Original Article

Efficacy of external application of oil and gel dosage forms of *Aragvadhadi* formulation in combination with *Rasayana Churna* in the management of *Shwitra* (vitiligo) - An open-labeled comparative clinical trial

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Abstract

Introduction: *Aragvadhadi Taila* (ART) is one of the herbomineral formulations mentioned in Chakradatta indicated in *Shwitra* (vitiligo). Modification of *Taila* form into gel form reduces the risk of contamination in view of arsenical contents (*Manahshila*, *Haratala*) assures precise dose administration at desired site (by avoiding spreading). The gel is a comparatively acceptable dosage form than that of medicated oil. **Aim:** The aim of the study is to evaluate the comparative efficacy of *Aragvadhadi* formulation in *Taila* (ART: *Aragvadhadi Taila*) and gel (ARG: *Aragvadhadi* gel) dosage forms with the internal administration of *Rasayana Churna* in the management of *Shwitra*. **Materials and methods:** The study was a randomized open labeled, involving 66 patients of *Shwitra* that were randomly divided into two groups. Patients registered in group A ($n = 34$) were treated with local applications of ART and group B ($n = 32$) with ARG for 2 months. *Rasayana Churna* (3 g), along with the equal quantity of honey and *Ghrita* was given twice a day after the meal in both groups. Wilcoxon signed-rank test was applied to evaluate the effect of therapy in the individual group for subjective criteria like vitiligo area scoring index score, size and number of patches, *Rukshata* (dryness), *Saparidaha* (burning sensation), *Bahalatva* (thickening), *Kandu* (itching) while the comparison of results between the groups for the same by applying Coefficient of Variation (CV). **Results:** Group B showed better and consistent results in all signs and symptoms except *Rukshata, Saparidaha* in terms of Coefficient of Variation. In both the groups, statistically highly significant improvement was found in signs and symptoms of *Shwitra* such as *Saparidaha, Kandu,* size of patches and number of patches; however, the difference between the groups was statistically insignificant. **Conclusion:** Both the forms (ART, ARG) of *Aragvadhadi* formulation along with *Rasayana Churna* were found as a safe and effective treatment in vitiligo with significant pigment regeneration capacity as topical use for application over 2 months.

Keywords: *Aragvadhadi* gel, *Aragvadhadi Taila*, Arsenical, *Rasayana Churna*, *Shwitra*, Vitiligo

Introduction

In Ayurveda, *Shwitra* has been listed to be the worst among *Kushtha* that causes ugly appearance of the body. Acharya Vagbhatta has described *Shwitra* as more dangerous than *Kushtha* as it's prognosis worsens with duration as it becomes incurable (*Asadhya*) very quickly.,[1] Vitiligo is an acquired skin disorder caused by the disappearance of pigment cells from the epidermis that gives rise to well-defined white patches, which are often symmetrically distributed. It can be cosmetically disfiguring and it is a stigmatizing condition, leading to serious psychological problems in daily life. In India, Gujarat is considered to have the highest incidence in the world, with 8.8% of people affected by vitiligo.[2]

The modern medical system has treatment modalities, including narrow-band ultraviolet B (311 nm) therapy, transplantation of

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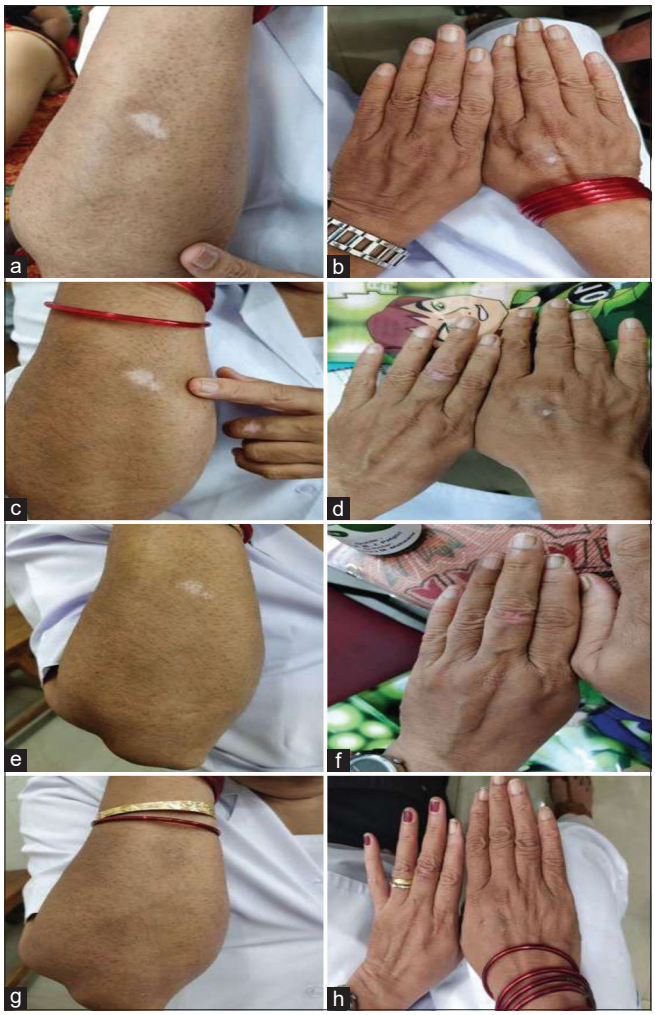

Figure 1: (a-h) Group A: Patient treated with external application of *Aragvadhadi Taila* and internal administration by *Rasayana Churna* (acute patient of vitiligo)

