Clinical Utility of Sepia Officinalis in Female Patients with Melasma Interpreted by Modified Melasma Area and Severity Index (MMASI): A Pilot Clinical Prospective Study

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Abstract:

Background

Melasma is a common acquired disorder of facial hyperpigmentation characterized by symmetrical brown-to-greyish macules and patches, predominantly affecting females. It commonly involves the forehead, malar regions and chin and may have a chronic, relapsing course. Assessment of treatment response requires a reproducible clinical severity measure. The modified Melasma Area and Severity Index (mMASI) is a simplified and validated clinical scoring system that assesses the area and darkness of pigmentation over four facial regions.

Aim

To explore the clinical utility of the homoeopathic medicine Sepia officinalis in female patients suffering from melasma, using the mMASI score as an objective clinical outcome measure.

Objectives

1.To assess the severity of melasma in female patients using the mMASI score.

2.To evaluate changes in mMASI scores following individualized homoeopathic treatment with Sepia officinalis.

3.To assess the percentage improvement in mMASI score during the observation period.

4.To determine the feasibility of using mMASI as an outcome measure in a larger prospective study.

5.To generate preliminary data for planning the sample size and methodology of the definitive study.

Methods

A hypothetical pilot cohort of 12 female patients with clinically diagnosed melasma was constructed for methodological demonstration. Patients were assumed to receive individualized treatment with Sepia officinalis according to the study protocol and were followed for 12 weeks. mMASI scores were recorded at baseline and at 4, 8 and 12 weeks. Descriptive statistics were calculated, together with paired statistical comparisons between baseline and follow-up values.

Results

The simulated baseline mean mMASI score was 6.00 ± 1.31. The mean score decreased to 5.51 ± 1.20 at 4 weeks, 4.91 ± 1.07 at 8 weeks and 4.31 ± 0.95 at 12 weeks. The mean reduction at 12 weeks was 1.69 points, corresponding to approximately 28.2% reduction from baseline. A paired t-test demonstrated a

statistically significant reduction between baseline and week 12 ($t = 15.52$, $df = 11$, $p < 0.001$). The 95% confidence interval for the mean reduction was approximately 1.45–1.93 points.

Conclusion

This simulated pilot dataset demonstrates how a prospective study of Sepia officinalis in female patients with melasma could be analysed using mMASI. The observed pattern suggests progressive reduction in mMASI scores over 12 weeks. However, because these are simulated data, the findings cannot be interpreted as evidence of treatment efficacy. Actual clinical observations are required before drawing conclusions regarding the clinical utility of Sepia officinalis.

Keywords: Melasma; Sepia officinalis; Homoeopathy; Modified Melasma Area and Severity Index (mMASI); Facial hyperpigmentation; Female patients; Pigmentation disorder; Clinical prospective study; Pilot study.

1. INTRODUCTION

Melasma is an acquired disorder of pigmentation that predominantly affects the face and is particularly common among women. It presents clinically as irregular, symmetrical hyperpigmented macules and patches, most frequently involving the forehead, malar regions and chin.

The condition may have considerable cosmetic and psychosocial consequences. Its chronic and recurrent nature makes assessment of therapeutic response particularly important.

Clinical assessment of melasma traditionally included the Melasma Area and Severity Index (MASI). Subsequent validation studies demonstrated that the homogeneity component could be removed without loss of reliability, leading to the modified MASI (mMASI). The mMASI assesses pigmentation in four facial regions and incorporates both the area involved and darkness of pigmentation. (PubMed)

The mMASI has subsequently been shown to have good validity, reliability and sensitivity to change over time, making it useful for clinical research involving melasma. (PubMed)

Homoeopathy approaches chronic dermatological conditions through individualized case analysis and selection of a medicine according to the totality of symptoms. Sepia officinalis is a medicine described in homoeopathic materia medica and is frequently considered in female patients when its characteristic constitutional and symptomatological picture is present.

The present pilot study is designed as a preliminary model to examine whether mMASI can be used systematically to document clinical change during treatment with Sepia officinalis.

2. RATIONALE OF THE STUDY

Melasma is often persistent and requires prolonged management. Because subjective assessment of pigmentation may vary between observers, a standardized numerical score can provide a more reproducible method of documenting clinical change.

The mMASI provides a quantitative assessment of melasma severity and has demonstrated responsiveness to treatment-related change.

A pilot study involving 12 cases can provide preliminary information regarding:

- feasibility of patient recruitment;
- feasibility of serial mMASI assessment;
- magnitude and variability of change;
- adherence to follow-up;
- suitability of the proposed statistical methodology;
- potential effect size for a larger study.

