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Research Protocol

Ayurveda Section

Pharmaceutico Analytical and Clinical Evaluation of Modified Dosage Forms (*Lepa guti*) of *Varun Twak* Lepa and *Krushnatiladi Lepa* in *Vyanga* (Melasma): A Research Protocol for Randomised Controlled Trial

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ABSTRACT

Introduction: *Vyanga*, also referred to as melasma, is a prevalent disorder characterised by skin discoloration on the face. According to Ayurveda, Acharya Sushruta and Vagbhata described *Vyanga* as one of the *Kshudra Rogas*. Melasma is a related pigmentary disease characterised by symmetrical hyperpigmented macules on the face. *Vyanga* has been treated in Ayurveda through *antah-parimarjan*a (internal therapy) and *bahi-parimarjana chikitsa* (external therapy), respectively.

Need of the Study: *Vyanga*, also known as melasma, is not a life threatening condition, but it can significantly impact an individual's appearance. Therefore, it is essential to explore effective management options. Modern treatments typically involve the use of topical steroids and antiseptics, which can lead to various side-effects such as irritation and rashes. In Ayurveda, several *Shodhana* (purification) and *Shamana* (alleviating) therapies are recommended for managing *Vyanga*. However, there are limitations regarding the use of *Shodhana* therapies in pregnant women, making *Shamana* therapies more preferable in such cases. *Krushnatiladi Lepa*, described in *Raja Martanda*, is noted for its properties, including *Kusthaghna* (antidermatological), *Kandughna* (anti-itch), *Raktashodhaka* (blood-purifying), *Twak Prasadaka* (skin-nourishing) and *Varnyakara* (skin-toning). Despite its potential benefits, no studies have assessed its efficacy in treating *Vyanga*.

Aim: To conduct a pharmaceutical and analytical evaluation of modified dosage forms (*Lepa guti*) of *Krushnatiladi Lepa* and *Varun Twak Lepa*, as well as, to assess their clinical efficacy in managing *Vyanga* (melasma).

Materials and Methods: A randomised double-blind, controlled clinical trial will be conducted Department of Rasa Shastra and *Bhaishajya Kalpana*, Mahatma Gandhi Ayurved College and Research Centre (MGACH and RC), Salod (H), Wardha, Maharashtra, India, from August 2024 to August 2025. A total of 62 patients aged between 18 years and 50 years with typical symptoms of *Vyanga* (melasma) will be selected from the Department of Kayachikitsa Outpatient Department (OPD) and Inpatient Department (IPD) and peripheral camps and divided equally into two groups. In group A (control group), *Varun Twak Lepa guti* will be administered for local application with cow's milk once a day, whereas in group B (interventional group), *Krushnatiladi Lepa guti* for local application with cow's milk once a day will be given. The parameters assessed will include *Shyavata* (discoloration), *Parush Sparsha* (dryness), *Daha* (burning sensation), *Kandu* (itching), *Snigdhata* (oiliness), size of patches, Von Luschan's colour scale, and Melasma Severity Index (MSI) score. For statistical analysis, paired and unpaired t-tests will be applied for intragroup and intergroup comparison. A p-value of <0.05 will be considered statistically significant.

Keywords: *Antah-parimarjan*, *Bahi-parimarjana*, *Chikitsa*, *Kshudra roga*, *Shodhan*, Melasma severity index

INTRODUCTION

Ayurveda, an ancient science, has significantly evolved in India. It is founded on traditional wisdom, clinical experience and scientific experimentation. This comprehensive natural healthcare and research system focuses on disease prevention and treatment while assisting in the maintenance of good health, including skin diseases. Ayurveda is evolving in the context of modern scientific, technological and medical considerations. Ayurveda has investigated skin issues, including their aetiology and treatment [1].

Rasashastra and *Bhaishajya Kalpana* (Alchemy and Pharmacy in India) are independent branches of Ayurveda. Ayurveda's weapon, Bhaishajya, is a natural resource provided by Mother Nature to combat the spread of dangerous diseases. The five basic preparations mentioned in Ayurveda compendia take various forms of medicine [2]. The use of these five basic preparations was severely restricted due to the medications' short shelf life, insufficient testing processes, and difficulty in usage. These aspects have contributed to the development of ideas and the generation of different formulations that can be made by modifying the five primary preparations [3].

