# Individualized Homeopathic Medicines in the Treatment of Tinea Corporis: Double-Blind, Randomized, Placebo-Controlled Trial

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## Abstract

**Introduction** Tinea corporis (TC; ringworm or dermatophytosis) is a superficial skin infection caused by *Microsporum*, *Epidermophyton* and *Trichophyton* genera of dermatophytes. We compared the effects of individualized homeopathic medicines (IHMs) in fifty-millesimal (LM) potencies against placebo in TC.

**Methods** A double-blind, randomized, placebo-controlled, two parallel arms trial was conducted on 62 individuals suffering from TC at the National Institute of Homoeopathy, India. Participants were randomized in a 1:1 ratio to receive either IHMs in LM potencies or identical-looking placebos for a period of 3 months. The primary outcome measure was the number of participants showing complete disappearance of skin lesions after 3 months. Secondary outcomes were a numeric rating scale (NRS) measuring intensity of itching and the Skindex-29 questionnaire (overall, and three sub-scales – degree of symptoms, psychological functioning, emotional status). All were assessed at baseline and every month, up to 3 months. The intention-to-treat sample was analyzed to detect inter-group differences using two-way repeated measures analysis of variance after adjusting for baseline differences.

**Results** The primary outcome revealed no improvement in either of the groups ($\chi^2 = 0.012$, $p = 0.999$). Inter-group differences in some of the secondary outcomes favored IHMs against placebo – itching NRS (mean group difference after 3 months: −0.7 (95% confidence interval [CI], −1.1 to −0.4; $p = 0.001$); Skindex-29 overall (mean group difference after 3 months: 3.2 [95% CI, −0.6 to 7.0; $p = 0.009$]); Skindex-

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29 degree of symptoms (mean group difference after 3 months: 0.9 [95% CI, −0.2 to 1.9; $p = 0.007$]); and Skindex-29 psychological functioning (mean group difference after 3 months: 1.7 [95% CI, 0–3.4; $p = 0.002$]).

**Conclusion** Results were negative on the primary outcome; however, secondary outcomes included some statistically significant results favoring IHMs against placebo after 3 months.

**Trial registration** CTRI/2019/11/021999; UTN: U1111–1242–0070.

## Introduction

Tinea corporis (TC; ringworm or dermatophytosis) is a superficial skin infection affecting mainly the keratin of the epidermis, hairs and nails after direct contact with infected soil, animals, or the skin of other humans,[1,2] mainly caused by the *Microsporum*, *Epidermophyton* and *Trichophyton* genera of dermatophytes.[3,4] *Trichophyton rubrum* is the causative organism in 70% of cases; and *Trichophyton mentagrophytes* and *Microsporum audouinii* are other common species.[5] Worldwide prevalence of superficial mycotic infection is 20% to 25%,[6] with lifetime risk of developing the infections estimated to be 10% to 20%.[7] In rural India, the prevalence of TC is 78%,[8] whereas in Kolkata it is 86.4%.[9] In south India, prevalence is 25.7%; the 21-30 years age group is the most commonly affected (24%), predominantly males (1.94:1), laborers (30.6%), rural people (54.6%), and those from a lower socioeconomic background (65.4%).[10,11] Conventional treatment suggests topical terbinafine and itraconazole and oral anti-fungal therapies for local lesions[12]; but if the lesion is multiple, extensive, deep, recurrent, chronic or unresponsive to topical anti-fungal treatment, or if the patient is immunodeficient, systemic anti-fungal treatment is suggested.[13] Studies have shown that this kind of treatment produces mild adverse reactions,[14] such as gastrointestinal upset, headache, and taste disturbances.[15]

One recent observational study conducted on 65 participants with dermatophytosis revealed promising results in favor of homeopathy.[16] Another observational study, using *Bacillinum* on 36 participants with tinea infection, produced equivocal results.[17] A recent case report on tinea with the medicine *Sepia succus* showed improvement.[18] One *in vitro* study documented positive effects of two homeopathic medicines—*Thuja occidentalis* and *Graphites*—on keratinophilic fungi.[19] Despite this preliminary evidence, we were unable to identify any published randomized, placebo-controlled, trial of individualized homeopathic medicines (IHMs) in TC, and so we aimed to rectify that deficiency in the research literature.

## Methods

### Trial Design

This double-blind, randomized (1:1), placebo-controlled, two-parallel arms trial was conducted from November 2019 to June 2021 at the dermatology out-patient department of the National Institute of Homoeopathy, Kolkata, India.

### Ethical Matters

The study protocol was approved by the Institutional Ethical Committee (IEC) [Ref. No. 5–23/NIH/PG/Ethical Comm. 2009/ Vol 6/ 49(PG); dated October 14, 2019] and was registered prospectively in the Clinical Trials Registry—India [CTRI/ 2019/11/021999] with a secondary identifier—UTN of U1111–1242–0070. The study complied with the Helsinki Declaration for ethical conduct of clinical trials involving human participants and adhered to the International Conference on Harmonization guideline for Good Clinical Practice. The trial protocol and the full project report were submitted as the postgraduate synopsis and thesis respectively of the corresponding author to the West Bengal University of Health Sciences, Kolkata. Provision was kept in the protocol to treat intercurrent illness, and adverse or serious adverse events, if any, as per homeopathic principles or by referral. No new drug was experimented on in this trial. Prior to enrollment, each patient was provided with an information sheet detailing the objectives, methods, risks and benefits of participating, and addressing matters of confidentiality; written informed consent was then obtained from each individual who agreed to participate in the trial.

