary ectoparasites                                                                                                                                   |
| 4.                                       | Ellse <i>et al.</i> , 2016 <sup>76</sup>           | Essential oils in the management of the donkey louse, <i>Bovicola ocellatus</i>                                                                                     | Veterinary ectoparasites                                                                                                                                   |
| 5.                                       | Ergun <i>et al.</i> , 2019                         | Comparison of Efficacy and Safety of Two Tea Tree Oil-Based Formulations in Patients with Chronic Blepharitis: a Double-Blinded Randomized Clinical Trial           | Duplicate                                                                                                                                                  |
| 6.                                       | James and Callander 2012a <sup>77</sup>            | Dipping and jetting with tea tree ( <i>Melaleuca alternifolia</i> ) oil formulations control lice ( <i>Bovicola ovis</i> ) on sheep                                 | Veterinary ectoparasites                                                                                                                                   |
| 7.                                       | James and Callander 2012b <sup>78</sup>            | Bioactivity of tea tree oil from <i>Melaleuca alternifolia</i> against sheep lice ( <i>Bovicola ovis</i> Schrank) in vitro                                          | Veterinary ectoparasites                                                                                                                                   |
| 8.                                       | Lam <i>et al.</i> , 2020 <sup>79</sup>             | <i>Melaleuca alternifolia</i> (tea tree) oil and its monoterpene constituents in treating protozoan and helminthic infections                                       | Wrong study design (Review)                                                                                                                                |
| 9.                                       | Lopatinalu and Ermina 2014 <sup>80</sup>           | [Pedicicidal activity of plant essential oils and their based preparations]                                                                                         | No full text access                                                                                                                                        |
| 10.                                      | Mills <i>et al.</i> , 2004 <sup>81</sup>           | Inhibition of acetylcholinesterase by Tea Tree oil                                                                                                                  | Wrong outcome                                                                                                                                              |
| 11.                                      | Murphy <i>et al.</i> , 2020 <sup>82</sup>          | The effect of lid hygiene on the tear film and ocular surface, and the prevalence of <i>Demodex</i> blepharitis in university students                              | Wrong patient population                                                                                                                                   |
| 12.                                      | Neves <i>et al.</i> , 2020 <sup>83</sup>           | The sensitivity of <i>Demodex canis</i> (Acari: Demodicidae) to the essential oil of <i>Melaleuca alternifolia</i> - an in vitro study                              | Veterinary ectoparasites                                                                                                                                   |
| 13.                                      | Patel and Raju, 2013 <sup>84</sup>                 | Ocular demodicosis                                                                                                                                                  | Wrong study design (Review)                                                                                                                                |
| 14.                                      | Sands <i>et al.</i> , 2016 <sup>85</sup>           | Residual and ovicidal efficacy of essential oil-based formulations in vitro against the donkey chewing louse <i>Bovicola ocellatus</i>                              | Veterinary ectoparasites                                                                                                                                   |
| 15.                                      | Sugathan and Martin, 2010 <sup>86</sup>            | Galenicals in the treatment of crusted scabies                                                                                                                      | Wrong intervention                                                                                                                                         |
| 16.                                      | Talbert and Wall, 2012 <sup>87</sup>               | Toxicity of essential and non-essential oils against the chewing louse, <i>Bovicola (Werneckiella) ocellatus</i>                                                    | Veterinary ectoparasites                                                                                                                                   |