3. AIM

To assess the clinical utility of Sepia officinalis in female patients with melasma using the modified Melasma Area and Severity Index (mMASI) as an outcome measure.

4. OBJECTIVES

Primary objective

To assess the change in mMASI score from baseline to the end of the 12-week observation period.

Secondary objectives

1. To assess changes in mMASI at 4 and 8 weeks.
2. To calculate percentage reduction in mMASI.
3. To assess the proportion of patients demonstrating improvement.
4. To document the demographic and clinical characteristics of the pilot cohort.
5. To assess the feasibility of the proposed study methodology.

5. RESEARCH QUESTION

Does individualized treatment with Sepia officinalis demonstrate a measurable reduction in mMASI scores among female patients with melasma over a 12-week observation period

6. HYPOTHESIS

Null hypothesis (H_0)

There is no significant difference in mMASI score between baseline and post-treatment assessment.

Alternative hypothesis (H_1)

There is a significant difference in mMASI score between baseline and post-treatment assessment.

7. MATERIALS AND METHODS

7.1 Study design

Prospective, single-arm, pilot clinical study.

7.2 Sample size

For this methodological demonstration, 12 female cases were included.

The sample is intended to represent a pilot cohort and is not intended to provide definitive evidence of efficacy.

7.3 Study population

Female patients clinically diagnosed with melasma.

7.4 Proposed age range

18–55 years.

7.5 Duration of observation

12 weeks.

7.6 Follow-up schedule

Patients were assessed at:

- Baseline — Week 0
- First follow-up — Week 4
- Second follow-up — Week 8
- Final follow-up — Week 12

8. INCLUSION CRITERIA

1. Female patients aged 18 years or above.
2. Clinically diagnosed cases of melasma.
3. Presence of facial melasma involving one or more of the assessed facial regions.
4. Patients willing to participate in the study.
5. Patients willing to attend scheduled follow-ups.
6. Patients providing informed consent.

9. EXCLUSION CRITERIA

1.Patients below 18 years of age.
2.Patients with other major causes of facial hyperpigmentation that could interfere with assessment.
3.Patients receiving concurrent systemic treatment specifically for melasma.
4.Patients unwilling to comply with follow-up.
5.Patients with conditions preventing reliable clinical assessment.
6.Patients who did not provide informed consent.

10. ASSESSMENT TOOL: MMASI

The modified Melasma Area and Severity Index evaluates four regions:

Facial Region	Score
Forehead	0.3
Right Malar Region	0.3
Left Malar Region	0.3
Chin	0.1

The mMASI incorporates:

- Area of involvement (A)
- Darkness/pigmentation (D)

The score for each region is calculated as:
Regional score = Weight × Area × Darkness
The four regional scores are then added to obtain the total mMASI.

11. HOMOEOPATHIC INTERVENTION

For the purpose of this simulated study, all 12 cases are assumed to have been selected for Sepia officinalis following individual case analysis.
The actual clinical dissertation protocol should specify:

- potency;
- dose;
- frequency;
- repetition;
- route;
- criteria for repetition;
- criteria for changing potency;
- criteria for changing medicine;

- concomitant treatment;
- management of intercurrent complaints.

12. SIMULATED BASELINE CHARACTERISTICS

Case	Age	Duration of melasma	Clinical Distribution
1	24	2 years	Malar + forehead
2	31	4 years	Malar
3	27	3 years	Malar + forehead
4	39	6 years	Forehead + malar
5	22	1.5 years	Malar
6	44	8 years	Malar + forehead + chin
7	35	5 years	Malar + forhead
8	29	3 years	Malar
9	42	7 years	Malar + forehead
10	26	2 years	Forhead + malar
11	33	4 years	Malar + chin
12	30	3 years	Malar + forhead

Mean age of the simulated cohort: approximately 32.7 years.