### Participants

Study inclusion criteria were: suffering from TC (ICD-10-CM code B35.4) for at least 3 months; aged between 18 and 65 years, and of either sex; literate, with the ability to read English and/or Bengali; consented to participate. A patient who was using topical agents for tinea lesions was eligible for inclusion after a washout period of 2 weeks. A potential participant was excluded if there was a complication such as lichenification or eczematization, a similar looking skin condition such as seborrheic dermatitis, pityriasis rosea or psoriasis, or if too sick for consultation, diagnosed with unstable mental or psychiatric illness, had any uncontrolled or life-threatening systemic illness affecting quality of life and/or any organ failure, was pregnant, puerperal or lactating, suffered from substance abuse and/or dependence, was in a self-reported immune-compromised state, or had been undergoing homeopathic treatment for any chronic disease at any time within the previous 6 months.

### Intervention

Both the medicines and the placebos were procured from Hahnemann Publishing Company Private Limited—a good manufacturing practice (GMP)-certified firm.

- *Verum:* Indicated IHMs were administered in fifty-millesimal (LM) potencies as decided appropriate to the individual case. Homeopathic medicines are produced through sequentially agitated ("succussed") dilutions in decimal (D), centesimal (C) or quinquagintamillesimal (Q or LM or 50-millesimal) potencies. In this trial, we used Q-potencies which were prepared by grinding the raw material (C1 until C3), followed by consecutive 1:50,000 agitated dilutions. Therefore, a Q1 corresponds to a $5 \times 10^{-10}$ fraction of the raw material ($Q2 = 2.5 \times 10^{-15}$, $Q3 = 1.25 \times 10^{-20}$, $Q4 = 6.25 \times 10^{-24}$, etc.). A single medicated cane sugar globule of poppy seed size (no.10) was dissolved in 80 mL of distilled water with addition of two drops of 90% v/v ethanol; 16 doses were marked on the vial. Each dose of 5 mL was instructed to be taken, after 10 uniformly forceful downward strokes to the vial, in 45 mL of clean room-temperature water in a clean cup; also to stir well, to take 5 mL of this liquid orally, and to discard the rest of the liquid from the cup. Medicine selection, dosage and repetition were decided by consensus among three qualified, experienced and affiliated homeopaths in every case. The duration of therapy for each patient was 3 months. Follow-ups took place in compliance with homeopathic principles.
- *Control*: This group received placebos, identical in appearance to the verum. In LM scale, a single non-medicated cane sugar globule of poppy seed size (no. 10) was dissolved in 80 mL distilled water with addition of two drops of 90% v/v ethanol, and the remaining instructions were similar to those of the verum group. The period of interventions for each patient was also 3 months.
- *Concomitant care:* Along with the medicines, each of the enrolled participants received advice on applying olive oil[20] or coconut oil[21] on the affected parts, which they were requested to do twice a day, keeping the area dry, avoiding the use of tight garments including synthetic clothes, and washing infected clothes and bed linen separately in hot water.

## Outcome Measures

- Primary: Number of participants in each group showing complete disappearance of the skin lesion at the end of 3 months of intervention, as assessed from naked eye examination by a conventionally trained dermatologist who was blinded to treatment group.
- Secondary:
  - 0 to 10 numeric rating scale (NRS), measuring intensity of itching: the NRS represented "no itch" (score of 0) to "worst imaginable itch" (score of 10). Subjects were asked to rate the intensity of their itch using this scale. It has high reliability and concurrent validity and was a popular choice for all participants due to its simple format.[22]
  - Skindex-29 questionnaire: the Skindex-29 is a health-related instrument designed to measure the effects of skin disease on a person's quality of life. The questionnaire covers areas considered crucial in an instrument designed to evaluate quality of life, such as degree of symptoms (seven items; question nos. 1, 7, 10, 16, 19, 24, 27), psychosocial functioning (12 items; nos. 2, 4, 5, 8, 11, 14, 17, 20, 22, 25, 29, 30) and emotional status (10 items; nos. 3, 6, 9, 12, 13, 15, 21, 23, 26, 28). Higher scores indicate greater impact of skin disease. All the questions are provided with a 5-point agreement Likert scale (never, 1; always, 5). All responses were transformed to a linear scale of 100 (never, 0; rarely, 25; sometimes, 50; often, 75; all the time, 100); thus, the range of scores was 0 (no effect) to 100 (effect experienced all the time). Item no. 18 was a single item, not included in the scoring. Any item with multiple responses was considered as missing. If responses to more than 25% of the items were missing overall, the questionnaire was eliminated from statistical evaluation. Scores were calculated as the average of non-missing items in a given scale.[23]

## Sample Size

Formal effect size calculation was not possible on account of an absence of any published study of similar design. We expected complete disappearance of tinea lesions, in 50% and 25% of participants in the verum and control groups respectively, within 3 months of intervention. Calculated effect size ($w$) became 0.5. To detect a significant difference between two proportions of events over 3 months of intervention through $\chi^2$ goodness-of-fit $2 \times 2$ contingency tables, a study with $2 \times 31$ participants would give 95% power based on a two-tailed significance level of 5%. To achieve the 62 total, screening and exclusion continued until the enrollment reached that number.