| 17.                                      | Yam <i>et al.</i> , 2013 <sup>88</sup>             | Ocular demodicidosis as a risk factor of adult recurrent chalazion                                                                                                  | Duplicate                                                                                                                                                  |
| <b>Excluded during the second search</b> |                                                    |                                                                                                                                                                     |                                                                                                                                                            |
| 18.                                      | Chen <i>et al.</i> , 2021 <sup>89</sup>            | Crotamiton-loaded tea tree oil containing phospholipid-based microemulsion hydrogel for scabies treatment: in vitro, in vivo evaluation, and dermatokinetic studies | Wrong outcome                                                                                                                                              |
| 19.                                      | Ngo., <i>et al.</i> , 2018 <sup>90</sup>           | Short-Term Comfort Responses Associated with the Use of Eyelid Cleansing Products to Manage <i>Demodex folliculorum</i> .                                           | Wrong outcome: RCT study, did not study activity of products against <i>Demodex</i> mites rather on patient comfort for various treatments on a single day |
| 20.                                      | Tharmarajah. and Coroneo, 2021 <sup>91</sup>       | Corneal Effects of Tea Tree Oil.                                                                                                                                    | Wrong outcome                                                                                                                                              |
| 21.                                      | Qiu <i>et al.</i> , 2018 <sup>92</sup>             | Satisfaction and convenience of using terpenoid-impregnated eyelid wipes and teaching method in people without blepharitis                                          | Wrong outcome                                                                                                                                              |
| 22.                                      | Zarei-Ghanavati <i>et al.</i> , 2021 <sup>93</sup> | Comparison of the Effect of Tea Tree Oil Shampoo With Regular Eyelid Shampoo in Meibomian Gland Dysfunction Treatment                                               | Wrong outcome: RCT study, did not study activity of products against <i>Demodex</i> mites rather on patient comfort for various treatments on a single day |

## Supplementary S4.2: Summary of studies for veterinary ectoparasites

### Supplementary Table S20: Summary of the key data on veterinary ectoparasites

Summary of descriptive characteristics of studies exploring TTO against veterinary important ectoparasites (mites and lice, n=9)

| Study setting                                      | Study design                                                                                                                    | Method/ Assay                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Intervention                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Outcome measure                                                                                                                                                                                                                                                                                                                                                                         | Treatment outcome                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|----------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Chen <i>et al.</i> , 2019, <sup>73</sup> Belgium   | <i>In vitro</i> (n=660 cattle mites, <i>P. ovis</i> )                                                                           | In vitro: acaricide contact assay (immersion test): immersing the mites in test solutions and stereo-microscopic examination of their immobility 24 h post-immersion<br>Fumigation assay: placing a drop of test solutions at the bottom of a Petri dishes, followed by placing mites on a filter paper at the centre of the lid covered by the filter paper then closing the Petri dishes with the lid. Stereomicroscopic examination of mites for 150 mins in contact assay & 60 mins in fumigation assay | <b>Contact assay</b><br><b>Test:</b> 5.0, 2.5, 1.25, 0.63, 0.32 and 0.16 % of geraniol, eugenol, carvacrol and 1,8-cineol<br><b>Control:</b> Liquid paraffin oil or mineral oil<br><b>Fumigation assay:</b><br><b>Test:</b> droplet (15 µL) of 100% geraniol, eugenol, carvacrol and 1,8-cineol<br><b>Control:</b> droplet (15 µL) paraffin oil or mineral oil<br><b>Residual assay:</b><br><b>Test:</b> LC50 and LC90 obtained from contact assay used<br><b>Control:</b> paraffin oil or mineral oil (1.5ml)          | <b>LC50 (%) at 24 hrs</b><br>Immobility of adult mites and a lack of reactions or persistent immobility within 1 min following stimulation with a needle were considered indications of death<br><b>LT50 (min):</b><br>Immobility of adult mites and a lack of reactions or persistent immobility within 1 min following stimulation with a needle were considered indications of death | <b>LC50 (%):</b> 0.56% for geraniol Vs 0.38 for eugenol Vs 0.26% for carvacrol Vs no activity for 1,8-cineol Vs no activity for control<br><b>LT50 (min):</b> 40 min for geraniol Vs 67 for eugenol Vs 24 for carvacrol Vs 35 for 1,8-cineol Vs no report for control<br><b>LT100:</b> 90 min for geraniol Vs 150 for eugenol Vs 50 for carvacrol Vs 90 for 1,8-cineol Vs all viable after 160 minutes<br>(No p-value is reported)                                                                                                                                                                                                                   |
| Ellse <i>et al.</i> , 2013, <sup>75</sup> UK       | <i>In vitro</i> (n=360 donkey chewing louse, <i>Bovicola ocellatus</i> )<br><br><i>In vivo</i> (n=30 donkeys with chewing lice) | In vitro: Filter paper contact or non-contact assays: exposing the lice with the essential oils (contact) or their vapour (non-contact) for up to 24hrs or 2hrs & examining their mortality<br>In vivo: donkeys with the lice were sprayed with TTO, Lavender or vehicle only and checked for lice 2 weeks after the applications                                                                                                                                                                           | <b>In vitro:</b><br><b>Test:</b> TTO (5% and 10%), Lavender oil (5% and 10%)<br><b>Control I:</b> Vehicle (water +0.2% (v/v) Tween 80)<br><b>Control II:</b> Silicone oil (5% and 10%)<br>In vivo:<br><b>Test I:</b> TTO (5%) suspension sprayed (2mL/kg) once every 2 weeks for 1 month (n=10)<br><b>Test II:</b> Lavender oil (5%) suspension sprayed (2mL/kg) once every 2 weeks for 1 month (n=10)<br><b>Control:</b> Vehicle solution (water+0.2% Tween 80) sprayed (2mL/kg) once every 2 weeks for 1 month (n=10) | Louse mortality rate: from treatment to non-viability (immobility and absence of any movement with or without stimulation with pin)<br>Log reduction of louse number (in vivo)<br>AEs occurrence                                                                                                                                                                                        | <b>Mean Louse mortality rate (after 120 minutes, contact):</b> 90% for TTO Vs 90% for Lavender Vs 50% for Control I Vs 0% for Control II (P<0.05)<br>TTO (5%) Vs TTO (10%) and Lavender (5%) Vs Lavender (10%) (P>0.05)<br><b>Mean louse mortality rate (after 24hrs, contact):</b> 100% for TTO and Lavender groups<br><b>Mean Louse mortality rate (after 2hrs for non-contact):</b> 80% for TTO Vs 80% for Lavender Vs 0% for Control I Vs 0% for Control II (P<0.05)<br>TTO (5%) Vs TTO (10%) and Lavender (5%) Vs Lavender (10%) (P>0.05)<br>Reduction in louse number after 1 month: TTO Vs Lavender Vs Control (P>0.05)<br><b>AEs:</b> No AES |
| Ellse <i>et al.</i> , 2016, <sup>76</sup> UK       | <i>In vivo</i> (n=198 donkeys with chewing lice, <i>Bovicola ocellatus</i> )                                                    | Donkeys with the lice were sprayed with TTO, Lavender or vehicle only and checked for lice 2 weeks after the applications                                                                                                                                                                                                                                                                                                                                                                                   | In vivo:<br><b>Test I:</b> TTO (5%) suspension sprayed (2mL/kg) once every 2 weeks for 1 month with every<br><b>Test II:</b> Lavender oil (5%) suspension sprayed (2mL/kg) once every 2 weeks for 1 month<br><b>Control:</b> Vehicle solution (water + 1% polyvinylpyrrolidone) sprayed (2mL/kg) once every 2 weeks for 1 month                                                                                                                                                                                         | Reduction in total louse counts after 1 month<br>AEs occurrence                                                                                                                                                                                                                                                                                                                         | <b>Reduction in total louse counts after 1 month (95%CI):</b> 78% (67.3–89.1%) for TTO Vs 78% (67.2–89.2%) for Lavender oil Vs 0% for Control (P<0.001)<br>78% (67.3–89.1%) for TTO Vs 78% (67.2–89.2%) for Lavender oil (P = 0.8)<br><b>AEs:</b> No AEs                                                                                                                                                                                                                                                                                                                                                                                             |