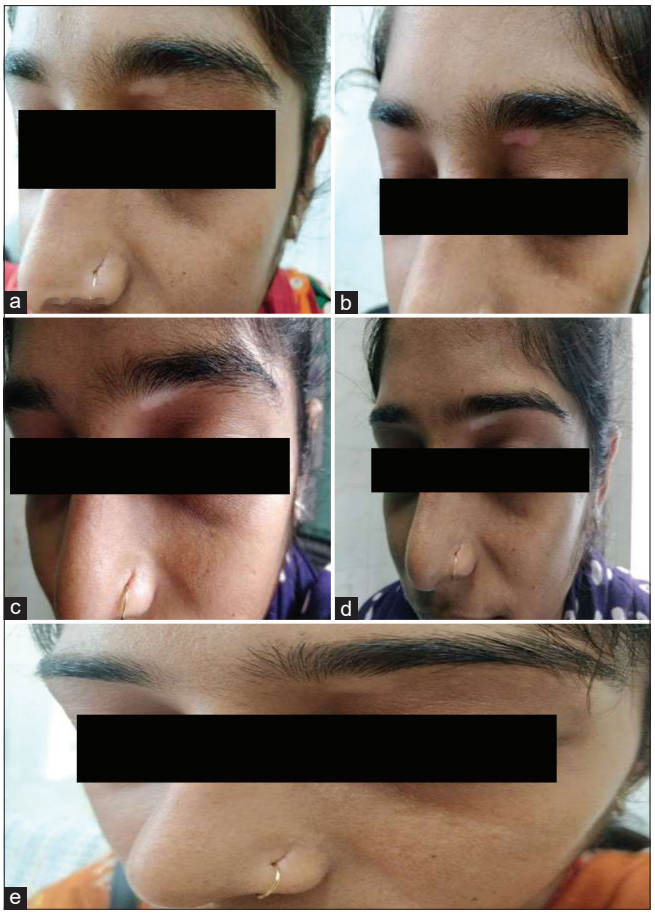

Figure 2: (a-e) Group B: Patient treated with external application of *Aragvadhadi* gel and internal administration by *Rasayana Churna* (acute patient of vitiligo)

autologous pigment cells, and thin split-thickness skin graft in various modalities.[3] According to a survey, these treatment modalities have limited use because of adverse events such as pruritis (37%), erythema (>grade 2, 22%), nausea (20%), and headache (8%).[4] Therefore, it is the need of time to look for treatment with less adverse events as well as more effective treatment from Ayurveda.[5]

Aragvadhadi Taila (ART) is one of the compound formulations mentioned in Chakradatta indicated in *Shwitra* (vitiligo).[6] This herbomineral formulation consists of two arsenicals, i.e., *Shuddha Manahshila* (processed realgar), *Shuddha Haratala* (processed orpiment). *Aragvadha* is considered *Kushthagna Dravya* in *Aragvadhiya* chapter in place of *Adhyaya* in text Charaka Samhita.[7] Acharya Sushruta has mentioned *Aragvdhadi Gana* which is separately used to cure skin diseases (*Kushtha*).[8] Acharya has advocated *Aragvadha* as external and internal remedies for skin diseases and injury, etc. Rasaratna Samuchhya has mentioned *Kushthahara* property of processed *Haratala*.[9] However, there is no published research work on modification of this formulation. Modification of *Taila* form into gel reduces the risk of contamination in view of arsenicals content (*Manahshila*, *Haratala*) assures precise dose administration at desired site (by avoiding spreading). Disadvantages of topical medicament oil are unwanted spreading, chances of irritation, hyperpigmentation of healthy skin, and inconvenience in public transport. Gel is a comparatively convenient dosage form than that of medicated oil.

Vitiligo may cause emotional, psychological consequences. *Rasayana Churna* containing *Guduchi* (*Tinospora cordifolia* Linn.), *Amalaki* (*Emblica officinalis* Linn.), and *Gokshura* (*Tribulus terrestris* Linn. in equal proportion has rejuvenation properties.[10] Therefore, *Rasayana Churna* has been selected in the study.

Consequently, the study is undertaken to evaluate the comparative clinical efficacy of *Aragvadhadi Taila* and its gel form along with *Rasayana Churna* in *Shwitra* (vitiligo).

Materials and method

The study was a randomized open labeled, involving 66 patients with vitiligo fulfilling the inclusion criteria. Each patient was examined in detail. Relevant pathological (total

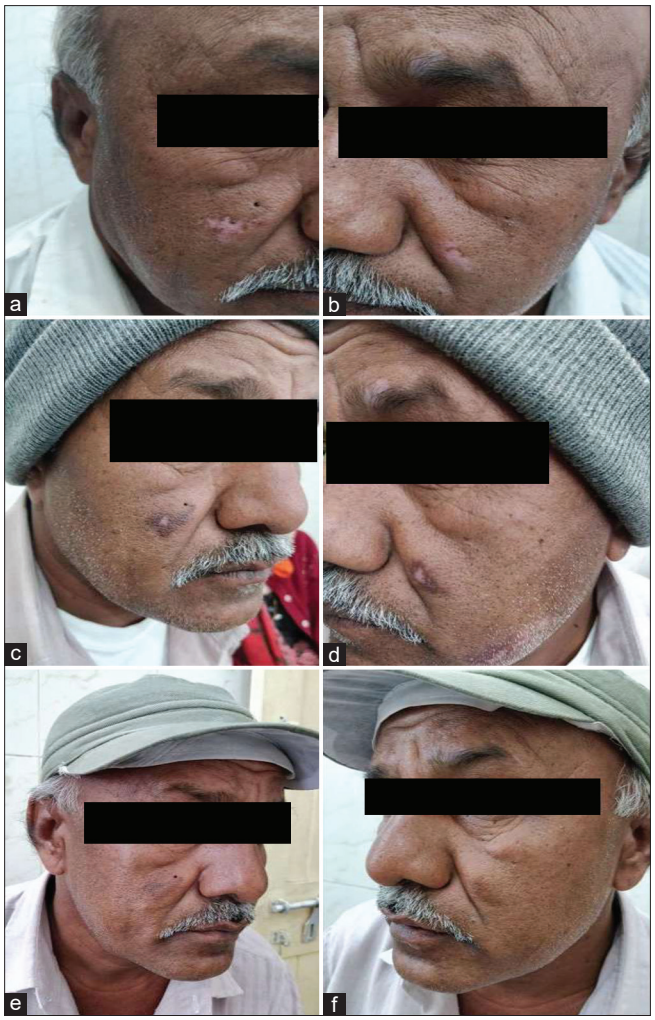

Figure 3: (a-f) Group A: Patient treated with external application of *Aragvadhadi Taila* and internal administration by *Rasayana Churna* (chronic patient of vitiligo)