## Randomization

A random sequence was generated by permuted block randomization maintaining 1:1 allocation, performed by an independent third party in strict confidentiality using the StatTrek random number generator, and was made available to the blinded pharmacist in coded form for dispensing from the coded vials as per the prescriptions.

## Blinding

The double-blinding method was ensured by masking both the participants and the investigators. The outcome assessors, the pharmacists and the data entry operators were also kept blinded throughout the trial. Identical looking vials were coded as "1" or "2" and contained either medicine or placebo. Codes were assigned randomly and confidentially by an independent third party. Both medicines and placebos were re-packed in identical glass bottles and labeled with code, name of medicine and potency, and were dispensed according to the random number list. The vials were destined for each patient in turn by the random number chart. Codes were broken at the end of the trial after the dataset was frozen.

 

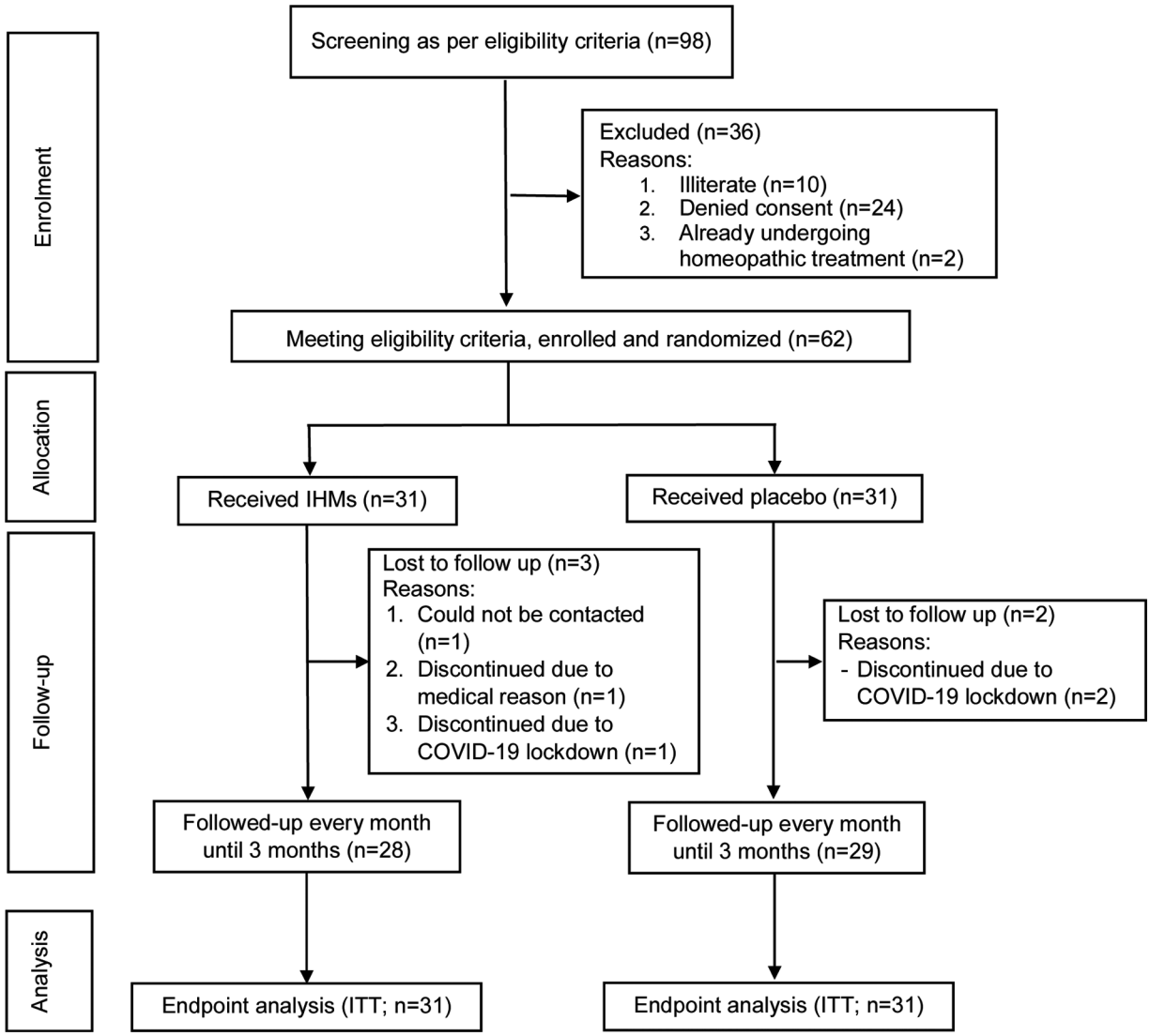


**Fig. 1** Study flow diagram. IHMs, individualized homeopathic medicines, COVID-19, coronavirus disease 2019; ITT, intention-to-treat.

### Allocation Concealment

Blinded postgraduate trainees were involved in participant screening, enrollment and assigning serial numbers to the enrolled participants. Subsequently, the blinded participants were interviewed by the blinded homeopaths for prescription. Allocation concealment was achieved by making both the recruiters and the physicians unaware of the randomization sequence. The blinded pharmacist was provided with the coded random number chart in strict confidentiality for dispensing of either medicines or alike placebos to the participants sequentially.