Having a smooth and glowing complexion enhances a person's beauty and boosts their self-esteem. *Vyanga* is a disease that damages the skin and interrupts the beauty of a naturally radiant face [4]. According to the perspectives of Acharya Sushruta and Vagbhata, *Vyanga* is considered a Kshudra roga. Thin, painless, bluish-black patches on the face are one of its distinctive characteristics. The condition is caused by the vitiation of the *Vata*, *Pitta*, and *Rakta doshas* [5].

Vyanga shows similarities to the clinical manifestations of cholasma and melasma. Present studies indicate that this condition produces hyperpigmented areas on the face [6,7]. Melasma produces hyperpigmented patches, usually appearing on areas such as the cheeks, nose, forehead, and upper and lower lips, which are exposed to the sun. Melasma has been believed to be a consequence of exposure to ultraviolet radiation from sunlight [8].

Studies have suggested that it is the most prevalent pigmented disorder among Indians. Dermatology clinics in Southeast Asia report a prevalence between 0.25% and 4%, with an average female-to-male ratio of 4:1. Melasma can affect 50-70%

of pregnant women and usually manifests in the postpartum period [9,10].

Complete knowledge regarding *Lepa Kalpana* has not been consolidated into a single chapter of Ayurvedic literature. As a result, understanding the theory of *Lepa Kalpana* requires reliance on various vague references. Numerous authors have elaborated on different treatment modalities for melasma. One of these treatments, *Lepa*, directly targets the lesions, making it more effective. Various herbal drugs and their active constituents are beneficial in managing melasma and may help lighten the skin's darker areas. *Varun Twak Lepa* is a topical herbal formulation used in Ayurveda for managing *Vyanga*, a condition characterised by hyperpigmented macules on the face, akin to melasma. This formulation typically contains *Varun* (Crataeva nurvala) along with other herbal ingredients known for their skin benefits [10-12].

Krushnatiladi Lepa includes some of the fundamental herbal preparations described in Ayurvedic literature for treating *Vyanga*. *Lepa Guti*, a modified dosage form, can be easily applied externally [13]. There is limited research on the efficacy of *Krushnatiladi Lepa* preparations in the market for treating melasma. Therefore, the present study will be aimed to conduct a pharmaceutical-analytical and comparative evaluation of the modified dosage forms (*Lepa guti*) of *Varun Twak Lepa* and *Krushnatiladi Lepa* in the treatment of *Vyanga* (melasma).

Primary objectives:

1. To procure and prepare authenticated drugs of *Krushnatiladi Lepa guti* and *Varun Twak Lepa guti*.
2. To assess the quality control parameters of *Krushnatiladi Lepa guti* and *Varun Twak Lepa guti*.

Secondary objective:

1. To evaluate and compare the efficacy of *Krushnatiladi Lepa guti* and *Varun Twak Lepa guti* in *Vyanga* (melasma).

Null hypothesis (H_0): The modified dosage form (*Lepa guti*) of *Krushnatiladi Lepa* will be less effective than or equally effective as *Varun Twak Lepa* in *Vyanga*.

Alternate hypothesis (H_1): The modified dosage form (*Lepa guti*) of *Krushnatiladi Lepa* will be more effective than *Varun Twak Lepa* in *Vyanga*.

REVIEW OF LITERATURE

The Ayurvedic approach to managing *Vyanga*, a condition characterised by skin discoloration and pigmentation, incorporates a variety of therapeutic interventions aimed at restoring the skin's natural tone and health. Key components of this management strategy include:

***Nidanparivarjan*:** This initial step focuses on the identification and removal of the underlying causes of *Vyanga*, which may include dietary factors, environmental influences, or lifestyle habits.