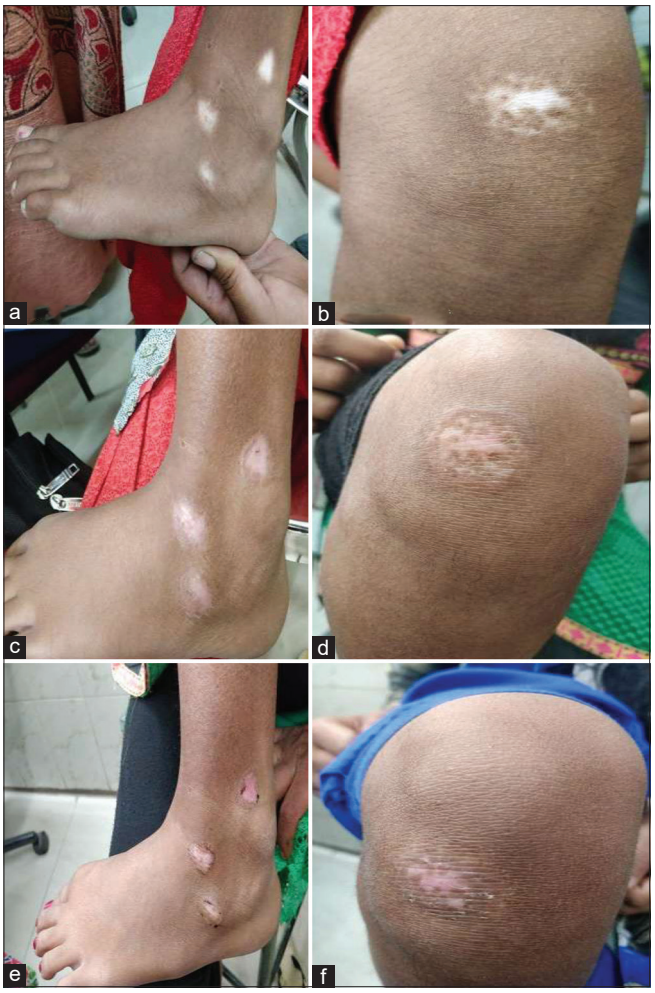

Figure 4: (a-f) Group B: Patient treated with external application of *Aragvadhadi* gel and internal administration by *Rasayana Churna* (chronic patient of vitiligo)

leukocyte count, differential leukocyte count, haemoglobin erythrocyte sedimentation rate, total red blood cells, absolute eosinophil count, and urine examinationand biochemical investigations (post prandial blood sugar, glutamic-oxalacetic transaminase, glutamic-pyruvic transaminase, alkaline phosphates, Sr creatinine, and blood urea) were done before and after treatment to assess the disease condition and to exclude any other pathology. Informed consent was obtained from all the patients before including in the trial. The study was also approved by Institutional Ethics Committee clearance (7/-A/ETHICS/2017-18/2093, dated: 23/11/2017) and registered at the clinical trial registry of India, ICMR, New Delhi, vide CTRI/2018/01/011120 dated 03/01/2018.

Inclusion criteria

Patients having classical signs and symptoms of *Shwitra* such as *Arunata* (vermilion colored), *Mandala* (circular), *Rukshata* (dryness), *Paridhvanshi* (when rubbed scales off morbid skin) for *Vatika Shwitra; Padmapatra Pratikasam* (eruptions resembling the petals of a lotus flower), *Sadaha* (burning sensation), *Romavidhvanshi* (loss of hairs), *Tamra* (coppery colored) for *Paitika Shwitra* and *Kandu* (itching), *Shweta* (white colored), *Bahala* (thick) and *Snigdha* (glossy) for *Shleshmika* type of *Shwitra* were included in the study. Patients in the age group between 16 and 60 years irrespective of sex and chronicity of <10 years were included.

Exclusion criteria

Patients having chronicity >10 years, patients of cardiac, renal, hepatic diseases, other conditions such as insulin-dependent diabetes mellitus (IDDM), non-IDDM, gravid and lactating women, women in fertile age planning for conception within the next 3 months. Patients of patches due to burning or chemical explosion, lesions at *Guhyanga* (genital organ), *Panipadatala* (sole of palm and feet), *Oshtha* (lips), *Sarvanga* (generalized lesion over the body), and patches with *Raktaroma* (reddish hair) and *Samsakta* (coalescent) were excluded.[11,12]

Method of preparation of the trial drugs

Aragvadhadi Taila (ART) was prepared as per reference of Chakradatta in compliance with classical guidelines, in 5

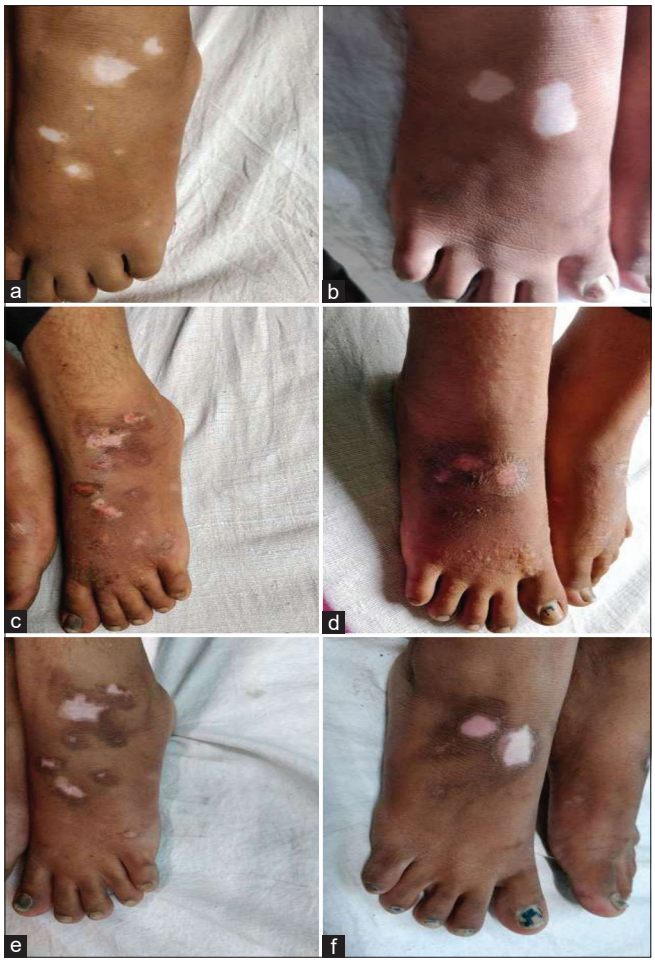

Figure 5: (a-f) Group A: Blister formation in a patient treated with external application of *Aragvadhadi Taila* and internal administration by *Rasayana Churna*