### Statistical Method

The intention-to-treat (ITT) approach was adopted; missing values were replaced by predicted values from a linear regression model. Baseline differences between groups were adjusted using analysis of covariance (ANCOVA) models. The intra-group changes were examined using one-way repeated measure analysis of variance (ANOVA). Inter-group differences were tested with Chi-square tests, unpaired *t*-tests and two-way repeated measures ANOVA. Effect sizes (Cohen's *d*: small, 0.2; medium, 0.5; large, 0.8) are also reported. Statistical Package for Social Sciences (SPSS version 20.0 statistics for Windows; IBM Corp., Armonk, NY) was used to analyze the data.

### Reporting Guidelines

Study reporting adhered to the CONSORT extension statement for randomized trials[24] and the RedHot guidelines[25] for reporting data on homeopathic treatments (►**Supplementary Tables 1** and **2**, available online only).

## Results

### Participant Flow

Out of the 98 participants screened, 36 were excluded because of various reasons; 62 were enrolled as per the eligibility criteria and subsequently randomized. Five participants dropped out (verum, 3; control, 2); 57 completed the trial (►**Fig. 1**).

 

**Table 1** Comparison of the socio-demographic characteristics between groups at baseline ($N = 62$)

| Features | IHMs group ($n = 31$) | Placebo group ($n = 31$) | *p*-Value |
|---|---|---|---|
| Age | 35.7 ± 10.7 | 33.9 ± 13.9 | 0.509 |
| Body mass index | 19.4 ± 2.2 | 19.7 ± 2.5 | 0.705 |
| Blood pressure | | | |
| • Systolic | 121.6 ± 9.0 | 121.7 ± 7.4 | 0.926 |
| • Diastolic | 77.8 ± 5.7 | 79.0 ± 5.7 | 0.481 |
| Sex[a] | | | 0.891 |
| • Male | 15 (48.4) | 14 (45.2) | |
| • Female | 16 (51.6) | 17 (54.8) | |
| Residence[a] | | | 0.822 |
| • Rural | 20 (64.5) | 18 (58.1) | |
| • Semi-urban | 7 (22.6) | 8 (25.8) | |
| • Urban | 4 (12.9) | 5 (16.1) | |
| Education[a] | | | 0.554 |
| • $8^{th}$ std. or less | 7 (22.6) | 10 (32.3) | |
| • $9^{th}$ to $12^{th}$ std. | 10 (32.3) | 11 (35.5) | |
| • Higher than $12^{th}$ std. | 14 (45.2) | 10 (32.3) | |
| Marital status[a] | | | 0.501 |
| • Single | 6 (19.4) | 8 (25.8) | |
| • Married | 25 (80.6) | 23 (74.2) | |
| Employment status[a] | | | 0.916 |
| • Employed | 5 (16.1) | 6 (19.4) | |
| • Business | 6 (19.4) | 6 (19.4) | |
| • Dependent | 20 (64.5) | 19 (61.3) | |
| Income status[a] | | | 0.212 |
| • Poor | 18 (58.1) | 12 (38.7) | |
| • Middle | 6 (19.4) | 11 (35.5) | |
| • Affluent | 7 (22.6) | 8 (25.8) | |

Abbreviation: IHMs, individualized homeopathic medicines.
[a]Continuous data presented as mean ± standard deviation and unpaired *t*-tests applied.
Note: Categorical data presented as absolute value (%) and Chi-square tests (Yates corrected) applied; *p* less than 0.05 (two-tailed) considered as statistically significant.

### Recruitment

The enrollment period spanned 17 months, from November 2019 until March 2021 inclusive. Follow-up of the last enrolled patient was completed in June 2021. Total study duration was 20 months.

### Baseline Data

There were no statistical differences between the groups at baseline (all $p > 0.05$) except Skindex-29 degree of symptoms ($p = 0.004$) and psychological functioning ($p = 0.019$) subscales (►**Tables 1**, **3**, **4**).

### Numbers Analyzed

Out of the 31 enrolled in each group, outcome data were complete for 28 and 29 participants in the IHMs and placebo groups respectively. ITT analysis included all the randomized participants ($n = 62$).

### Outcomes and Estimation

- Primary: After 3 months of intervention, complete disappearance of the skin lesions was observed in one patient only (in the placebo group); thus, no significant group difference could be detected ($\chi^2 = 0.012$, $p = 0.999$) (►**Table 2**).
- Secondary:
  - *Itching NRS*: Intra-group improvement over time was significant in both the IHMs ($F_{3, 27} = 206.984$, $p < 0.001$) and placebo groups ($F_{3, 27} = 113.352$, $p < 0.001$). Inter-group differences were significant, with large effect sizes, after the first (mean difference: 1.1; 95% CI, 0.8 to 1.5; $p < 0.001$; $d = 1.714$), the second (mean difference: 1.2; 95% CI, 0.8 to 1.5; $p < 0.001$; $d = 1.833$) and the third month (mean difference: −0.7; 95% CI, −1.1 to −0.4; $p < 0.001$; $d = 1.064$). Placebos were significantly

 

**Table 2** Intra- and inter-group comparison of presence or absence of lesion at different time points between groups ($N = 62$)

| | Baseline; *n* (%) | After 1 month; *n* (%) | After 2 months; *n* (%) | After 3 months; *n* (%) | $\chi^2$ | *p*-Value |
|---|---|---|---|---|---|---|
| IHMs group ($n = 31$) | 31 (100) | 31 (100) | 31 (100) | 31 (100) | 0.012 | 0.999 |
| Placebo group ($n = 31$) | 31 (100) | 31 (100) | 31 (100) | 30 (96.8) | | |

Abbreviation: IHMs, individualized homeopathic medicines.