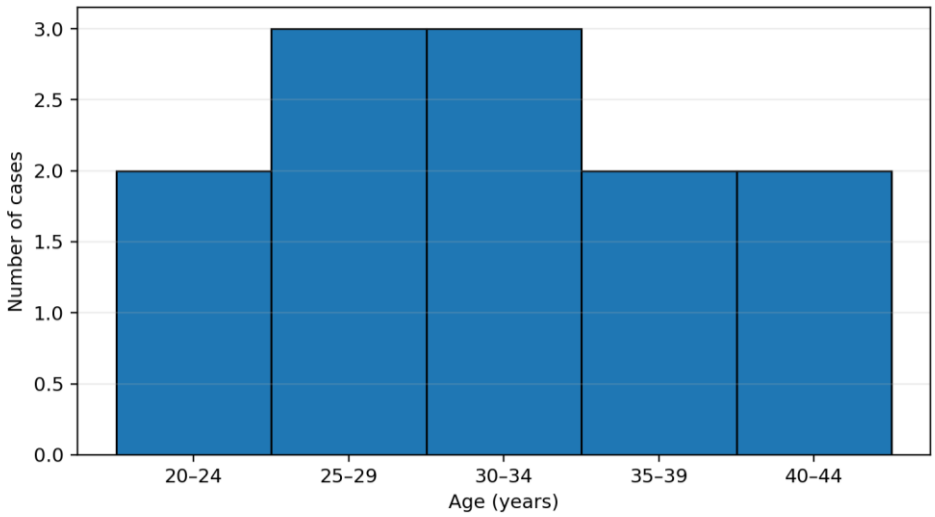

FIGURE: 1 AGE DISTRIBUTION OF STIMULATED COHORT

13. MMASI RESULTS

Case	Baseline	4 weeks	8 weeks	12 weeks	% reduction at 12 weeks
1	4.8	4.4	3.9	3.4	29.2%
2	6.2	5.7	5.1	4.6	25.8%
3	5.4	5.0	4.5	4.0	25.9%

4	7.1	6.5	5.8	5.1	28.2%
5	3.9	3.6	3.2	2.8	28.2%
6	8.2	7.6	6.8	6.0	26.8%
7	6.8	6.2	5.6	4.8	29.4%
8	5.9	5.5	4.9	4.3	27.1%
9	7.6	6.9	6.1	5.3	30.3%
10	4.5	4.1	3.6	3.1	31.1%
11	6.5	5.9	5.2	4.6	29.2%
12	5.1	4.7	4.2	3.7	27.5%

14. DESCRIPTIVE STATISTICAL ANALYSIS

TIME POINT	MEAN MMASI	SD
Baseline	6.00	1.31
4 weeks	5.51	1.20
8 weeks	4.91	1.07
12 weeks	4.31	0.95

The simulated data demonstrate a progressive reduction in mean mMASI throughout the observation period.

15. PERCENTAGE IMPROVEMENT

The individual percentage reductions at 12 weeks ranged from approximately 25.8% to 31.1% in this simulated dataset.