***Shodhan chikitsa*:** This purification therapy encompasses several techniques designed to cleanse the body of toxins. It includes:

- ***Siravedhana*:** A method of bloodletting that helps detoxify the bloodstream and improve circulation.
- ***Abhyanga*:** An Ayurvedic oil massage that nurtures and nourishes the skin while promoting relaxation.
- ***Nasya*:** This therapy involves administering medicinal oils or powders through the nasal passages to enhance respiratory health and systemic balance.

***Shamana chikitsa*:** This palliative treatment focuses on alleviating symptoms and restoring balance to the body without removing doshas. It utilises herbal remedies and lifestyle modifications to provide relief.

***Lepa*:** The application of herbal pastes or formulations directly to the affected areas of the skin. This topical treatment aids in healing and restoring skin colour.

***Udvartana*:** A therapeutic massage using herbal powders that helps improve circulation, exfoliate the skin and reduce excess fat [14].

Research studies have highlighted the efficacy of specific herbal formulations in the management of *Vyanga*:

A study published by Patil YR and Passalwad VP investigated the synergistic effects of *Arjuna* (Terminalia arjuna) and *Manjistha* (Rubia cordifolia) *Lepa*. Both herbs possess *pitta-shamak* properties, helping to cool the skin and *rakta-prasadak* qualities that purify the blood. Their combined use is believed to be effective in restoring the skin's natural colour and alleviating the symptoms of *twak vaivaryata* (skin discoloration) [15].

A study conducted by Chavan VM and Nimbalkar M, focused on the usage of Eladi *Lepa* and *Raktapachak Kwath* in the treatment of *Vyanga*. Both formulations are effective due to their properties as *raktaprasadak* (blood-purifying), *twaka-prasadak* (skin-enhancing) and *varnyakara* (colour-restoring). Together, they work to cleanse the blood, calm the aggravated doshas, and restore the skin's natural tone, showcasing the holistic benefits of Ayurvedic treatment in dermatological conditions [16].

Mundhe SS and Ade V investigated the effectiveness of *Varun Twak Lepa* in managing *Vyanga*; 40 patients from the OPD and IPD of Kayachikitsa were included. The study found significant results on the 20th and 30th days in all three types of melasma, with more significant results in the epidermal type [10]. Overall, the Ayurvedic management of *Vyanga* employs a comprehensive and multifaceted approach that not only addresses the symptoms but also promotes overall skin health and vitality.

MATERIALS AND METHODS

A randomised double-blind standard controlled clinical trial will be conducted Department of Rasa Shastra and *Bhaishajya Kalpana*, MGACH and RC, Salod (H), Wardha, Maharashtra, India, from August 2024 to August 2025. Sixty-two patients between the ages of 18 years and 50 years of either gender with typical symptoms of *Vyanga* (Melasma) will be selected from the Department of Kayachikitsa OPD and IPD and peripheral camps. Informed consent will be obtained from all participants before conducting the study. The study has been registered on the Clinical Trials Registry India (CTRI) website (CTRI/2023/12/060971) and ethical clearance has been obtained from the Institute Ethical Committee (IEC) (MGACHRC/IEC/Sep-2023/745).

Inclusion criteria:

1. Patients willing to participate in the study and ready to provide written informed consent.
2. Patients from the age group of 18-50 years will be selected for the study.
3. Patients irrespective of gender, caste, religion, occupation and economic status will be selected for the study.
4. Patients with a chronicity of less than five years will be selected.
5. Patients exhibiting clinical features of *Vyanga* as per Ayurvedic classics will be included [2].
6. Patients with a Von Luschan's chromatic scale ranging from 17 to 30 will be included [17].

Exclusion criteria:

1. Patients with a past and present history of any skin diseases, e.g., psoriasis, dermatitis, vitiligo, etc.
2. Individuals suffering from any bacterial, fungal, or viral infections who are currently taking antibiotics, antifungal, or antiviral drugs.
3. Patients with rashes or open wounds on the face.
4. Patients with a history of hyperpigmentation since birth, such as Nevus of Ota, tumours like malignant melanoma, or drug-induced pigmentation changes.