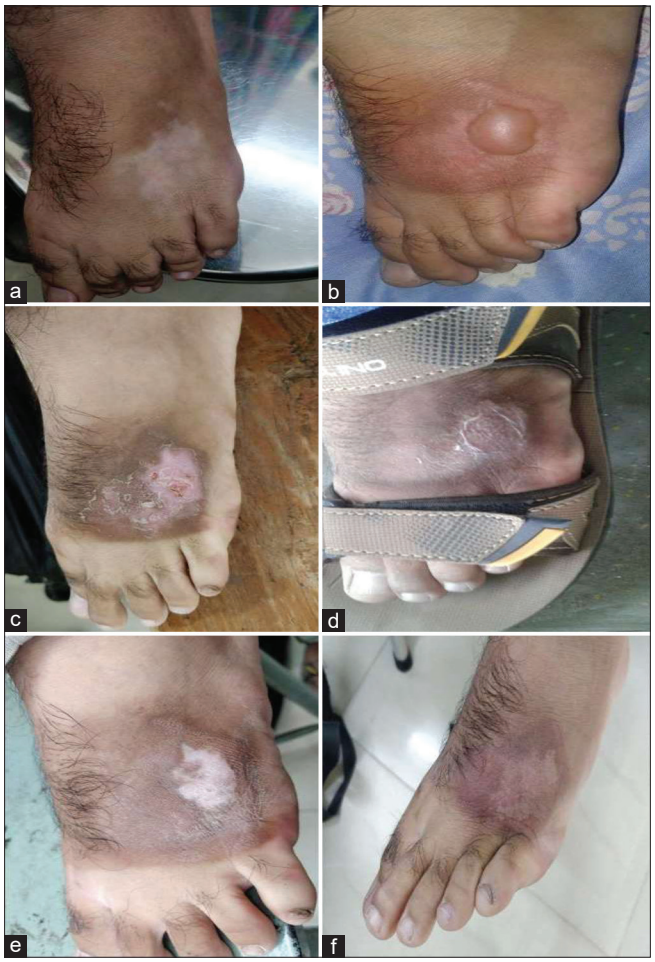

Figure 6: (a-f) Group B: Blister formation in a patient treated with external application of *Aragvadhadi* gel and internal administration by *Rasayana Churna*

batches of 2 lit. each at the institutional Bhaishajya Kalpana laboratory. *Aragvadhadi Taila* contains *Sarshapa Taila* (mustard oil), *Aragvadha* fruit (*Cassia fistula* Linn.), *Dhava* (*Anogeissus Latifolia* Linn.) bark, *Kushtha* (*Saussurea lappa* C.B. Clarke), *Haridra* (*Curcuma longa* Linn.), *Daruharidra* (*Berberis aristata* DC), *Shodhita Manahshila* (Processed red arsenic sulfide), *Shodhita Haratala* (Processed yellow arsenic sulfide), and *Gomutra* (cow's urine). Pharmaceutical and analytical standardization were carried out for the ART.[13] *Aragvadhadi* gel (ARG) was prepared by adding 15% of Aerosil in *Aragvadhadi Taila*. Both the trial drugs were stored in airtight container.

Material

Of the 66 registered patients in group A (n = 34), patients of *Shwitra* were treated with external application of ART and internal administration of *Rasayana Churna*[14] 3 g with *Sahapana* (vehicle) of honey and *Ghrita* 2 times/day, and in group B (n = 32), *Aragvadhadi* gel (ARG) Q. S. for external application and *Rasayana Churna* for internal administration.

Posology

In group A, patients were treated with external application of ART and internal administration of *Rasayana Churna* 3 g with *Sahapana* of *Madhu* and *Ghrita* with equal quantity after meal 2 times/day and in group B were treated with ARG Q. S. for external application and *Rasayana Churna* for internal administration after the meal. The quantity sufficient drug was advised to apply locally over patches in the morning with exposure to sunlight for 30 min for 2 months. Follow-up was taken at weekly intervals for VASI (Vitiligo Area Scoring Index) score, signs and symptoms and probable ADRs for 1 month. Other medicines were stopped, and dietary restrictions were advised in both the groups as stated in classics.[15]

Wholesome diet

Patients were advised to take in diet such as old rice (*Puranashali*), wheat (*Godhuma*), green gram (*Mudga*), light food (*Laghuahara*), and *Patola* (bitter gourd), old cereals, seasonal fruits, green vegetables such as *Methika* (*Trigonella foenum-graecum* Linn.), *Patola* (*Trichosanthes dioica* Roxb.), and *Amalaki* (*Phyllanthus emblica* Linn.).

Unwholesome diet

Viruddhahara (incompatible food), *Guru Ahara* (heavy food), *Vidahi Ahara* (spicy, pungent food), *Vishtambhi*

Ahara (constipatives), *Anupamamsa* (sea food), *Kanda-Moola* (roots and tubers), *Amla–Katu-Lavana Rasa* (sour, pungent, salty food), curd, fish, canned food, junk foods, milk and milk products, oily and fermented food products, consumption of food at inappropriate time, late, and day sleep were advised to avoid.

Criteria for assessment

Special vitiligo area scoring index (VASI)[16] scoring pattern was adopted for evaluation of the status of affected area. The score was given based on size and number of patches, percentage of body area involvement, and chronicity of patches. For the assessment of the involvement of body surface area, the rule of nine[17] used to calculate the percentage of burn was considered with certain modifications. The whole body was allocated in scores, but looking into the nature of the disease, score was further specified regions to the organs. Subjective criteria involve *Rukshata* (dryness of the skin), *Saparidaha* (burning sensation), *Kandu* (itching), and *Bahalatva* (thickening of the skin) were assessed before and after the treatment [Tables 1-3].

Overall effect of therapy

1. Complete remission: 100% improvement in subjective and objective parameters
2. Marked improvement: >75%–99% in subjective and objective parameters
3. Moderate improvement: >50%–75% in subjective and objective parameters
4. Mild improvement: >25%–50% in subjective and objective parameters
5. Unchanged: Up to 25% improvement in subjective and objective parameters.

