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Research Article

Comparative Study of Efficacy and Safety of Coded Unani Formulations–UNIM-001 + UNIM-003 with Methoxsalen in Cases of Bars (Vitiligo)

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A B S T R A C T

Background: Vitiligo is a common acquired disorder of skin depigmentation in varying patterns, varying from small maculae's with scalloping borders to near total depigmentation of body. The prevalence of vitiligo in India has been invariably reported between 0.25% and 4% of dermatology outpatients across studies from India and up to 8.8% in Gujarat and Rajasthan. The study was conducted to compare the coded Unani formulation UNIM-001 (tablet) and UNIM-003 (ointment) with Melanocyl tablet (10mg each) (Methoxsalen) as standard control.

Methodology: Sixty Five patients of trial group (UNIM-001+ UNIM-003) and sixty seven patients of control group (Comparator group) of 12-50 years of either sex were selected from patients attending the Out Patient Department (OPD), at RRIUM, Aligarh during 2015-18. The patients were treated for eight months with instructions and are followed every month for efficacy and safety of the drug(s). The CRF was maintained, and post treatmet followup was done at 3 months for the repigmentaion retained by the patient.

Result: The UNIM-001 (tablets) and UNIM -003 (ointment) and standard control drug Melanocyl tablets (methoxsalen) showed same results and did not show any side effects.

Conclusion: The trial drug and the standard control drugs both possess same anti- vitiligo efficacy and are also safe for the patients.

Keywords: Vitiligo (Bars), Temperament (Mizaj), Dermatomal, Non-dermatomal Bilateral symmetrical

Introduction

Vitiligo is a common acquired disorder of skin depigmentation in varying patterns, varying from small maculae's with scalloping borders to near total depigmentation of body. The disorder affects nearly 1%-2% of the world population

irrespective of race and ethnicity with highest incidence recorded in Indian subcontinent followed by Mexico and Japan.[1,2,4] Vitiligo occurs worldwide with an overall prevalence of 1%. However, its incidence varies from 0.1 to > 8.8%.[3] The prevalence of vitiligo in India has been invariably reported between 0.25% and 4% of dermatology outpatients across studies from India and up to 8.8% in Gujarat and Rajasthan.[2,5,6] It has a familial incidence of 25 to 30%.[7] A multitude of plausible theories have been put forward to explain the pathogenesis of vitiligo and mechanisms that finally lead to the loss of functional melanocytes from the epidermis.[8] The important ones include a genetic predisposition, autoimmune destruction of melanocytes,[9] zinc-α2-glycoprotein deficiency hypothesis,[10] altered redox status[11] and free radical mediated melanocytes damage,[12] heightened sympathetic response and catecholamine's/ neurotransmitter mediated melanocytes damage[13] and impaired melanocytes adhesion or melanocytorrhagy.[14] The fusion of all these effectively explains the vitiligo pathogenesis the combination theory.[15] The medication of vitiligo comprises medical, phototherapeutic and surgical modalities. In some situations, a combination of these methods works the best.[16] The clinically characteristic symptoms of the vitiligo are pale or milk-white maculae or patches due to the selective destruction of melanocytes. They occur on the skin in different parts of the body and sometimes also on the mucous membranes.[17]

In modern medicine system various therapy such as topical corticosteroids,[18-21] systemic drug: Methotrexate vs. maniple dexamethasone and minocycline vs. minipulse dexamethasone,[22,23] ultraviolet light therapy,[24] Monochromatic Excimer Light laser (MEL) therapy,[25] combination of UV and topical or systemic therapies[26] and combination of Monochromatic Excimer Light laser (MEL) and topical therapies[27] have recently been used for treatment of vitiligo, but they all have certain side effects.

Most of the Unani physicians including *Jālinūs*, as mentioned in *Mu„ālajāt-i Buqrāṭiyāh,*[28] *Ibn Sīnā* in *Al-Qānūn fi"l-Ṭib,*[29] *Jurjānī* in his book *Ḍhakhīra Khawārizm Shāhī,*[30] *Hakīm Akbar Arzānī* in his book *Ṭibb-i Akbar*,[31] and *Sadīd al-Dīn Gāzrūni* in the book Al-Sadīdī,[32] described the cause of vitiligo as *Ḍu,,af-i Quwwat-i Mughayyira-i Badan* (transformative faculty,[33] the power that brings changes, and shapes the nutrients into tissues) and *Mushabbiha-i Badan* (power of resemblance[34]). This *Ḍu,af* (weakness) may be due to accumulation of *Balgham-i Ghalīz* (viscous phlegm), *Fasād al-Dam* or *Barūdat al-Dam* in the body.