5. Patients suffering from systemic disorders such as renal failure or hepatic disorders.
6. Patients with known cases of endocrine disorders, such as Addison's disease or Cushing's disease.

Sample size calculation: The sample size is determined using the formula for the mean difference:

$$n1=n2=2\frac{(Z_\alpha+Z_\beta)^2\sigma^2}{(\delta)^2}$$

Z_α=1.96, α=Type I error at 5% at both sides two tailed

Z_β=1.28, =Power at 90%

Primary variable effect on MSI:

Change in MSI score Mean difference (δ)±SD (δ) in Melasma

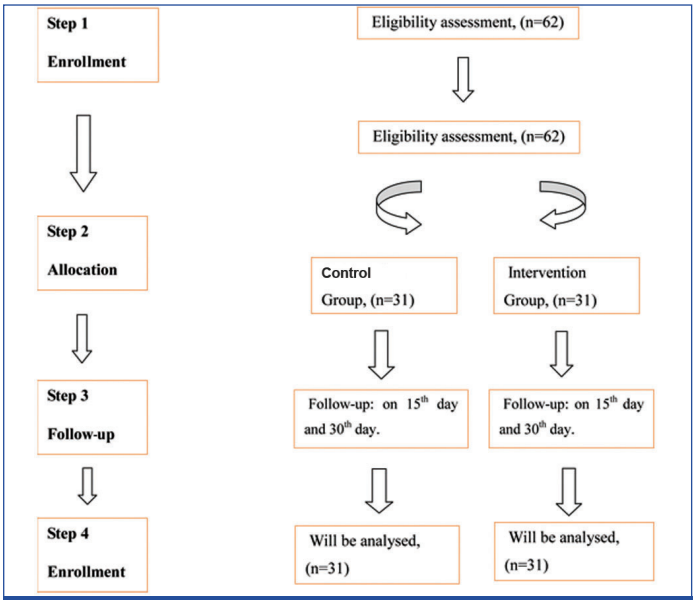
Severity Index (MSI) score for *Varun Twak Lepa*=7.55±8.53 [10];

$$\text{Sample size N= } n1=n2=2\frac{(1.96+1.28)^2(8.53)^2}{(7.55)^2}=28 \text{ per group}$$

Taking 10% of dropouts=3

The required total sample size for each group is 28+3=31 per group.

Randomisation will be done using a computer-generated table method. The subject's enrollment and allocation criteria is illustrated in [Table/Fig-1].



[Table/Fig-1]: Treatment period and follow-up period.

The research drugs *Krushna Tila, Krushna Jeeraka, Shweta Jeeraka, Shweta Sarshapa* and *Varun Twak* will be procured from reliable sources. The Taxonomist/Dravyaguna Department will authenticate the drugs. The central research lab of Datta Meghe Institute of Higher Education and Research (DMIHER), Wardha, and MGACH and RC, Wardha, Maharashtra, India, analytical labs, or Active Pharmaceutical Ingredient (API), will standardise the raw drugs.

The ingredients and properties of *Varun Twak Lepa guti* are listed in [Table/Fig-2] [18], while the ingredients of *Krushnatiladi Lepa guti* include *Krushna Tila, Krushna Jeeraka, Shweta Jeeraka* and *Shweta Sarshap*. The properties, along with the names, are enlisted in [Table/Fig-3] [18].

Classical method of preparation of *Varun Twak Lepa Guti* and *Krushnatiladi Lepa Guti:*

A) Preparation of *Varun Twak Lepa Guti*:

a) The *raw drug* (*Varun*) will be taken in the required quantity and triturated in a grinder separately before being sieved through an 80 mesh. The fine powder of *Varun* will be taken and mixed homogeneously. Wet levigation will be done with *Varun Kwatha* for three days, after which the *Lepa guti* will be prepared and stored in an airtight, wide-mouthed container for further therapeutic use [19].

b) **Preparation of *Krushnatiladi Lepa Guti*:**

All raw drugs (*Krushna Tila, Krushna Jeeraka, Shweta Jeeraka* and *Shweta Sarshapa*) will be taken in equal quantities and triturated in a grinder separately before being sieved through an 80 mesh. Fine powders of all drugs will be combined in equal proportion and mixed homogeneously. Bhavana will be given with the *Kwath* of *Krushna Tila*, *Krushna Jeeraka*, *Shweta Jeeraka*, and Shweta Sarshap for three hours. The *Lepa guti* will then be prepared and stored in an airtight container for further therapeutic use.