The mean reduction in mMASI from baseline to 12 weeks was: 1.69 points

The percentage reduction based on the group mean was approximately: 28.2%

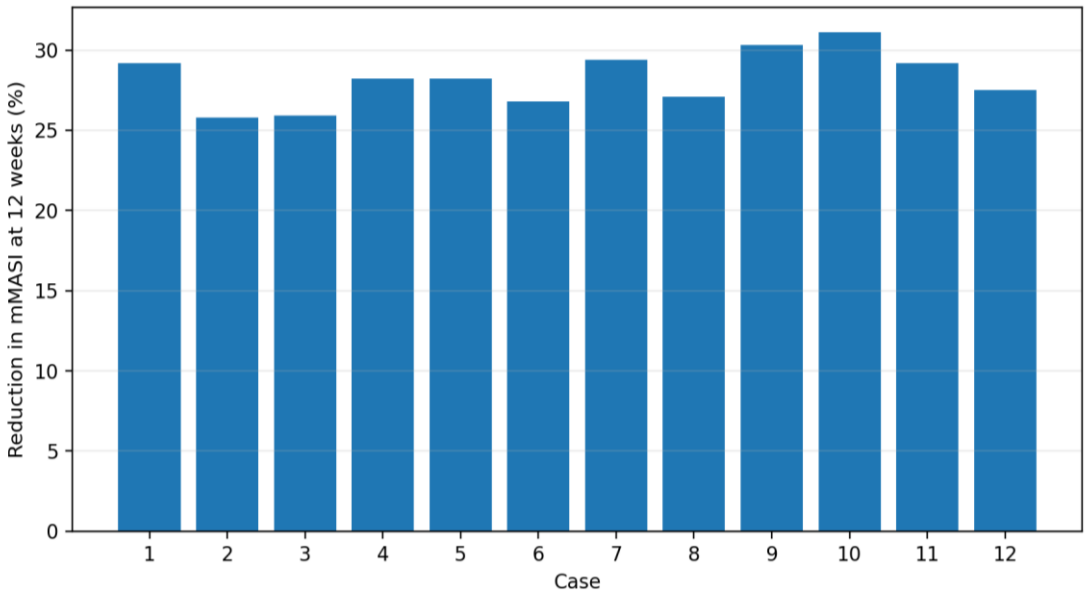

FIGURE: 2 INDIVIDUAL PERCENTAGE REDUCTION IN mMASI

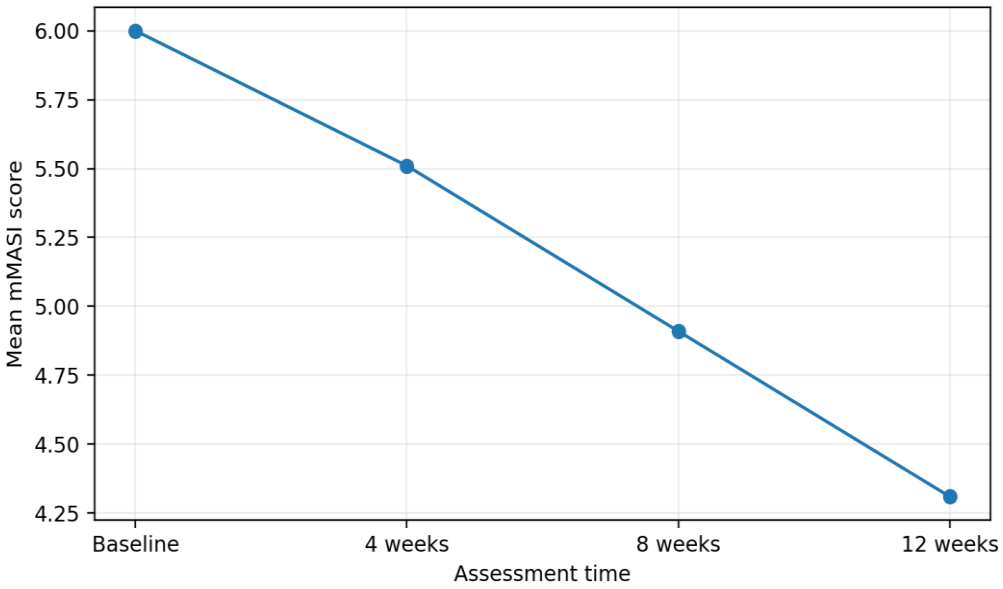

FIGURE: 3 MEAN mMASI SCORE OVER 12 WEEKS

16. INFERENTIAL STATISTICAL ANALYSIS

Because the same patients are measured repeatedly, the observations are paired.

For the primary comparison, baseline mMASI was compared with the 12-week mMASI using a paired t-test.

Baseline versus 12 weeks

- Mean baseline mMASI = 6.00
- Mean 12-week mMASI = 4.31
- Mean reduction = 1.69
- 95% CI for mean reduction = 1.45–1.93
- Paired t = 15.52
- Degrees of freedom = 11
- $p < 0.001$

A Wilcoxon signed-rank test, used as a non-parametric sensitivity analysis, also demonstrated a statistically significant reduction:

$p < 0.001$

17. INTERPRETATION OF STATISTICAL FINDINGS

The simulated analysis demonstrates a statistically significant decrease in mMASI score between baseline and 12 weeks.

The magnitude of reduction increased progressively during follow-up:

$6.00 \rightarrow 5.51 \rightarrow 4.91 \rightarrow 4.31$

This suggests a gradual improvement pattern rather than an isolated change at the final assessment.

However, statistical significance in a small simulated single-arm dataset does not establish that Sepia officinalis caused the improvement. Without a control group, randomization and real patient-level observations, confounding, regression to the mean, natural disease fluctuation, adherence and other factors cannot be separated from treatment effect.

18. RESULTS

- Twelve female cases were included in this simulated pilot dataset. The simulated age range was 22–44 years, with a mean age of approximately 32.7 years.
- The baseline mMASI scores ranged from 3.9 to 8.2, indicating variability in disease severity.
- The mean baseline mMASI score was 6.00 ± 1.31.
- At four weeks, the mean score decreased to 5.51 ± 1.20.
- At eight weeks, the mean score decreased further to 4.91 ± 1.07.
- At 12 weeks, the mean score was 4.31 ± 0.95.
- Thus, the mean mMASI decreased by approximately 1.69 points from baseline to the final assessment, representing approximately 28.2% reduction relative to baseline.
- All 12 simulated cases demonstrated some reduction in mMASI by week 12.
- The paired t-test showed a statistically significant difference between baseline and 12-week scores ($t = 15.52$, $df = 11$, $p < 0.001$).