In Unani System of Medicine (USM), many single drugs such as Habbul-Neel (*Ipomoea nil*), Atrilal (*Ammi majus*), Babchi (*Psoralea corylifolia*), Panwar (*Cassia tora*), Kharbaq Syah (*Helleborus niger*), Sheetraj (*Plumbago zeylanica*), Saqmooniya (*Convulvulus scammonia*)[35-37] as well as compound formulations (systemic) Safoof Bars[38] topical application: Zamad Bars have been used in the therapeutic management of vitiligo.

Methodology

The study was conducted between 2015 and 2018 at RRIUM, Aligarh. The coded Unani formulation UNIM-001+ UNIM-003 was procured from Central Council for Research in Unani Medicine, New Delhi. The UNIM-001 is in tablet forms and UNIM-003 is in ointment form. Melanocyl tablet (10mg each) (Methoxsalen) was purchased from Aligarh. Sixty Five patients of trail group (UNIM-001+ UNIM-003) and sixty seven patients of control group (Comparator group) of 12-50 years of either sex were selected from patients attending the Out Patient Department (OPD). Study participant will be asked not to take any anti-vitiligo therapy during the trial period. The study is a single blind study. Participants are allocated to the treatment group by pre-randomized schedule. One group was received (UNIM-001+ UNIM-003) and other group was received Melanocyl Tablet (10mg each) (Methoxsalen) as a comparator drug.

Total 260 cases were screened and 260 cases were registered on the basis of inclusion and exclusion criteria, 65 and 67 cases completed the study in both the group (trail and control group) respectively. The efficacy and safety of Unani formulation (UNIM-001+ UNIM-003) as a trial drug and allopathic drug Melanocyl Tablet (Methoxsalen) as a comparator drug were evaluated on the basis of biochemical, haematological parameters as well as percentage repigmentation response .

Selection Criteria

Patients of were enrolled on the basis of following inclusion and exclusion criteria:

Inclusion Criteria

- Patients with clinically diagnosed segmental and non-dermatomal vitiligo.
- Patients of either sex in the age group 12-50 years.
- Patients with any duration of disease, site, extension and distribution of lesions.
- Willingness to give written informed consent form.

Exclusion Criteria

- Patients with active Vitiligo treatment with other drugs/ systems.
- Non-cooperative patients.
- History of drug or alcohol abuse, chronic smokers not willing to abstain from smoking during the study period.
- Any clinically significant abnormality identified on physical examination or laboratory Tests.
- Patients having any systemic disease and other skin diseases.
- Patients with known allergies.

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- Patients with impaired cardiac, hepatic and renal function.
- Patients with history of malignancy.
- Concomitant use of any other antioxidants.
- Patients with history of hypersensitivity to any other investigational drugs/ herbal medicine.
- Patients receiving any other investigational product within 4 weeks.
- Patients with any medical condition, where physician feels participation in the study could be detrimental to patients well being.
- Patients with uncontrolled infection
- Pregnant and lactating women.

Ethical Consideration

All patients were included in the study after obtaining written informed consent and study was conducted. This research study is also registered under Clinical Trial Resistry-India (CTRI) (CTRI/ 2013/ 12/ 004215 dated 13/ 12/ 2013.

Drug, Dose and Mode of Administration

UNIM-001 (800 mg each) was given to the patients in a dose of one to four tablets orally two-three times a day after meal for a period of 240-days. UNIM-003 topical drug were in lotion form given for topical application and it was applied every alternate day followed by exposure to sun light. Patients were advised to apply on one patch and expose to sunlight at least for 3-5 days in order to ascertain the sensitivity of an individual, based on further application may be planned. The exposure time was adjusted according to the skin sensitivity of an individual permits which could range from 3-30 minutes in the early hours in the morning.

Melanocyl Tablet (10mg each) (Methoxsalen) was given orally two tablet BD after meal.

Treatment allocation: RRIUM had 20 patients per block. Block randomization technique was used to allocate the treatment schedule to the patients. Pre-randomization was done by using statistical graph pad. Randomization chart will be kept with a third person who is not involved directly in the trial.

Blinding: The assessor will not know the treatment allocation the patients.

Assessment of *Mizaj* (Temperament)

Assessment of *Mizāj* (Temperament) was done at baseline.

Follow-up evaluation

The patients will be assessed clinically at day 0, 30th-day, 60th-day, 90th-day, 120th-day, 150th-day a 180th-day, 210th-day and 240th-day. The subjective and objective clinical observations were recorded in the follow-up sheet.

Criteria for Assessment of Efficacy

To assess the response of treatment in patients of Vitiligo, the following parameters were used.

1. Efficacy evaluation: By observation and percentage Repigmentation by digital photography.
2. Safety Evaluation:

- Adverse drug reaction/ Adverse drug event was reported by the patients in the case report form. It was reported to the Institutional Ethics committee (IEC) 39. IEC was reviewed according to its SOP.
- Biochemical and hematological investigation were carried out at baseline and once a month at every follow-up.