Table 1: Criteria for assessment of involvement of body surface area

Extent of re-pigmentation (%)	Clinical observation	Scoring given
0	No change in the pigmented area	0
10	Specks of re pigmentation or concavity of margins	1
25	Area of re pigmentation less than the residual depigmented area	2
50	Area of re pigmentation almost equal to that of residual depigmentation	3
75	Area of re pigmentation less than the residual depigmented area	4
90	Some specks of depigmentation left	5
100	Complete re pigmentation	6

Table 2: Scoring pattern of patches

Percentage of area as per rule of nine (%)	Size (cm)	Number of patches	Chronicity of patches (years)	Score
<5	1	1-2	1-2	1
5-25	2	3-4	3-4	2
25-50	3	5-6	5-6	3
50-75	4	7-8	7-8	4
>75	>4	>9	9-10	5

Statistical analysis

The percentage of improvement in each parameter in all the treated groups was calculated. Wilcoxon signed-rank test was applied to evaluate the effect of therapy in the individual group for subjective criteria such as VASI score, size, and number of patches, *Rukshata* (dryness), *Saparidaha* (burning sensation), *Bahalatva* (thickening), *Kandu* (itching) while the comparison of results between the groups in subjective criteria was done by applying coefficient of variation (CV). The overall effect of therapy on each scale was calculated with reference to percentage improvement in all symptoms. Finally, the overall effect of therapy was evaluated by enumerating the number of patients in improvement categories.

Observations and Results

In the present clinical study, a total of 80 patients were assessed for eligibility. Among them, 72 patients were registered, i.e., 35 in group A and 37 in group B. Thirty-four patients in group A and 32 patients in group B had completed the treatment. One patient in group A and five patients in group B left the treatment in between. In group A, one patient refused to continue medicine. In group B, from three patients were resided much far from Jamnagar city and could not came regularly, one patient was migrated to another city for further study purposes, and 1 discontinued without any reason [Chart 1]. Detailed demographic data are introduced in Table 4. There is no statistically significant difference ($P > 0.05$) in the effect of therapies in group A and B on biochemical parameters such as FBS, S. cholesterol, S. triglyceride, and hematological parameters like Hb%, ESR., TLC., neutrophils, lymphocytes, eosinophils, and monocytes. All changes were within normal biological ranges.

Comparison of effect of treatment within same group (paired 't' test) showed that ART treated group A exhibited highly significant improvement in burning sensation (45.9%, $P < 0.0001$) and ART gel treated group B showed highly significant reduction in size of patches (45.94%, < 0.001), number of patches (34.25%, $P < 0.001$), VASI Score (52%, $P < 0.0001$), itching (17.99%, $P < 0.001$) and significant reduction in thickening of skin (43.33%, $P < 0.0038$). Upon comparison of effect of treatments among groups, group A exhibited better result in dryness, burning sensation whereas group B in VASI score, number of patches, thickening of skin and itching. There was statistically insignificant difference (unpaired 't' test) ($P > 0.999$) in effect of treatment in between two groups on parameters VASI score, size of patches, number of patches, burning sensation, thickening and itching of skin whereas significant difference was noted in reduction in dryness in between groups. [Table 5].

Upon consideration of overall effect of treatment, ART (group A) showed mild improvement in 46.87%, moderate improvement

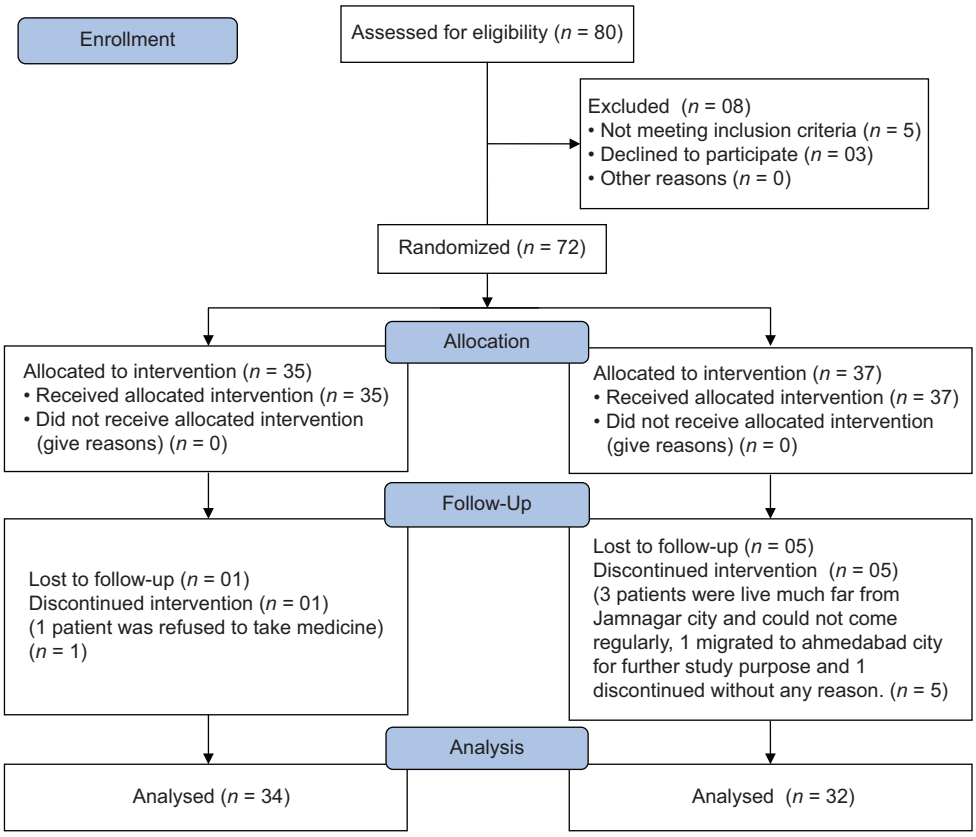

Chart 1: CONSORT flow diagram

in 43.75%, and marked improvement in 3.12% of patients. While, in 6.25% of the patients remained unchanged. ART gel (group B) showed mild improvement in 32.35%, moderate improvement in 52.94%, and marked improvement in 11.76% of patients Whereas merely 2.94% of the patients remained unchanged. None of the patients showed complete remission in either groups. [Table 6 and Chart 2]

On applying coefficient of variation (CV), group B showed better and consistent results in all parameters except dryness, burning sensation. The major difference was found in the thickening of skin between comparisons of both the groups as that of other symptoms. It may be due to better localized action of the gel dosage form). [Table 7]

Photographs of acute and chronic patients from group A and B are presented in Figures 1, 2, 3, and 4. Patient suffered from blister formation depicted in figures 5,6. None of the patients reported complete cure with the treatment of 2 months duration. It was assesed in pilot study.