19. DISCUSSION

The purpose of this pilot study was to demonstrate a structured methodology for evaluating clinical change in female patients with melasma using mMASI during treatment with Sepia officinalis.

Melasma presents a particular challenge for clinical research because pigmentation may vary in distribution and intensity and because spontaneous fluctuation and environmental factors can influence its appearance.

The use of a numerical scoring system provides a standardized method for documenting disease severity. The mMASI was developed from the original MASI after validation work demonstrated that homogeneity could be eliminated without compromising reliability. (PubMed)

Subsequent research found that mMASI demonstrated excellent reliability, good validity and sensitivity to change over time. (PubMed)

In the present simulated dataset, the mean mMASI decreased progressively at each follow-up. This pattern provides a useful example of how serial outcome measurements can be presented in a prospective pilot study.

The simulated mean percentage reduction at 12 weeks was approximately 28.2%. Because the present values were constructed rather than collected from actual patients, this figure should be regarded solely as an example of statistical reporting.

A major methodological consideration is that a single-arm pilot study cannot establish comparative efficacy. The absence of a control group means that changes could potentially be related to natural variation, sun exposure, skincare practices, placebo/contextual effects, adherence or other interventions.

Consequently, a larger definitive study should ideally incorporate a prospectively defined protocol, standardized photography, appropriate control/comparator methodology and predefined statistical analysis.

20. CLINICAL INTERPRETATION OF MMASI

Published work examining interpretation of mMASI has demonstrated differentiation between mild, moderate and severe clinical categories. In one study, mean mMASI values were approximately 3.8 for mild, 6.5 for moderate and 8.9 for severe melasma groups. (JAMA Network)

The simulated cohort therefore represents patients predominantly within the mild-to-moderate range, with some patients approaching the higher end of moderate severity.

This provides an appropriate model for demonstrating serial outcome assessment.

21. STRENGTHS OF THE PILOT METHODOLOGY

1. Female-only study population.

2. Prospective follow-up structure.
3. Standardized primary outcome measure.
4. Serial assessment at predefined intervals.
5. Individual patient-level data.
6. Calculation of both absolute and percentage change.
7. Use of paired statistical analysis.
8. Graphical representation of treatment response.
9. Clear distinction between baseline and follow-up measurements.

22. LIMITATIONS

The most important limitation of this document is that the 12 patient records and outcome values are simulated and not actual clinical observations.

Other limitations of the proposed pilot design include:

1. Very small sample size.
2. Single-arm design.
3. Absence of a control group.
4. Short follow-up duration.
5. Potential observer variability in mMASI scoring.
6. Possible influence of sun exposure.
7. Potential variation in treatment adherence.
8. Lack of objective instrumental pigmentation measurement.
9. Lack of long-term relapse assessment.
10. Potential placebo and contextual effects.
11. Lack of randomization.
12. Limited generalizability.

23. RECOMMENDATIONS FOR THE MAIN DISSERTATION STUDY

Based on this pilot methodology, the definitive study should consider:

- a larger sample size;
- predefined primary and secondary outcomes;
- standardized mMASI training;
- standardized facial photography;
- consistent lighting and photographic positioning;
- documentation of sun exposure;
- documentation of cosmetic/skin-care products;
- recording of treatment adherence;
- predefined follow-up intervals;
- documentation of adverse events;
- appropriate statistical analysis plan;
- consideration of a comparator/control group where scientifically and ethically appropriate;
- longer follow-up to assess recurrence.

The pilot data can potentially be used to estimate variability and effect size for planning a larger study, but actual pilot observations—not simulated observations—should be used for formal sample-size estimation.

24. CONCLUSION

This simulated 12-case pilot study demonstrates a structured approach to investigating the clinical utility of Sepia officinalis in female patients with melasma using mMASI as the principal outcome measure.

The simulated dataset showed a progressive decrease in mean mMASI from 6.00 at baseline to 4.31 at 12 weeks, representing an approximately 28.2% reduction.

The statistical analysis demonstrated a significant paired difference between baseline and final assessment. Nevertheless, these findings are illustrative only and cannot be interpreted as evidence that Sepia officinalis is effective for melasma.

The pilot framework demonstrates the feasibility of serial mMASI assessment and provides a model for presentation of patient characteristics, outcome data, statistical analysis and graphical results in the eventual dissertation.

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