Primary outcomes: analytical study (physico-chemical parameters)

Analytical parameters of *varun twak lepa guti* and *krushnatiladi lepa guti*:

A. Organoleptic parameters:

1. *Sparsh* (Touch)
2. *Rupa* (Appearance)
3. *Gandha* (odour)

B. Physicochemical parameters:

1. Loss on drying at 105°C (%): A shallow petri plate will be filled evenly with 10 grams of the chemical. Then, the dish will be placed in a desiccator to cool for a while before being subjected to a controlled heating environment at 105°C. This process will be repeated until two successive weight readings are stable. After this, the percentage of weight loss will be compared to the initial weight [20].

Drug/Latin Name (Material)	*Rasa* (Taste)	*Guna* (Quality)	*Virya* (Potency)	*Vipak* (Bio-transformed rasa)	*Doshaghnata* (Regulatory functional factors of the body)	Proportion
Varun (Crataeva religiosa Forst.)	*Tikta,* (bitter), *Kashay* (astringent)	*Laghu* (light), *Ruksha* (dry)	*Ushna* (hot)	*Katu* (pungent)	*Kapha-Vatahara*	1 part

[Table/Fig-2]: Ingredients and properties of *Varun Twak Lepa guti.*

Drug/latin name (Material)	*Rasa* (Taste)	*Guna* (Quality)	*Virya* (Potency)	*Vipak* (Bio-transformed rasa)	*Doshaghnata* (Regulatory functional factors of the body)	Proportion
Krushna Tila (Sesamum indicum Linn.	*Madhura,* (sweet), *Kashaya,* (astringent) *Tikta* (bitter)	*Guru,* (heavy), *Snigdha* (unctuousness)	*Ushna* (hot)	*Madhura* (sweet)	*Vatahara*	1 Part
Krushna Jeeraka (Carum carvi Linn.)	*Katu* (pungent)	*Laghu* (light), *Ruksha* (dry)	*Ushna* (hot)	*Katu* (pungent)	*Kaphahara*	1 Part
Shweta Jeeraka (Cumin cyminum Linn.	*Katu* (pungent)	*Laghu* (light), *Ruksha* (dry)	*Ushna* (hot)	*Katu* (pungent)	*Kapha-vatahara*	1 Part
Shweta Sarshap (Brassica alba Linn.)	*Katu* (pungent) *Tikta* (bitter)	*Laghu* (light), *Snigdha* (unctuousness)	*Ushna* (hot)	*Katu* (pungent)	*Kapha-vatahara*	1 Part