3. Assessment of safety

Biochemical Analysis

Serum Glutamate Pyruvate Transaminase (SGPT, E.C. 2.6.1.2) and Serum Glutamate Oxaloacetate Transaminase (SGOT, E.C. 2.6.1.1.) were done by the method described by International Federation of Clinical Chemistry (IFCC) 40, Blood Urea by the method of Tiffany et al.[41] Serum Creatinine by Bowers method,[42] Serum Total Bilirubin by Pearlman and Lee,[43] Total protein by Biuret method and point,[44] Albumin by BCG Dye method and point.[45]

Haematological Analysis

Haematological parameters were done according to the method described by Mukherjee.[45] It included Haemoglobin (Hb), Erythrocyte Sedimentation Rate (ESR), Total Leucocytes Counts (TLC), Red Blood Corpuscles (RBC), Platelets Count and Differential Leucocytes Counts (DLC): Polymorphs, Lymphocyte and Eosinophil Counts.

Collection of Blood Serum

Blood samples were collected by puncturing the vein at each investigation. 1.0 ml of blood with Ethylene Diamine Tetra Acetic Acid (EDTA) was used for various haematological parameters and another 2.0-2.5 ml of blood sample was allowed to clot and serum was separated by centrifugation, which was used for various biochemical parameters. Biochemical and haematological investigations were carried out.

Statistical Analysis

Data were analyzed statistically by one-way Analysis of Variance (ANOVA) followed by Dennett's' test. The values were considered significant when the P-value was found less than 0.05.

Result and Discussion

Clinical Findings

Demographic Study

Out of 65 patients of Vitiligo (Bars) of trail group, 32 (49.23%), mean age 27.06 years were male and 33 (50.77%),

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mean age 27.06 years were female and out 67 patients of Vitiligo (Bars) of control group 26 (38.81%), mean age 27.92 years were male and 41 (61.19%), mean age 20.90 years were female which shows that females of age group (12-20 years) have higher incidence 17 (26.15%) with mean age 16.18 years and 27 (40.30%) with mean age 16.44 years as compared to male in both the groups (Trail and control group) respectively. Shah et.al., 2008[46] had reported similar type of observations.

21-40 years of trial group 16 (24.62%) with mean age 30.25 years were male and 15 (22.39%) with mean age 31.12 years were female, whereas out 67 patients of Vitiligo (Bars) of control group 15 (22.39%) with mean age 31.12 years were male and 13 (19.40%) with mean age 28.42 years were female.

41-50 years of trial group 04 (6.15%) with mean age 45.0 years were male and 04 (6.15%) with mean age 47.5 years were female, whereas out 67 patients of Vitiligo (Bars) of control group 03 (4.48%) with mean age 46.33 years were male and 01 (1.49%) with mean age 50.00 years were female (Table 1).

The age of onset of Vitiligo ranged from 12 to 20 years of female of trail group and control group have higher incidence 22 (33.85%) (Mean age 10 years) and 35 (52.24%) (Mean age 12 years) respectively, whereas the age of onset of Vitiligo of male of both trail and control group have similar incidence. The age of onset of Vitiligo ranged from 21 to 40 years of male of trail group and control group have higher incidence 15 (23.08%) (Mean age 29 years) and 11 (16.42%) (Mean age 32 years) respectively. Trail group of 17 (26.15%) patients, mean age 25.18 year had family history and 48 (73.85%) patients, mean age 25.94 years had no history, whereas in Control group of 17 (25.37%), patients, mean age 21.65 years had family history and 50 (74.63%) patients, mean age 24.3 years had no history. Sehgal and Srivastava, 2007[47] had observed similar type of results.

In socio-economic status study, Out of 65 patients of Vitiligo (Bars) of trail group, 47 (72.31%) patients, mean age 24.64 years were lower income group followed by middle income group 17 (26.15%) patients, mean age 29.35 years and higher income group 01 (1.54%) patients, 16.00 years. In total 67 patients of control group 50 (74.63%) patients, mean age 23.54 years were lower income group followed by middle income group 17 (25.37%) patients, mean age 24.59 years. Lower income group in both groups have higher incidence than middle income group. Similar type of observation had been reported by Almomani et. al., 2015.[48]

Non-vegetarian patients of Vitiligo of trial group as well as control group had more incidences 39 (60%) and 43 (66.15%) than vegetarian 26 (40.00%) and 24 (35.86%) respectively (Table 2) Jimi et al., 2011[49] had reported similar type of observation.

Both trial as well as control group patients had a history of previous treatment in different system of medicine. Out of 65 patients of Vitiligo (Bars) of trail group, 05 (7.69%) patients, mean age 21.6 years had tried Allopathic treatment, 23 (35.39%) patients, mean age 26.61 years were received Unani treatment, 07 (10.77%) patients, mean age 26.14 years were received Ayurvedic treatment and 30 (46.15%) patients, mean age 25.67 had without treatment.