Discussion

Psychological factors and incompatible food (salty and milk food together) are mentioned in classics as the prime causative factors for this disease. Acharya Charaka also stated that psychological factors may induce stress in the patients and become the triggering factor that triggers the disease manifestation mechanism.[18] 68.35% of patients

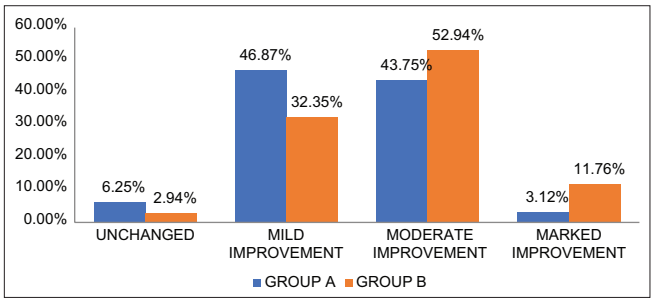

Chart 2: Overall effect of therapies in group A and group B

had sour taste dominancy followed by sweet taste (55.69%) and salty taste (45.56%) in their diet. It revealed that *Madhura* (sweet), *Amla* (sour), and *Lavana* (salty) *Rasa* causes aggravation of *Kaphadosha*, *Amla Rasa* (sour taste) causes *Rakta Dushti*. Excessive taking of *Amla*, *Lavana* (salty taste), and *Katu Rasa* pungent taste causes *vitiation of Pitta*. Acharya Charaka has also mentioned these foods play an important role in the pathogenesis of *Shwitra*. About 65.82% of patients were observed in taking salty diet and milk while 21.51% were observed in taking sour food and milk together. These combinations food lead to vitiation of blood hence leads to *Shwitra* disease.[19] Acharya Charaka has mentioned the role of incompatible food in the manifestation of *Shwitra*.[20] This process plays an important role in the initiation of the pathogenesis of *Shwitra*. All these factors might have contributed to disturb the immunological balance

Table 3: Subjective criteria relief in associated signs and symptoms of *Shwitra* as per gradation pattern

Associated signs & symptoms	Score
Rukshata (dryness of skin)	
No line on scrubbing with nail	0
Faint line on scrubbing with nail	1
Lining and even words can be written by nail	2
Excessive *Rukshata* leading to *Kandu*	3
Rukshata leading to crack formation	4
Saparidaha (burning sensation)	
No burning sensation	0
Occasional localized burning sensation	1
Localized mild burning sensation in a particular hr. of day	2
Burning sensation throughout the day but tolerable and relieved after cold medications	3
Intolerable burning sensation throughout the day which can't be relieved by cold medications	4
Kandu (itching)	
No itching	0
Mild/occasional itching	1
Moderate frequent itching	2
Severe frequent itching	3
Very severe itching which disturbs sleep and other routine activities	4
Bahalatva (thickening of skin)	
No thickening	0
Mild thickening	1
Moderate thickening	2
Very thick	3
Very thick with induration	4

Table 4: General observations (baseline data of both the groups) (*n*=72)

Observations	Maximum percentage
Age: 18-25 years	35.44
Occupation: Brass company employee	16.45
Agni: *Mandagni* (low digestive fire)	45.56
Prakriti: *Vata Pitta*	49.36
Family history	17.72
Ahara Vihara Nidana (improper food habits and lifestyles)	
Atisevita Ahara and *Vihara* (excessive intake of food habits and activities)	
Amla Rasa (sour taste of food)	68.35
Madhura Rasa (sweet taste of food)	55.69
Lavana Rasa (salty taste of food)	45.56
Usna Shita Krama Viruddha Sevana	17.72
Guda (jaggery)	83.54
Divaswapa (day sleep)	56.96
Viruddhahara (incompatible diet)	
Lavana (salty food) + milk	65.82
Amla Rasa (sour food) + milk	21.51
Milk + fish	6.32
Swetabha Vaivarnyata patches	55.69
Kandu (itching)	34.17
Rukshata (dryness of skin)	15.18
Onset of disease: Gradual	72.15
Chronicity (years)	
<1	41.77
6-10	17.72
Distribution of patches	
Exposed	79.74
Localized	93.67
Type	
Segmental vitiligo	54.43
Non-segmental vitiligo	40.50
Active vitiligo	39.24
Symmetrical distribution	54.43
Level of stress: Moderate	73.41
Associated disease	
Worm manifestation	12.65
Sun exposure time (h)	
<1	73.41
Excessive 4-5	2.53

of the body, thus causing autoimmune or process to paralyze the affected patient's melanocytes system to produce the lesions of vitiligo.[21]

In the present study, 35.44% of patients were reported in the age group of 18–25 years. Ayurvedic classics have stated *Shwitra* as the disease of dominant *Pitta* in *Dosha* triad. This is evident from the above data as *Shwitra* is more prevalent in the age group, which was *Pitta Pradhana*.[22] About 16.45% of patients were employee of brass industries. One cross-sectional descriptive research attributed to the use of raw materials, such as copper, in industries, which the workers grind and clean producing dust, which leads to black stain also over hands. Occupational dermatosis, i.e., vitiligo was found in 20 workers (1.9%), and a higher percentage of workers had found occupational dermatoses in this research.[23]

17.72% of patients had positive family history of disease. Among them, 11.39% of patients were having family history of vitiligo in 1st-degree relatives and 5.06% of patients had family history in 2nd-degree relatives. The occurrence of vitiligo is in the ratio of 1:3 when it comes to inheritance.[24] Comparatively less incidence of heredity in terms of % of the history of heredity (14%) in the present study and previous all thesis of the institute (mean 15.8 ± 0.98 of percent of patients with heridity) are suggestive of lower hereditary prevalence, which itself suggest that prevalence of locally adopted lifestyle could be a major player in increasing prevalence of nonhereditary vitiligo.[25] Familial occurrence has been reported to be in the range of 6.25% to 30% in many previous researches. 17.72% of patients had taken >1 h sun exposure time, and only 2.53% had taken excessive 4–5 h. Sun may affect highly reactive chemicals (called reactive oxygen species) in the skin that may play a role in triggering the disease in a genetically susceptible patients.[26] Normally, excessive sun exposure first causes skin reddening, followed by peeling of the outer skin layers and the formation of darker skin in the exposed area (tanned skin). However, in some cases, a reaction occurs in which the melanin