[Table/Fig-3]: Ingredients and properties of *Krushnatiladi Lepa guti.*

2. **pH value:** The pH will be measured using a digital pH meter that has an integrated electrode assembly. Buffer solutions with pH values of 4.0, 7.0 and 9.20 will be used for calibration to verify the instrument's accuracy prior to the experiment [20].
3. **Hardness:** Hardness is an important quality control parameter for tablets since the compression process affects stability, disintegration, and all other aspects of tablet performance. It also indicates how brittle, strong and well-bound the tablets are. Tablets must be handled and transported without breaking until they are provided to the customer. A Monsanto tablet hardness tester will be used to determine the hardness of the medication [21].
4. **Water soluble extractive value (%):** The substance (5 grams) will be mixed with 100 mL of distilled water and alcohol in a conical flask with a glass stopper. Over six hours, the mixture will be gently shaken regularly. It will then be left undisturbed for eighteen hours. Next, the mixture will be filtered, and a water bath will be used to evaporate 25 mL of the residual solution until it is completely dry. After being dried for six hours at 105°C, the leftover residue will be cooled for thirty minutes in a desiccator, and it will then be promptly weighed. The weight of the air-dried medication will be used to compute the percentage of water-soluble materials [20].
5. **Alcohol soluble extractive value (%):** Alcohol will be used in place of water in the procedure for determining the water extractive values, and the percentage of alcohol-soluble materials will be calculated using the previously described method [20].
6. **Acid-insoluble ash (%):** The residues that come from the total ash calculations will be boiled in hydrochloric acid. The insoluble ingredients will then be washed with hot water, poured into a crucible, dried and weighed. The value for acid-insoluble ash will be obtained by calculating the weight difference between the crucible containing the burned sample and the empty crucible [21,22].
7. **Total ash (%):** Each sample of ash will be weighed at exactly two grams and then placed into silica crucibles. After being evenly distributed across the bottoms of the crucibles, the samples will be burned, allowed to cool, and then weighed. The total ash value will be calculated by deducting the weight of the empty crucible from the weight of the crucible containing the burned sample [20].
8. **Disintegration time:** Disintegration time is a crucial factor in determining how well dosage forms-such as tablets, capsules, boluses, pessaries and suppositories-break down in a certain amount of time when submerged in a liquid medium under specific experimental conditions. This measurement provides an indication of the drug's quality, as well as, the characteristics of the binding agent used [22].
9. **Uniformity of weight:** The drug content of half-tablets will be compared to half of the mean drug content obtained from the full sample of whole tablets to assess the consistency of the drug content. The weights of the half-tablets will be compared to half of the mean weight determined for the entire tablets in the sample, using a Mettler analytical balance to assess weight consistency [23].
10. **HPTLC:** The application of High-performance Thin Layer Chromatography (HPTLC) is essential for drug quality assessment and adulterant identification. This method facilitates the separation of different chemical components, which allows for the calculation of Rf values after spot detection. This will be crucial for verifying the authenticity, purity and potency of the drug [20].

Treatment application: *Varun Twak Lepa guti* in group A and *Krushnatiladi Lepa guti* in group B will be applied topically to the face in an upward movement with cow's milk once a day for 30 days. The *Lepa guti* will be rubbed on a piece of stone with a small quantity of cow's milk until a thick paste is prepared. This paste will then be applied to the affected area until it reaches a semi-dry condition. The face will be cleansed with warm or lukewarm water once the *Lepa* has partially dried.

The patients will be advised to avoid using any soap, beauty creams, face packs, etc., during the therapy. At the beginning of the investigation, all baseline parameters will be documented. Treatment for patients in both groups will be administered. On the 15th and 30th days, all parameters will be recorded [Table/Fig-4]. A Complete Blood Count (CBC) and Erythrocyte Sedimentation Rate (ESR) will be performed before beginning medication to rule out any infectious conditions.

Group	Sample size (n)	Intervention	Dose and frequency	Duration	Follow-up
Group A (Control group)	31	*Varun Twak Lepa guti*	Local application once at day time	30 days	0th, 15th, 30th day during treatment.
Group B (Intervention group)	31	*Krushnatiladi lepa guti*	Local application once at day time	30 days	0th, 15th, 30th day during treatment.

[Table/Fig-4]: Showing the grouping and posology.

Secondary outcomes: Subjective criteria for melasma assessment are illustrated in [Table/Fig-5] [24].

Symptoms	Grade-0 (Normal)	Grade-1 (Mild)	Grade-2 (Moderate)	Grade-3 (Severe)
Shyavata (Discolouration)	No *Shyavata* (Discolouration)	Reddish brown colour	Brown colour	Blackish brown colour
Parush Sparsh (Dryness)	Normal	Not visible, but perceptible by touch	Skin that a person feels stretched	Recognisable chapping, dryness, and roughness of the skin
Daha (Burning Sensation)	No *Daha* (No burning sensation)	Mild *Daha*	Moderate *Daha*	Severe *Daha*
Kandu (Itching)	No *Kandu* (No itching)	Occasionally itching (moderate in frequency and intensity)	Moderately itchy (increased in frequency or intensity)	Intense itching
Snigdhata (Oiliness)	Normal	Sensed through touch but not seen. There's no need to cleanse your face more than once or twice a day.	Skin that is oily needs to be washed often (three to four times a day)	Skin that is excessively oily is visible. Growth of acne Face cleaning should be done more than four times a day.