Out of 65 patients of Vitiligo (Bars) of control group, 06 (8.96%) patients, mean age 23.67 years had tried Allopathic treatment, 32 (47.76%) patients, mean age 22.50 years were received Unani treatment, 05 (7.46%) patients, mean age 25.40 years were received Ayurvedic treatment and 24 (35.82%) patients, mean age 24.75 had without treatment (Table 1).

Temperament (humors) Study

In both trial and control group the incidence of Balghami (*Phlegmatic*) temperament (humors) affected with Vitiligo were 65 (100.00%), mean age 25.74 years and 66 (98.51%), mean age 23.30 years respectively. Balghami (*Phlegmatic*) temperament had higher incidence. Thulasamma et al., 2017[50] had reported similar type of observation (Table 1).

Clinical Patterned

Out of 65 patients of Vitiligo (Bars) of trail group, 29 (44.62%), mean age 26.10 years were dermatomal type of Vitiligo and 36 (55.39%), mean age 25.44 years were non-dermatomal type of Vitiligo whereas in total 67 patients of control group 34 (50.75%), mean age 23.56 years were dermatomal type of Vitiligo and 33 (49.25%), mean age 23.70 years were non-dermatomal type of Vitiligo (Table 1). Non-dermatomal type of Vitiligo had more incidences in trail group. Similar results had been reported by an authors.[51] In control group dermatomal type of Vitiligo had more incidences. Similar inference had been found by Khaitan et al.[52]

Out of 65 patients of Vitiligo (Bars) of trail group, 37 (56.92%) patients, mean age 26.62 years had extensive pattern of lesion and 28 (43.08 %) patients, mean age 24.17 years had non-extensive type of lesion. In total 67 patients of control group 35 (52.24%) patients, mean age 24.57 years had extensive type of lesion and 32 (47.76%) patients mean age 23.70 years had non-extensive type of lesion. In both the group, extensive pattern of lesions had more incidences than non extensive type.

Out of 65 patients of Vitiligo (Bars) of trail group, 23 (35.39%) patients, mean age 25.96 years had unilateral type of distribution of lesion and 25 (38.46 %) patients, mean age 25.20 years had bilateral type of distribution of lesion, 16 (24.62%) patients, mean age 26.00 years had bilateral symmetrical type of distribution of lesion and 01 (1.54%) patients, mean age 30.00 years had had bilateral

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asymmetrical type of distribution of lesion whereas in total 67 patients of control group 24 (35.82%) patients, mean age 24.62 years had unilateral type of distribution of lesion, 21 (31.34%) patients, mean age 23.43 years had bilateral type of distribution of lesion, 22 (32.84%) patients, mean age 23.83 years had bilateral symmetrical type of distribution of lesion (Table 1).

Table 1.Demographic study of Vitiligo

	Trial Group n=65, % age	Mean age±S.D.	Control Group n=67, %age	Mean age±S.D.
Sex Wise				
Female	33 (50.77%)	25.21±10.66	41 (61.19%)	20.90±8.14
Male	32 (49.23%)	27.06±12.32	26 (38.81%)	27.92±11.06
Age wise distribution (in years)				
12-20	F 17 (26.15 %) M 12 (18.46 %)	16.18±2.40 15.75±2.34	F 27 (40.30%) M 08 (11.94%)	16.44±2.49 14.88±2.36
21-40	F 12 (18.46%) M 16 (24.62%)	30.77±6.44 30.25±5.79	F 13 (19.40%) M 15 (22.39%)	28.42±6.22 31.12±7.18
41-50	F 04 (6.15%) M 04 (6.15%)	45.00±2.94 47.50±3.5	F 01 (1.49%) M 03 (4.48%)	50.00 46.33±3.21
Age onset of the disease				
12-20	F 22 (33.85%) M 17 (26.15%)	10.14±4.08 14.06±3.96	F 35 (52.24%) M 15 (23.40%)	12.29±4.39 12.33±5.23
21-40	F 06 (9.23%) M 15 (23.08%)	31.00±6.95 28.92±4.98	F 05 (7.50%) M 11 (16.42%)	29.33±5.85 32.00±5.46
41-50	F 03 (4.62%) M 02 (3.08%)	48.00±3.46 43.50±2.12	F Nil M 01 (1.49%)	Nil 44.00±0.00