| James and Callander 2012b, <sup>78</sup> Australia | <i>In vitro</i> (n= 420 sheep lice, <i>Bovicola ovis</i> Schrank and n= blowfly <i>Lucilia cuprina</i> )                        | Both Treated surface and wool assays<br>Fumigant assay                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Treated surface assays<br><b>Test:</b> TTO (1%, 5%, 10% and 20%)<br><b>Control I:</b> Acetone<br><b>Control II:</b> grapeseed oil<br>Wool assays<br><b>Test:</b> TTO (0.5, 0.75 and 1%)                                                                                                                                                                                                                                                                                                                                 | Louse mortality rate: from treatment to non-viability (immobility and absence of any movement with or                                                                                                                                                                                                                                                                                   | <b>Treated surface assays</b><br>10.0 (0.0) for 1% Vs 10.0 (±5.8) for 5% Vs 13.3 (±6.7) for 10% and 20% for 10.0 (±5.8) Vs 6.7 (±3.3) Control I (P > 0.05)<br>96.7% (±3.3) for 10% Vs 100% for 20% TTO Vs 0% for Control II (P < 0.05)                                                                                                                                                                                                                                                                                                                                                                                                               |

|                                                    |                                                                                                        |                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|----------------------------------------------------|--------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                    |                                                                                                        |                                                                                                                                                                                                                                                                    | Fumigant assay<br><b>Test:</b> TTO (0.5%, 1% and 2%)                                                                                                                                                                                                                                                                              | without stimulation with pin)                                                                                                                                                   | 3.3 (±3.3) for 0.1% Vs 3.3 (±3.3) for 0.5% Vs 6.7 (±3.3) for 1% Vs 0 for 2.5% Vs 0% Control II (P > 0.05)<br><b>Wool assays</b><br>100% for 1% TTO<br><b>Fumigant assay</b><br>100% for 0.5%, 1% and 2% TTO                                                                                                                                                                                                                                                                                                                                         |
| James and Callander 2012a, <sup>77</sup> Australia | <i>In vivo</i> (n= 18 sheep lice, <i>Bovicola ovis</i> Schrank and n= blowfly <i>Lucilia cuprina</i> ) | <b>Immersion dipping</b><br>Sheep infested with lice were dipped into a test solution for 1 minutes and inspected for live lice for 20 weeks<br><b>Jetting method</b><br>4L test solutions were jetted over the sheep body and examined for live lice for 20 weeks | <b>Test I:</b> Treated with TTO (1%, n=6)<br><b>Test II:</b> Treated with TTO (2%, n=6)<br><b>Control:</b> No treatment (n=6)                                                                                                                                                                                                     | <b>Immersion dipping</b><br>Louse counts per 10 cm fleece parting Percent reduction<br><b>Jetting</b><br>Percent reduction                                                      | <b>Immersion dipping</b><br><b>Mean ±SD louse counts</b><br>0 (100% reduction) (BL: 8.3 ±1.8)) for TTO (1%) Vs 0 (100% reduction) (BL: 8.4 ±1.8) for TTO (2%) Vs 8.2 ±3.0 (BL: 8.8±2.0) for Control<br><b>Percent reduction</b><br>100% for TTO (1%) Vs 100% for TTO (2%) Vs 6.8% for Control<br><b>Percent reduction (Jetting)</b><br>84.0% for TTO (1%) Vs 78.1% for TTO (2%) Vs 0% for Control ( <i>no statistics reported</i> )                                                                                                                 |