**Table 3** Intra- and inter-group comparison of pruritus intensity scores (0-10) at different time points between groups ($N = 62$) (baseline differences adjusted using ANCOVA model)

| | Baseline mean ± SD | After 1 month; mean ± SD | After 2 months; mean ± SD | After 3 months; mean ± SD | Wilks' lambda | Partial eta-square | $F_{3, 27}$ | $p^c$ |
|---|---|---|---|---|---|---|---|---|
| • IHMs group ($n = 31$) | 8.3 ± 0.7 | 8.2 ± 0.7 | 6.9 ± 0.6 | 3.9 ± 0.8 | 0.043 | 0.957 | 206.984 | <0.001*** |
| • Placebo group ($n = 31$) | 8.2 ± 1.1 | 7.0 ± 0.7 | 5.8 ± 0.6 | 4.7 ± 0.7 | 0.076 | 0.924 | 113.352 | <0.001*** |
| Mean inter-group difference ± SE | 0.2 ± 0.2 | 1.1 ± 0.2 | 1.2 ± 0.2 | −0.7 ± 0.2 | | | | |
| 95% CI | −0.3, 0.6 | 0.8, 1.5 | 0.8, 1.5 | −1.1, −0.4 | | | | |
| $t_{60}$ | 0.689 | 6.607 | 7.338 | −4.087 | | | | |
| $p^a$ | 0.493 | <0.001*** | <0.001*** | <0.001*** | | | | |
| Effect size (Cohen's *d*) | – | 1.714 | 1.833 | 1.064 | | | | |
| Two-way repeated measures ANOVA | | | | | | | | |
| • $F_{1, 60}$ | | | | 12.574 | | | | |
| • Partial eta-square | | | | 0.173 | | | | |
| • $p^b$ | | | | 0.001** | | | | |

CI, confidence interval; IHMs, Individualized homeopathic medicines; NRS, Numeric rating scale; SD, standard deviation; SE, standard error.
[a]Unpaired *t*-tests; $t_{60}$: *t* score at 60 degrees of freedom; *p*: inter-group differences detected by unpaired *t*-tests.
[b]*p*: inter-group differences detected by two-way repeated measures ANOVA models.
[c]*p*: intra-group changes detected by one-way repeated measures ANOVA.
*$p < 0.05$.
**$p < 0.01$.
***$p < 0.001$.

superior to IMHs for the first and second months of the study in reducing the intensity of pruritus; however, the situation was reversed after the third month. Overall analysis favored homeopathy against placebo ($F_{1, 60} = 12.574$, $p = 0.001$) (►**Table 3**).

◦ *Skindex-29 questionnaire*: Intra-group changes at different points in time of the overall score and the sub-scales were statistically significant in both the groups (all $p < 0.001$). Inter-group differences in overall score and two sub-scales after 3 months of intervention favored IHMs significantly against placebo: Skindex-29 overall scores (mean group difference after 1 month, 5.5 [2.5 to 8.5]; after 2 months, 7.1 [3.4 to 10.7]; after 3 months: 3.2 [−0.6 to 7.0]; $F_{1, 60} = 7.231$, $p = 0.009$); Skindex-29 degree of symptoms sub-scale scores (mean group difference after 1 month, 0.5 [−0.5 to 1.5]; after 2 months, 1.2 (0.3 to 2.1); after 3 months, 0.9 (−0.2 to 1.9); $F_{1, 60} = 7.908$, $p = 0.007$); and Skindex-29 psychological functioning sub-scale scores (mean group difference after 1 month, 1.9 [0.3 to 3.6]; after 2 months, 3.4 (1.6 to 5.2); after 3 months, 1.7 (0 to 3.4); $F_{1, 60} = 10.328$, $p = 0.002$). No significant inter-group difference was observed for the Skindex-29 emotional status sub-scale scores: mean group difference after 1 month, 2.3 (1.1 to 3.5); after 2 months, 1.8 (0.5 to 3.2); after 3 months, 0.4 (−0.9 to 1.8); $F_{1, 60} = 2.312$, $p = 0.134$. Inter-group differences at individual time points were mostly statistically significant, except the Skindex-29 degree of symptoms sub-scale score after 1 month ($p = 0.335$) and 3 months ($p = 0.094$), the Skindex-29 emotional status sub-scale scores after 3 months ($p = 0.556$), and the Skindex-29 overall score after 3 months ($p = 0.094$) (►**Table 4**).