Variables	Trial Group (n=65, %age)	Control Group (n=67, %age)
Family History		
Yes	17 (26.15%)	17 (25.37%)
No	48 (73.85)	50 (74.63%)
Economic Status		
High Economy group (HEG)	01 (1.54%)	Nil
Medium Economy Group (MEG)	17 (26.15%)	17 (25.37%)
Low Income Group (LEG)	47 (72.31%)	50 (74.63%)
Dietary Habits		
Non-Vegetarian	39 (60.00%)	43 (66.15%)
Vegetarian	26 (40.00%)	24 (35.82%)
Types of Medication		
Allopathic	05 (7.69%)	06 (8.96%)
Unani	23 (35.39%)	32 (47.76%)
Ayurvedic	07 (10.77%)	05 (7.46%)
No medicine	30 (46.15%)	24 (35.82%)
Assessment of Mizaj (Temperament)		
Balghami (Phlegmatic)	65 (100.00%)	66 (98.51%)
Safrawi (Bilious)	Nil	01 (1.49%)

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Clinical pattern of Vitiligo		
Variables	**Trial Group (n=65, %age)**	**Control Group (n=67, %age)**
Types of Vitiligo		
Dermatomal	29 (44.62%)	34 (50.75%)
Non-Dermatomal	36 (55.39%)	33 (49.25%)
Extension of lesion		
Extensive	37 (56.92%)	35 (52.24%)
Non-Extensive	28 (43.08%)	32 (47.76%)
Distribution of lesion		
Unilateral	23 (35.39%)	24 (35.82%)
Bilateral	25 (38.46%)	21 (31.34%)
Bilateral symmetrical (B.S)	16 (24.62%)	22 (32.84%)
Bilateral asymmetrical (B.AS)	01 (1.54%)	Nil

Biochemical Studies

Liver Function Tests and Kidney Function Tests

UNIM-001 (800 mg each) was given to the patients in a dose of two to four tablets orally two times a day after meal for a period of 240-days according to age. *UNIM-003* topical drug were in lotion form given for topical application and it was applied every alternate day followed by exposure to sun light. Patients were advised to apply on one patch and expose to sunlight at least for 3-5 days in order to ascertain the sensitivity of an individual, based on further application may be planned. Melanocyl Tablet (10mg each) (Methoxsalen) was given orally two tablet BD after meal.

In both trial and control group, no significant alterations in liver function tests, kidney function tests as well as protein, albumin, globulin and A/G ratio had been observed. Therefore, it can be inferred that it did not induce any negative or unfavorable response. The safety of the drug is therefore conformed (Table 2 & 3). Similar observation had been reported by other authors.[53,54,55]

Table 2.Effect of Unani coded drug UNIM-001+ UNIM-003 on the levels of SGPT, SGOT, Bilirubin, Blood Urea and Serum Creatinine, Protein, Albumin, Globulin and A/G ratio in vitiligo patients

Group Parameter	BL 0-Day	1st F-Up 30th day	2nd F-up 60th day	3rd F-up 90th day	4th F-up 120th day	5th F-up 150th day	6th F-up 180th day	7th F-up 210th day	8th F-up 240th day
SGOT (IU/L)	25.75 ±7.70	35.44 ±64.87	27.13 ±17.52	25.72 ±9.72	39.95 ±29.01	25.91 ±0.28	24.9 ±12.86	24.44 ±10.99	23.38 ±9.10
SGPT (IU/L)	23.72 ±12.91	33.26 ±66.23	31.09 ±55.6	24.60 ±11.56	26.02 ±21.51	26.05 ±24.48	26.16 ±19.39	23.79 ±22.3	23.73 ±15.97
Bilirubin (mg/dl)	0.76 ±0.21	0.81 ±0.26	0.78 ±0.22	0.79 ±0.44	0.78 ±0.24	0.75 ±0.21	0.78 ±0.24	0.77 ±0 .21	0.76 ±0.23
Blood Urea (mg/dl)	23.33 ±5.75	22.12 ±5.91	23.58 ±8.43	23.05 ±7.87	22.68 ±6.42	23.36 ±7.23	21.44 ±6.41	21.38 ±5.80	23.18 ±5.50
Creatinine (mg/dl)	0.89 ±0.14	0.91 ±0.15	0.92 ±0.16	0.92 ±0.17	0.91 ±0.17	0.93 ±0.14	0.93 ±0.17	0.92 ±0.16	0.94 ±0.18
Protein (gm/100ml)	7.04 ±0.45	6.92 ±0.55	7.08 ±0.51	6.97 ±0.50	7.12 ±0.48	7.20 ±0.59	7.20 ±0.52	7.21 ±0.52	7.07 ±0.52
Albumin (gm/100ml)	3.98 ±0.42	3.96 ±0.38	3.85 ±0.38	3.89 ±0.45	3.88 ±0.50	3.80 ±0.48	3.91 ±0.43	3.80 ±0.45	3.85 ±0.44
Globulin (gm/100ml)	3.09 ±0.57	3.02 ±0.52	3.24 ±0.62	3.03 ±0.62	3.21 ±0.61	3.34 ±0.56	3.27 ±0.58	3.37 ±0.59	3.20 ±0.49
A/ G Ratio	1.34 ±0.37	1.38 ±0.36	1.24 ±0.37	1.33 ±0.45	1.26 ±0.44	1.17 ±0.31	1.22 ±0.35	1.15 ±0.34	1.21 ±0.29