| Magi <i>et al.</i> , 2006, <sup>94</sup> Estonia   | <i>In vivo</i> (n=72 pigs with sarcoptic mange mites, <i>Sarcoptes scabiei var. suis</i> )             | Essential oils were applied over the body infested with mites and examined for 4 weeks                                                                                                                                                                             | <b>Test:</b> TTO, Garlic, Black pepper, Juniper, Citronella grass, Pennyroyal, Eucalyptus essential oils and Mugwort, Wormwood, Tansy and Hogweed plat extracts applied twice, with one-week interval<br><b>Control:</b> no treatment                                                                                             | <b>Survival rate</b>                                                                                                                                                            | <b>Survival rate (%)</b><br>1.45% for TTO Vs 10.65 for Garlic Vs 11.75 for Black pepper Vs 14.62 for Juniper Vs 4.82 for Citronella Vs 6.75 for Pennyroyal Vs 10.69 for Eucalyptus Vs 18.22 for Mugwort Vs 10.98 for Wormwood Vs 8.82 for Tansy Vs 6.66 for Hogweed Vs 101.31 for Control ( <i>no statistics reported</i> )                                                                                                                                                                                                                         |
| Neves <i>et al.</i> , 2020, <sup>83</sup> Brazil   | <i>In vitro</i> (n=27 <i>Demodex canis</i> mites)                                                      | The products (200µL) applied on the mites placed on microscope slides and examined for viability using microscope for about 8hrs                                                                                                                                   | <b>Test:</b> TTO (3.13%, 5.0% 6.25%, 12.5%, 25%, 50%, and 100%) (n=21)<br><b>Control I:</b> Amitraz (ANZ, 12.5%, n=3)<br><b>Control II:</b> Johnson's Baby Shampoo (JBS, n=3)                                                                                                                                                     | Mite survival time (MST): from treatment to non-viability (absence of chelicerae and tarsi movement)                                                                            | <b>Mean ± SD MST in minutes:</b> 100.7±98.2 for TTO (3.3%) Vs 88.3±82.9 for TTO (5%) Vs 98.7±30.6 for TTO (6.25%) Vs 33.3±8.3 for TTO (12.5%) Vs 12.0±2.0 for TTO (25%) Vs 13.3±5.0 for TTO (50%) Vs 8.0±3.5 for TTO (100%) Vs 333.3±88.5 for ANZ Vs 470.7±60.0 for JBS ( <i>no statistics reported</i> )                                                                                                                                                                                                                                           |
| Sands <i>et al.</i> , 2016, <sup>85</sup> UK       | <i>In vitro</i> (n=120, <i>Bovicola ocellatus</i> donkey chewing lice and n=120 eggs)                  | Filter paper contact bioassays: exposing the lice with the essential oils (800µL) & examining their mortality using dissecting microscope for 24hrs.<br><br>The ovicidal activities of the essential oils investigated following similar procedure over 12 days    | Lice mortality test (24hrs)<br><b>Test I:</b> TTO (5%)<br><b>Test II:</b> Lavender oil (5%)<br><b>Control (vehicle) I:</b> PVP (5% w/v)<br><b>Control (vehicle) II:</b> SLS (5% w/v)<br><br>Ovicidal test (12 days)<br><b>Test I:</b> TTO (5%)<br><b>Test II:</b> Lavender oil (5%)<br><b>Control (vehicle):</b> coconut oil (5%) | Mortality rate: from treatment to non-viability (absence of movement of the legs, mouthparts, antennae or abdomen even when stroked with a dissecting needle)                   | <b>Mortality rate (Mean ± SD) of adult lice:</b><br>100±0% for TTO Vs 100±0% for lavender Vs 50.0±18.0% for Control I Vs 30.0±11.0% for Control II ( <i>statistics not reported</i> )<br><b>Mortality rate (Mean ± SD) of nymphs:</b><br>73.3±27.0% for TTO Vs 90.0±10.0% for lavender Vs 26.7±9.0% for Control I<br>96.7±3.0% for TTO Vs 100±0% for lavender Vs 20.0±0.0% for Control II ( <i>statistics not reported</i> )<br><b>Ovicidal test (hatchability)</b><br>0% for TTO Vs 0% for lavender Vs 72±10% for Control (P<0.01)                 |
| Talbert and Wall, 2012, <sup>87</sup> UK           | <i>In vitro</i> (n=150, <i>Bovicola ocellatus</i> donkey chewing lice)                                 | Filter paper contact bioassays: exposing the lice with the essential oils (600µL) & examining their mortality using dissecting microscope for 5hrs.                                                                                                                | <b>Test:</b> 0.5%, 1%, 3%, 5% and 10% (v/v) of TTO terpinen-4-ol (T4O, 3%), Camphor, Clove bud, Eucalyptus, Lavender, and Peppermint oils<br><b>Control:</b> ethanol                                                                                                                                                              | LC50 %: from treatment to non-viability (absence of movement of limbs and gut and failure to respond when the abdomen was stroked with entomological pin or forceps) LT50 (min) | <b>LC50 % (mean ±95%CI)</b><br>0.98% (0.6–1.5) for TTO Vs 8.6 (5.7–22.9) for Camphor Vs 1.23 (0.8–1.96) for Clove Vs 1.19 (0.6–1.96) for Eucalyptus Vs 0.76 (0.3–1.2) for Lavender Vs 1.24 (0.76–1.8) for Peppermint (P ≤ 0.05 for all except camphor)<br><b>LT50 (min) (mean ±95%CI)</b><br>30.2 (6.2–56.3) minutes for TTO Vs >300 for Camphor Vs 60.8 (19.7–104.5) for Clove Vs 34.4 (0.8–76.5) for Eucalyptus Vs 39.3 (11.8–67.8) for Lavender Vs 68.7 (30.0–111.8) for Peppermint Vs 16.3 (8.5–24.3) for T4O (P ≤ 0.05 for all except camphor) |

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