 

**Table 4** Intra- and inter-group comparison of Skindex-29 scores at different time points between groups ($N = 62$) (baseline differences adjusted using ANCOVA model)

| | Baseline; mean ± SD | After 1 month; mean ± SD | After 2 months; mean ± SD | After 3 months; mean ± SD | Wilks' lambda | Partial eta-square | $F_{3,\ 28}$ | $p^c$ |
|---|---|---|---|---|---|---|---|---|
| **Degree of symptoms (0–100)** | | | | | | | | |
| IHMs group ($n = 31$) | 26.2 ± 1.5 | 21.3 ± 1.2 | 17.9 ± 1.6 | 15.7 ± 1.9 | 0.031 | 0.969 | 287.368 | <0.001*** |
| Placebo group ($n = 31$) | 24.6 ± 2.7 | 20.8 ± 2.5 | 16.7 ± 1.9 | 14.8 ± 2.2 | 0.088 | 0.912 | 96.970 | <0.001*** |
| Mean inter-group difference ± SE | 1.6 ± 0.5 | 0.5 ± 0.5 | 1.2 ± 0.5 | 0.9 ± 0.5 | | | | |
| 95% CI | 0.5, 2.7 | −0.5, 1.5 | 0.3, 2.1 | −0.2, 1.9 | | | | |
| $t_{60}$ | 2.935 | 0.971 | 2.716 | 1.701 | | | | |
| $p^a$ | 0.004** | 0.335 | 0.009** | 0.094 | | | | |
| Effect size (Cohen's *d*) | – | 0.255 | 0.683 | 0.438 | | | | |
| Two-way repeated measures ANOVA | | | | | | | | |
| • $F_{1,\ 60}$ | | | | 7.908 | | | | |
| • Partial eta-square | | | | 0.116 | | | | |
| • $p^b$ | | | | 0.007** | | | | |
| **Psychological functioning (0–100)** | | | | | | | | |
| IHMs group ($n = 31$) | 40.3 ± 3.1 | 33.2 ± 2.7 | 29.8 ± 3.0 | 26.9 ± 2.8 | 0.040 | 0.960 | 225.993 | <0.001*** |
| Placebo group ($n = 31$) | 37.3 ± 6.2 | 31.3 ± 3.7 | 26.4 ± 3.9 | 25.2 ± 3.8 | 0.192 | 0.808 | 39.328 | <0.001*** |
| Mean inter-group difference ± SE | 3.0 ± 1.2 | 1.9 ± 0.8 | 3.4 ± 0.9 | 1.7 ± 0.8 | | | | |
| 95% CI | 0.5, 5.5 | 0.3, 3.6 | 1.6, 5.2 | 0, 3.4 | | | | |
| $t_{60}$ | 2.410 | 2.305 | 3.806 | 2.027 | | | | |
| $p^a$ | 0.019* | 0.025* | < 0.001*** | 0.047* | | | | |
| Effect size (Cohen's *d*) | – | 0.587 | 0.977 | 0.509 | | | | |
| Two-way repeated measures ANOVA | | | | | | | | |
| • $F_{1,\ 60}$ | | | | 10.328 | | | | |
| • Partial eta squared | | | | 0.147 | | | | |
| • $p^b$ | | | | 0.002** | | | | |
| **Emotional status (0–100)** | | | | | | | | |
| IHMs group ($n = 31$) | 35.3 ± 3.2 | 29.9 ± 2.2 | 25.9 ± 2.3 | 23.0 ± 1.9 | 0.068 | 0.932 | 128.661 | <0.001*** |
| Placebo group ($n = 31$) | 36.2 ± 4.3 | 27.6 ± 2.6 | 24.1 ± 3.1 | 22.6 ± 3.4 | 0.067 | 0.933 | 129.721 | <0.001*** |
| Mean inter-group difference ± SE | −0.9 ± 0.9 | 2.3 ± 0.6 | 1.8 ± 0.7 | 0.4 ± 0.7 | | | | |
| 95% CI | −2.8, 0.9 | 1.1, 3.5 | 0.5, 3.2 | −0.9, 1.8 | | | | |
| $t_{60}$ | −0.983 | 3.728 | 2.665 | 0.593 | | | | |
| $p^a$ | 0.330 | < 0.001*** | 0.010* | 0.556 | | | | |
| Effect size (Cohen's *d*) | – | 0.955 | 0.659 | 0.145 | | | | |
| Two-way repeated measures ANOVA | | | | | | | | |
| • $F_{1,\ 60}$ | | | | 2.312 | | | | |
| • Partial eta-square | | | | 0.037 | | | | |
| • $p^b$ | | | | 0.134 | | | | |



 

**Table 4** (*Continued*)

| | Baseline; mean ± SD | After 1 month; mean ± SD | After 2 months; mean ± SD | After 3 months; mean ± SD | Wilks' lambda | Partial eta-square | $F_{3, 28}$ | $p^c$ |
|---|---|---|---|---|---|---|---|---|
| **Overall (0–100)** | | | | | | | | |
| IHMs group ($n = 31$) | 101.4 ± 6.3 | 87.3 ± 5.3 | 76.2 ± 6.6 | 67.9 ± 6.1 | 0.036 | 0.964 | 248.305 | <0.001*** |
| Placebo group ($n = 31$) | 100.4 ± 11.2 | 81.7 ± 6.5 | 69.1 ± 7.9 | 64.6 ± 8.6 | 0.083 | 0.917 | 103.689 | <0.001*** |
| Mean inter-group difference ± SE | 0.9 ± 2.3 | 5.5 ± 1.5 | 7.1 ± 1.8 | 3.2 ± 1.9 | | | | |
| 95% CI | −3.7, 5.5 | 2.5, 8.5 | 3.4, 10.7 | −0.6, 7.0 | | | | |
| $t_{60}$ | 0.406 | 3.661 | 3.838 | 1.702 | | | | |
| $p^a$ | 0.686 | 0.001** | < 0.001*** | 0.094 | | | | |
| Effect size (Cohen's *d*) | – | 0.944 | 0.975 | 0.443 | | | | |
| Two-way repeated measures ANOVA | | | | | | | | |
| • $F_{1, 60}$ | | | | 7.231 | | | | |
| • Partial eta-square | | | | 0.108 | | | | |
| • $p^b$ | | | | 0.009** | | | | |