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Table 3.Effect of allopathic drug Melanocyl Tablet (Methoxsalen) on the levels of SGPT, SGOT, Bilirubin, Blood Urea and Serum Creatinine, Protein, Albumin, Globulin and A/ G ratio in vitiligo patients

Group Parameter	BL 0-Day	1st F-Up 30th day	2nd F-up 60th day	3rd F-up 90th day	4th F-up 120th day	5th F-up 150th day	6th F-up 180th day	7th F-up 210th day	8th F-up 240th day
SGOT (IU/L)	24.20 ±8.35	25.54 ±8.29	26.29 ±10.02	24.3 ±8.97	24.85 ±9.04	23.69 ±10.98	23.78 ±12.00	24.21 ±12.03	23.1 ±7.89
SGPT (IU/L)	25.04 ±13.13	24.9 ±10.79	24.04 ±15.34	24.97 ±14.19	23.39 ±21.51	24.18 ±24.48	23.91 ±19.39	22.48 ±22.3	20.40 ±15.97
Bilirubin (mg/dl)	0.73 ±0.22	0.71 ±0.22	1.09 ±2.97	0.69 ±0.22	1.11 ±3.16	0.74 ±0.25	0.70 ±0.23	0.71 ±0.22	0.71 ±0.24
Blood Urea (mg/dl)	21.74 ±6.47	21.49 ±6.34	22.09 ±7.76	23.01 ±6.92	21.14 ±6.66	21.95 ±8.19	21.14 ±6.22	22.03 ±6.26	23.16 ±6.88
Creatinine (mg/dl)	0.90 ±0.16	0.91 ±0.16	0.86 ±0.15	0.90 ±0.15	0.88 ±0.16	0.92 ±0.13	0.87 ±0.15	0.90 ±0.16	0.92 ±0.17
Protein (gm/100ml)	7.03 ±0.55	7.08 ±0.55	7.14 ±0.56	7.15 ±0.68	7.14 ±0.61	7.01 ±0.51	7.17 ±0.53	7.06 ±0.50	7.16 ±0.53
Albumin (gm/100ml)	4.00 ±0.43	4.03 ±0.42	3.87 ±0.37	3.92 ±0.48	3.86 ±0.50	3.84 ±0.44	3.91 ±0.44	3.88 ±0.38	3.95 ±0.80
Globulin (gm/100ml)	3.06 ±0.68	3.04 ±0.59	3.27 ±0.60	3.24 ±0.63	3.26 ±0.66	3.17 ±0.55	3.26 ±0.58	3.19 ±0.51	3.25 ±0.59
A/ G Ratio	1.37 ±0.38	1.37 ±0.38	1.22 ±0.35	1.27 ±0.39	1.23 ±0.37	1.22 ±0.30	1.23 ±0.35	1.24 ±0.28	1.25 ±0.26

Table 4.Effect of Unani coded drug UNIM-001+ UNIM-003 in the levels of Haemoglobin, R.B.C. Count, Total Leukocyte Count (T.L.C.), Erythrocyte Sedimentation Rate (E.S.R.), Polymorph, Lymphocyte and Eosinophil count in Vitiligo patients

Group Parameter	Haemoglobin (gm %)	R.B.C. (106 mm3)	T.L.C. (103/mm3)	ESR (mm /hr)		Platelets (Lac/mm3)	Polymorphs (%)	Lymphocyte (%)	Eosinophil (%)
				1st hrs	2nd hrs				
BL (0-Day)	12.53±1.97	4.16±0.61	7.91±1.9	31.0± 15.18	42.0 ±13.23	2.11±0.64	62.0 ±9.37	34.0 ±8.50	4.0 ±2.03
1st F-Up (30th-days)	11.99±2.22	4.01±0.72	7.85±1.71	33.0± 13.55	43.0 ±12.15	2.01±0.64	61.0 ±7.30	34.0 ±1.78	5.0 ±7.41
2nd F-up (60-Days)	12.34±1.81	4.09±0.65	7.75±1.88	32.0± 13.16	44.0 ±11.99	2.13±0.67	61.0 ±9.36	33.0 ±9.01	6.0 ±2.54
3rd F-up (90th-days)	12.33±1.90	4.12±0.66	7.68±1.60	32.0± 13.89	42.0 ±12.81	2.13±0.70	62.0 ±9.21	34.0 ±9.51	4.0 ±2.28
4rth F-up (120th-days)	12.20+1.77	4.06±0.61	7.68±1.89	34.0± 13.29	45.0 ±12.57	2.12±0.74	61.0 ±9.22	34.0 ±9.64	4.0 ±2.19
5th F-up (150th-days)	12.37±1.85	4.12±0.60	7.60±1.75	31.0± 14.19	42.0 ±13.47	2.11±0.54	63.0 ±8.39	32.0 ±8.81	5.0 ±2.43
6th F-up (180th-days)	12.47±1.81	4.16±0.59	7.55±1.55	32.0± 12.65	43.0 ±11.57	2.14±0.57	63.0 ±10.27	32.0 ±9.42	5.0 ±2.38
7th F-up (210th-days)	12.62±1.80	4.22±0.61	7.66±1.91	30.0± 14.78	41.0 ±13.91	2.09±0.66	63.0 ±9.70	32.0 ±8.83	5.0 ±2.06
8th F-up (240th-days)	12.40±1.77	4.22±0.59	7.42±1.36	30.0± 13.56	42.0 ±13.17	2.08±0.63	64.0 ±9.08	31.0 ±8.32	5.0 ±2.37