[Table/Fig-5]: Gradation of subjective criteria [24].

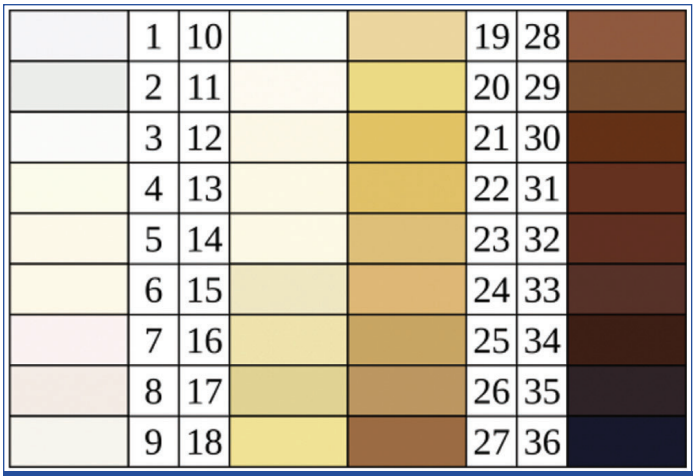
Objective criteria: Objective parameters will be assessed according to the gradation illustrated in [Table/Fig-6] [25].

Von Luschan's colour scale:

The change in complexion will be recorded using a digital Fujifilm camera in daylight on the 0th, 15th and 30th days, as depicted in [Table/Fig-7] [17].

Grade	Size of patches
Zero	0-1 cm
One	1.1-3 cm
Two	3.1-6 cm
Three	More than 6 cm

[Table/Fig-6]: Size of patches [25].



[Table/Fig-7]: Von Luschan's colours scale [23].

MSI score [26]:

The MSI score formula is as follows:

$0.4(a\times P^2)\ I+0.4(a\times P^2)\ r+0.2\ (a\times P^2)\ n$

The pigmentation severity and affected area will be scored in the manner illustrated in [Table/Fig-8].

Grade	Area of involvement (A)
Zero	Involvement of <10% area
One	Involvement of 11-30% area
Two	Involvement of 31-60% area
Three	Involvement of >60% area
Grade	**Pigmentation**
Zero	Absence of prominent pigmentation
One	Very dull pigmentation
Two	Minimal pigmentation
Three	moderate skin pigmentation
4	Intense pigmentation

[Table/Fig-8]: Melasma severity assessment.

Study design: Gnatt chart of the present study has been presented in [Table/Fig-9].

Scholar/Investigator	Dr. Pratiksha Mahure					
Title	Pharmaceutico analytical study of modified dosage forms (*Lepa guti*) of *Varun Twak Lepa* and *Krushnatiladi Lepa* and their comparative clinical evaluation in *Vyanga* (Melasma)- A randomised controlled trial					
Steps	Q1	Q2	Q3	Q4	Q5	Q6
IEC approval						
Review of literature						
Preparation of drugs						
Patient enrollment						
Data gathering						
Statistical analysis						
Writing a thesis						
The submissions						

[Table/Fig-9]: Gnatt chart.

Allocation implementation: The subjects will be enrolled by the researcher, who will administer the intervention and determine the allocation order.

Blinding: A double-blind standard Randomised Controlled Trial (RCT).

STATISTICAL ANALYSIS

Statistical Package for Social Sciences (SPSS) software software will be used for the statistical analysis. Paired and unpaired t-tests will be applied for intragroup and intergroup comparisons, respectively. A p-value greater than 0.05 will be considered statistically significant.

Repository name:

Title of project: Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist for the study of a pharmaceutico-analytical study of modified dosage forms (*Lepa guti*) of *Varun Twak Lepa* and *Krushnatiladi Lepa*, and their comparative clinical evaluation in *Vyanga* (Melasma)-A randomised controlled trial.

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