Table 5: Effect of both trial drugs on sign and symptoms of *Shwitra*

Groups	Sign and symptom	Before treatment versus after treatment			Initial versus at the end of follow up		
		Percentage change	*P*	Significance	Percentage change	*P*	Result
Group A	VASI score	30.24↑	<0.0001	HS***	20.23↑	0.0125	S**
Group B	VASI score	52↑	<0.0001	HS***	52.0↑	<0.0001	HS***
Group A	Size of patches	38.47↓	<0.0001	HS***	-	-	-
Group B	Size of patches	45.94↓	0.0004	HS***	-	-	-
Group A	Number of patches	28.72↓	<0.0001	HS***	-	-	-
Group B	Number of patches	34.25↓	<0.0001	HS***	-	-	-
Group A	*Rukshta* at patches	12.95↑	0.5625	NS****	60.7↑	0.1294	NS****
Group B	*Rukshta* at patches	4.28↑	0.8552	NS****	14.28↑	0.8469	NS****
Group A	*Saparidaha* over and around patches	45.9↑	<0.0001	HS***	23.99↑	0.0063	S**
Group B	*Saparidaha* over and around patches	34.9↑	0.0004	HS***	11.33↑	0.0065	S**
Group A	*Bahalatva* over and around patches	8.59↑	0.1726	NS****	8.56↑	0.1294	NS****
Group B	*Bahalatva* over and around patches	43.33↑	0.0038	S**	43.33↑	0.0052	S**
Group A	*Kandu* over and around patches	13.33↑	0.0005	HS***	30.94↓	0.0052	S**
Group B	*Kandu* over and around patches	17.99↑	0.0002	HS***	26.66↑	0.0037	S**

Group A: *n*=34, Group B: *n*=32. VASI: Vitiligo area scoring index, S: Significant **, NS: Non significant ****, HS: Highly significant ***. ↑: Percentage increase, ↓: Percentage decrease

Table 6: Overall effect of therapy (*n*=66)

GradationRelief	Number of patients, *n* (%)
Unchanged	3 (4.54)
Mild improvement	26 (39.39)
Moderate improvement	32 (48.48)
Marked improvement	5 (7.57)
Complete remission	0

Table 7: Comparison of results between the groups in subjective criteria by applying coefficient of variation

Symptoms	Group	*n*	Mean difference	SD	CV (%)	Better group
Rukshata	A	34	0.1500	0.06250	41.66	A
	B	32	0.1600	0.08824	55.15	
Saparidaha	A	34	0.1121	0.7188	15.59	A
	B	32	0.1336	0.6176	21.63	
Bahalata	A	34	0.1139	0.1875	60.74	B
	B	32	0.1035	0.3824	27.06	
Kandu	A	34	0.1739	0.7500	23.186	B
	B	32	0.1035	0.7941	21.11	
VASI score	A	34	0.6920	3.969	17.4	B
	B	32	0.7058	4.971	12.78	
Size	A	34	0.1519	1.188	12.78	B
	B	32	0.1506	1.324	11.37	
Number of patches	A	34	0.1626	0.8438	19.26	B
	B	32	0.1485	1.088	13.64	

CV: Coefficient of variation, SD: Standard deviation, *n*: Sample size, VASI: Vitiligo area scoring index

production is blocked and the skin loses its color. The patches of white are usually at the site of the burn, but it is also possible for additional patches to begin appearing elsewhere.[27]

Prima facia results of therapy in all patients could be still very significantly better than those are acknowledged after analysis of the overall results of all patients within the group. Better results were observed in VASI score in patients with chronicity of 6 to10 years after follow-up period of 1 month, as compared to results on VASI score in same patients after treatment of drugs for 2 months which were insignificant in either group. It is suggestive that drug will not achieve a maximum therapeutic effect with 2 months of treatment and with more duration of treatment, there may be still better clinical efficacy and it may be recommended to increase the duration of treatment as well as follow-up in future studies so as to achieve still better results. Prima facia results of therapy in terms of overall reduction in VASI score in all patients could be still very significantly better than those are acknowledged after analysis of the overall results of all patients within the group. This is evident from very high increase in VASI score in patients of lesser (1–5 years) and less chronicity (<1 year) [Table 8]. Improvement in VASI score is reducing sequentially with increase in chronicity, but it is noteworthy that there is improvement in VASI score even in patients with chronicity of 6–10 years [Table 9].

Hence, fewer score in ARG suggests better management in Group B. This is evident from very high increase in VASI score in patients of lesser (1–5 years) and less chronicity (<1 year) [Table 8]. It could be recommended that a study should be conducted on chronic cases of vitiligo (more than 6 years chronicity) as there are poor clinical outcomes in such chronic cases with all possible treatment modalities with restrictions and along with treatment-related risks specifically in the younger population requiring long term management. *Aragvadhadi Taila* treated group showed more improvement in *Rukshta* parameter. As *Rukshata* may be dependent on treatment modality and it is likely a local or systemic response of the body or local skin to treatment, which may also be adverse effects of drug treatment (adverse drug effect-arsenicals).