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Haematological Studies

In both trial and control group, no significant alterations in the level of hemoglobin, Red Blood Corpuscles (RBC), Total Leucocytes Counts (TLC), Erythrocyte Sedimentation Rate (ESR) and Differential Leucocytes Counts (DLC) had been observed. When compared with the values of baseline and different follow-up of treatment (Table 4 and 5). Similar observation had reported by other authors.[53,54,55]

Repigmentation Response

In trial group out 65 patients studied, 32 patients showed 0-20% Repigmentation, 27 patients showed 21-70% Repigmentation and 06 patients showed 71-100% Repigmentation. In control group out 67 patients studied, 36 patients showed 0-20% Repigmentation, 23 patients showed 21-70% Repigmentation and 08 patients showed 71-100% Repigmentation (Table 6). Nazim et al., 2018[56] had reported the safety and efficacy of many Unani drugs with different percentage of Repigmentation.

Conclusion

In modern medicine system various therapy such as topical corticosteroids, systemic drug, ultraviolet light therapy, Monochromatic Excimer Light laser (MEL) therapy, Combination of UV have recently been used for treatment of Vitiligo, but they all have certain side effects. Thus there is an urgent demand to identify herbal drugs and its active constituents, used as potential therapeutic agents for treatment of Vitiligo (bars).

On the basis of this study, it may be concluded that UNIM-001 Tablet and UNIM-003 topical drug. As well as comparator Drug (Melanocyl Tablet (Methoxsalen)) Possesses anti-Vitiligo effect. It can also be inferred that both the drug are safe as they did not induce any toxic effect, particularly on liver and kidney functions. Further studies are warranted in large group.

Table 5.Effect of Melanocyl tablets (methoxsalen) in the levels of Haemoglobin, R.B.C. Count, Total Leukocyte Count (T.L.C.), Erythrocyte Sedimentation Rate (E.S.R.), Polymorph, Lymphocyte and Eosinophil count in Vitiligo patients

Group Parameter	Haemoglobin (gm %)	R.B.C. (106/mm3)	T.L.C. (103/mm3)	ESR (mm/hr) 1st hrs 2nd hrs	Platelets (Lac/mm3)	Polymorphs (%)	Lymphocyte (%)	Eosinophil (%)	Group Parameter
BL (0-Day)	12.14±1.72	8.11 ±0.61	4.12 ±2.1	31.0 ±12.95	42.0 ±11.70	2.11 ±0.67	62.0 ±8.50	34.0 ±8.63	4.0±2.30
1st F-Up (30th-days)	12.01±1.81	4.07 ±0.63	7.54 ±2.00	31.00 ±12.69	42.0 ±11.96	2.07 ±0.72	61.0 ±9.34	35.0 ±9.73	4.0±2.38
2nd F-up (60th-Days)	12.00±1.86	4.03 ±0.61	7.70 ±2.00	30.0 ±13.37	41.0 ±12.67	2.05 ±0.69	61.0 ±9.45	34.0 ±9.47	5.0±2.46
3rd F-up (90th-days)	11.96±1.64	4.03 ±0.59	7.64 ±2.27	31.0 ±14.17	41.0 ±13.25	2.15 ±0.75	61.0 ±9.77	35.0 ±10.24	4.0±2.05
4rth F-up (120th-days)	12.09±1.67	4.08 ±0.55	7.45 ±1.88	30.0 ±14.21	41.0 ±13.38	2.15 ±0.77	61.0 ±7.81	35.0 ±8.15	4.0±1.95
5th F-up (150th-days)	12.10±1.73	4.08 ±0.56	7.16 ±1.60	31.0 ±14.46	42.0 ±13.35	2.15 ±0.70	61.0 ±9.27	34.0 ±9.51	5.0±2.55
6th F-up (180th-days)	12.12±1.72	4.04 ±0.51	7.42 ±2.13	31.0 ±14.46	42.0 ±13.35	2.15 ±0.70	61.0 ±9.27	34.0 ±9.51	5.0±2.55
7th F-up (210th-days)	12.14±1.70	4.09 ±0.55	7.39 ±1.88	30.0 ±13.98	41.0 ±13.29	2.14 ±0.76	63.0 ±9.93	33.0 ±9.69	4.0±2.39
8th F-up (240th-days)	12.22±1.85	4.14 ±0.61	7.41 ±1.65	30.0 ±13.49	42.0 ±12.39	2.19 ±0.68	61.0 ±9.53	34.0 ±9.86	5.0±2.34