Abbreviations: CI, confidence interval; IHMs, individualized homeopathic medicines; sd, standard deviation; SE, standard error.
[a]Unpaired *t*-tests; $t_{60}$: *t* score at 60 degrees of freedom; *p*, inter-group differences detected by unpaired *t*-tests.
[b]*p*: inter-group differences detected by two-way repeated measures ANOVA models.
[c]*p*: intra-group changes detected by one-way repeated measures ANOVA.
*$p < 0.05$.
**$p < 0.01$.
***$p < 0.001$.

## Medicines Used

The most frequently prescribed medicines were *Sulphur* ($n = 8$; 12.9%), *Bacillinum* ($n = 7$; 11.3%), *Thuja occidentalis* ($n = 7$; 11.3%), and *Kali arsenicum* and *Tellurium* ($n = 6$ each; 9.7%). The baseline prescription invariably started with the LM1 potency. Potencies were increased during follow-up after consensus agreement among the physicians. The highest potency used in this study was LM8 (►**Table 5**) (►**Supplementary Table 3**, available online only).

## Adverse Events

No serious adverse events occurred that could be attributed causally either to the intervention or to the comparator.

**Table 5** List of the most frequently prescribed medicines at baseline between groups ($N = 62$)

| Medicines | Total ($n = 62$); *n* (%) | IHMs group ($n = 31$); *n* (%) | Placebo group ($n = 31$); *n* (%) | *p* |
|---|---|---|---|---|
| 1. *Sulphur* | 8 (12.9) | 4 (12.9) | 4 (12.9) | 1.000 |
| 2. *Bacillinum* | 7 (11.3) | 4 (12.9) | 3 (9.7) | 0.688 |
| 3. *Thuja occidentalis* | 7 (11.3) | 2 (6.5) | 5 (16.1) | 0.229 |
| 4. *Kali arsenicum* | 6 (9.7) | 4 (12.9) | 2 (6.5) | 0.390 |
| 5. *Tellurium* | 6 (9.7) | 3 (9.7) | 3 (9.7) | 1.000 |
| 6. *Lycopodium clavatum* | 5 (8.1) | 3 (9.7) | 2 (6.5) | 0.641 |
| 7. *Natrum muriaticum* | 5 (8.1) | 2 (6.5) | 3 (9.7) | 0.641 |
| 8. *Pulsatilla nigricans* | 5 (8.1) | 1 (3.2) | 4 (12.9) | 0.162 |
| 9. *Lachesis mutus* | 4 (6.5) | 3 (9.7) | 1 (3.2) | 0.301 |
| 10. *Sepia succus* | 4 (6.5) | 3 (9.7) | 1 (3.2) | 0.301 |
| 11. *Arsenicum album* | 2 (3.2) | 1 (3.2) | 1 (3.2) | 1.000 |
| 12. *Arsenicum iodatum* | 2 (3.2) | 0 (0.0) | 2 (6.5) | – |
| 13. *Psorinum* | 1 (1.6) | 1 (3.2) | 0 (0.0) | – |

Abbreviation: IHMs, individualized homeopathic medicines;
Note: Chi-square (Yates corrected) applied; *p* less than 0.05 (two-tailed) considered as significant.

 

## Discussion

In this randomized double-blind clinical trial conducted on 62 participants suffering from TC, no inter-group differences could be detected for complete disappearance of the skin lesions, the primary outcome. However, the secondary outcomes revealed some statistically significant improvements in the IHMs group in comparison with placebos. Placebos were superior to IMHs for the first and the second months of the study in reducing the intensity of pruritus, but the situation was the opposite for the third month, in which pruritus was significantly less intense for patients taking IHMs compared with those receiving placebos. These contradictory results preclude any definitive conclusion, but several observations can be made. The apparent discrepancy might be due to the lack of effect of the highly diluted IHMs on the selected primary outcome measure, or a different set of remedies or different potencies/dosage might have been required to produce detectable effects in the defined timeframe of 3 months. However, some improvement in itching severity and Skindex-29 scores with homeopathy is consistent with the premise that homeopathy treats the whole person rather than acting on specific symptoms of disease: that is, a curative response after administration of homeopathic medicines follows Hering's law of cure – from above downward, from within outward, from more vital to less vital organs, and in reverse order of the appearance of symptoms.[26]