Table 8: Comparative effect of drugs in patients of *Shwitra* at different period of assessment

Group/ chronicity	Effect (VASI score) at different time of assessment					
	After treatment ($n=66$)			At the end of follow up ($n=66$)		
	VASI score (mean±SE difference)	Percentage change	Significance *P*	VASI score	Percentage change	Significance
ART	3.969±0.6920	30.24↑	<0.0001 (HS)	1.156±0.8981	6.82↓	0.1054 (IS)
ARG	4.971±0.7058	52↑	<0.0001 (HS)	1.294±0.3174	8.90↓	<0.0001 (HS)

ART: *Aragvadhadi Taila*, ARG: *Aragvadhadi* gel, SE: Standard error, VASI: Vitiligo area scoring index, NS: Nonsignificant, HS: Highly significant. ↑: Percentage increase, ↓: Percentage decrease

Probable mode of action of the drug

Most of the ingredients in this *Aargvadhadi Taila* are *Kushthaghna* (indicated for skin diseases), *Krimighna* (anthelmintic), and *Kandughna* (pacifying itching) by virtue of dominancy of *Rasadi Panchaka* (pungent-bitter taste, *Katu Vipaka* [pungent postdigestive effect], *Ushna Veerya* [hot potency], and *Sara-Tikshna Guna* [mobile and sharp qualities]) and that acts on *Bhrajaka Pitta* (maintenance of normal skin color). Most of the drugs have *Kapha Pittahara* properties. Hence, *Shwitra* is *Tridoshaja Pitta Pradhana Kushtha.* Accordingly, this formulation might have helped in breaking the pathogenesis of *Shwitra*. *Manahshila, Haratala,* and *Gomutra* (cow's urine) are specially indicated for *Shwitra*.[28] *Rasayana Churna* is a polyherbal formulation consists immunomodulatory drugs, i.e.; *Guduchi* (*Tinospora cordifolia* Linn.), *Amalaki* (*Emblica officinalis* Linn.), and *Gokshura* (*Tribulus terrestris* Linn.).[29] This combination may be helpful to flush out the toxins from the body and correct the digestive fire, unblocks the body channels for the nutrients to reach the tissues (*Strotas*), and balances three fundamental bodily bio-elements (*Tridosha*). Its constituents individually are reported to be potent immune-modulators. This formulation is reported to possess adaptogenic and anti-ulcer activity in experimental models.[30] This formulation helps in the proper functioning of subtype of *Pitta,* i.e.,; *Bhrajaka Pitta* and giving rise to normal color, texture, and luster to skin and reduces emotional and psychological consequences.

In LC-MS analysis of the formulation *Aragvadhadi Taila* of present study showed vitamin D_3 derivatives, i.e., 26, 26, 26, 27, 27, 27-hexafluoro-1alphaa-hydroxyvitamin D3, and alpha-(4-dimethylaminophenyl 1 alpha, 25 dihydroxy Vitamin D_3.[31] Therapeutic effects of topical Vitamin D occur via Vitamin D receptor-mediated genomic mechanism resulting in inhibition of keratinocyte proliferation. Vitamin D levels have been found to be reduced in various autoimmune disorders. Hence, cow's urine and *Daruharidra* (*Berberis aristata* DC) posseses melanogenesis process due to having Vitamin D_3 derivatives.[32] Derivatives of salicylic acid were found in mustard oil, *Aragvadha* and *Dhava.* It is monocarboxylic acid which causes shedding of the outer layer of skin. It may cause skin irritation (itching, inflammation) within a day or longer afterward. It is lipophilic in nature, oil soluble. Hence, it can penetrate into the pores of the skin. One it has penetrated in skin, the acid part of the molecule can dissolve some of the intracellular "glue" that holds skin cells together.[33] Mustard oil is one of the most important liquid media in this formulation. Mustard oil has a scraping action and is useful in the management of diseases caused by *Kapha*, dearrangement of *Vata*, itching, vitiligo and chronic diseases.[34] Alpha-lipoic acid (from eicosapentaenoic acid) is organo-sulfur compound with important antioxidant properties. It is present in mustard oil. Due to its properties, it can prevent the destruction of melanocytes by free radicals.[35] Cow's urine acts as chemical drug penetration enhancer and thus enhances the activity and bioavailability of the drug in the body.[36]

Adverse drug reaction

Small size blisters, irritation, itching, and rashes were found in three patients in group A [Figure 5] and 2 in group B [Figure 6]. Arsenic trisulphide is reported to cause irritation, burns, itching, and rashes on topical application.[37] Maximum patients were having excessive sun exposure (2 h to 7 h/day), and one patient had job in brass company involving work with molten brass. After blister formation, the treatment of local application was stopped till completely disappear of symptoms. For the management of the condition, affected lesions were irrigated with freshly prepared *Panchavalkala* decoction. Then, *Yashtimadhu Churna* with *Ghee* was applied over the affected area once a day.

Conclusion

Both the trial drugs; *Aragvadhadi Taila* (group A) and *Aragvadhadi* gel (group B), along with internal administration of *Rasayana Churna* were found highly significantly effective on improvement in VASI score, number, area and size of patches where *Aragvadhadi* gel was comparatively better in all above parameters and it was even comparatively better in the management of other associated signs and symptoms like *Rukshata, Saparidaha* and *Kandu* whereas *Aragvadhadi Taila* was better in the management of *Bahalatva*. Improvement in VASI (vitiligo area scoring index) score was significantly persisted till the end of follow up in patients with less chronicity and persisted even in patients with chronicity of 1–5 years and 6 -10 years. However, the findings can be revalidated through well-designed clinical trials involving a larger sample size.

Table 9: Comparative effect of drugs on vitiligo area scoring index score in patients with varying chronicity of *Shwitra* (effect after treatment)

Group/ chronicity	ART (*n*=34)		ARG (*n*=32)		Effect (VASI score) as that of initial in patients (Isolated as per chronicity)							
	Average (all enrolled pts)				<1 year (*n*=33)			1-5 years (*n*=26)			6-10 years (*n*=7)	
	VASI score (mean±SE difference)	Percentage change	Significance *P*		VASI score	Percentage change	Significance	VASI score	Percentage change	Significance	VASI score	Percentage change	Significance
ART	3.969±0.6920	30.2↑	<0.0001 (HS)		13.333±2.045	49.58↑	0.0001 (HS)	5.500±2.112	33.33↑	0.0161 (HS)	2.250±0.2500	14.75↑	0.1250 (NS)
ARG	4.971±0.7058	52↑	<0.0001 (HS)		8.500±1.020	79.83↑	0.0001 (HS)	6.786±1.085	41.1↑	0.0001 (HS)	3.333±0.6667	28.56↑	0.2500 (NS)

ART: *Aragvadhadi Taila*, ARG: *Aragvadhadi* gel, SE: Standard error, VASI: Vitiligo area scoring index, NS: Nonsignificant, HS: Highly significant. ↑: Percentage increase, ↓: Percentage decrease

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Conflicts of interest

There are no conflicts of interest.

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