The strengths of the current study include enrollment of persons who may need a wide range of different individualized remedies rather than only one, thus reflecting classical homeopathy practice, which in our trial required the agreement of three homeopaths on each remedy selection to ensure high confidence in the prescription. Moreover, we used daily, flexibly dosed LM potencies to obviate homeopathic methodological concerns such as remedy anti-doting or aggravations, and included both categorical and continuous variables as trial outcome measures. LM potencies were used mainly because of their low dose, ensuring minimal chances of homeopathic aggravations, with provision for repetition on a regular basis. The most marked divergence between active and placebo treated groups occurred in the intensity of itching and quality of life. The findings are consistent with homeopathic theories of healing.[27] Within homeopathic thinking, the remedy is not chosen for the diagnosis of TC, but for the unique person who has TC. Consequently, IHMs are expected clinically to cause gradual improvements in different aspects of health before eventual disappearance of lesions.[28]

An intervention period of 3 months, while choosing a strict dichotomous variable as the primary outcome measure and adhering to LM potencies only, may be considered as important study limitations. However, extending the intervention period in a placebo-controlled trial would have raised ethical concerns. The superiority of placebos against IHMs in reducing the intensity of pruritus in the first 2 months may be explained by the fact that IHMs can take some time to initiate their action in a chronic disease like TC. It probably necessitates observations for a longer period of time. Choice of the dichotomous outcome was based on prior assumptions and the experience of the investigators; however, that approach did not seem to work optimally. Time to disappearance of TC lesions after administering IHMs in centesimal potencies would be worth pursuing in future studies.

The trial's secondary outcome findings were similar to those of the observational study by Gupta et al[16]: both revealed promising effects of IHMs in TC, though the latter did not apply any validated outcome measures or randomized design. Another observational study used only *Bacillinum*,[17] which is contrary to the practice of classical homeopathy, and the outcome measures were subjective only. A case report on tinea using *Sepia* showed improvement,[18] but again validated outcomes were not used. In our trial, *Thuja occidentalis* was one of the most frequently prescribed homeopathic medicines, supported by an *in vitro* study using *Thuja occidentalis* on keratinophilic fungi.[19]

Experts have held different "miasms" responsible for tinea infection—"sycosis" by Allen,[29] "tubercular" by Burnett,[30] and "psora" and "latent psora" by Hahnemann[31]; but all concurred that treating tinea lesions with external applications gives rise to several unfavorable consequences, citing many instances. Burnett tagged the condition as "sub-tuberculosis" and recommended its treatment with the "pathologic similimum" *Bacillinum* in high potency and administered infrequently. While analyzing miasmatic dominance in the enrolled cases in our trial, the findings were as follows: predominantly psoric (61.3%), tubercular (23.2%), sycotic (13.4%) and syphilitic (2.1%). Douglass suggested "lymphatic temperament" as a predisposing condition of tinea.[32] Lilienthal advocated *Calcarea carbonicum*, *Sepia officinalis* and *Tellurium* as the most frequently indicated remedies for tinea infections.[33] Raue suggested several remedies—*Calcarea carbonica*, *Hydrastis canadensis*, *Natrum carbonicum*, *Natrum muriaticum*, *Sepia succus*, *Tellurium* and *Chrysophanic acid*[34]; several of these remedies were prescribed in our trial as well. Different authors like Kippax,[35] Dearborn,[36] Bernstein[37] and Morrison[38] have suggested different groups of remedies in treatment of TC. Homeopathic repertories represent the condition under different rubrics, such as "ringworm",[39] "herpes circinatus",[40–43] "trichophytosis"[40] and "tetters",[44] with a very similar group of medicines as were used in our trial.

Thus, robust trials on larger samples and for longer periods of time are now indicated, especially in view of emerging basic scientific evidence that homeopathic remedies have physical–chemical properties that differ from those of placebos.[45,46] We recommend that a confirmatory diagnosis of dermatophytosis, from skin scrapings examined microscopically on a 10–20% potassium hydroxide mount, should be incorporated in future trials.[47]

## Conclusion

In this randomized double-blind clinical trial, conducted on 62 individuals suffering from TC, inter-group differences could not be detected on the primary outcome after 3 months of homeopathic intervention; however, secondary outcomes

 

included some statistically significant improvement in the IHMs group in comparison with placebos. Independent, more robust, trials are warranted to inform more rigorous conclusions about the clinical effect of IHMs on TC.

Highlights

- A double-blind, randomized, placebo-controlled trial of individualized homeopathic medicines in LM potencies was conducted on 62 patients suffering from TC.
- Though no inter-group differences could be detected on the primary outcome measure, the secondary outcomes revealed some significantly better effects of homeopathic medicines than placebo.
- *Sulphur*, *Bacillinum* and *Thuja occidentalis* were the most frequently prescribed medicines.

## Supplementary material

**Supplementary Table 1.** CONSORT 2010 checklist of information to include when reporting a randomised trial.
**Supplementary Table 2.** RedHot checklist of information to include when reporting randomised trials of homeopathy.
**Supplementary Table 3.** Indications of the prescribed medicines.

Authors' Contributions

B.L., S.P., A.C. and N.K.S. contributed toward concept, literature search, and preparation of the article; B.L., S. P., A.C., A.K., D.B., P.B., S.D., and S.P. contributed toward the clinical study and data acquisition; M.K. and S.S. developed the concept and did the study design, data interpretation, statistical analysis, and preparation of the article. All the authors reviewed and approved the final article.

Author Disclosure Statement

None declared.

Conflict of Interest

None declared.

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