Table 6.Effect of Unani coded drug UNIM-001+ UNIM-003 (Trial Group) and allopathic drug Melanocyl Tablet (Methoxsalen) (Control group) on percentage Repigmentation after post-treatment (240-days) in Vitiligo patients

Pigmentation in %age	Trial Group (n = 65)	Control Group (n = 67)
0-20% (No response)	32	36
21-70% (Partial Response)	27	23
71-100% (Response)	06	08

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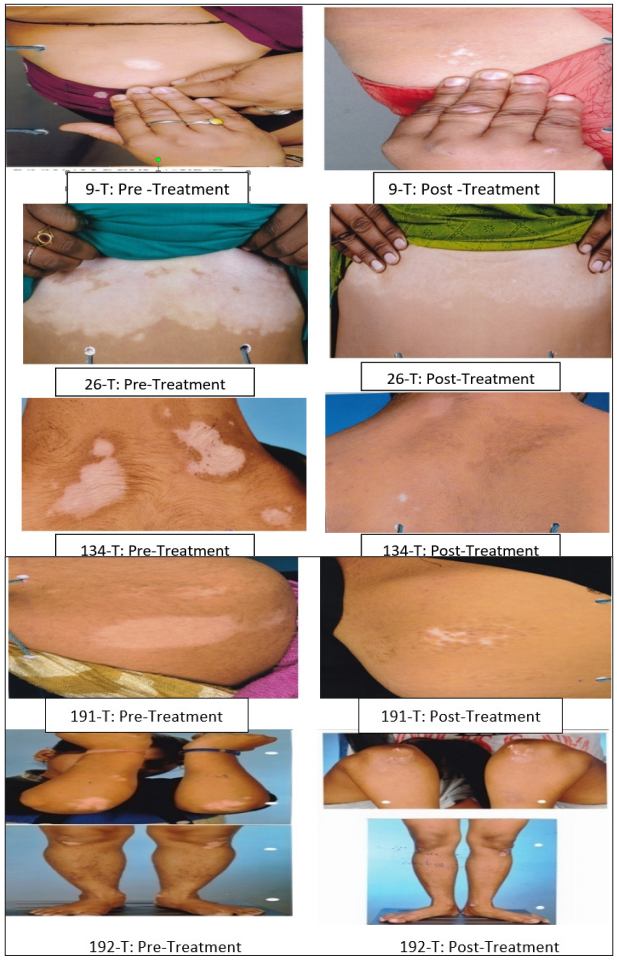

Figure 1.Photographs of trial group showing response to Unani coded drugs UNIM-001 Tablet and UNIM-003 topical in vitiligo patients. (pre-treatment= 0-day, post-treatment=240-days)

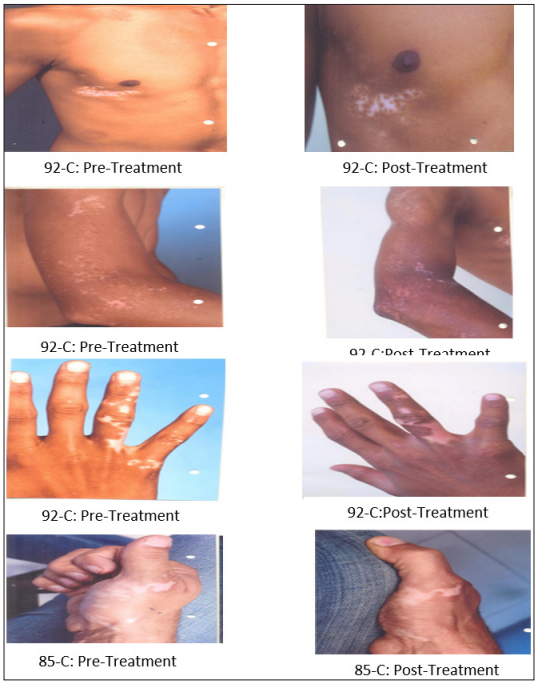

Figure 2.Photographs of Control group showing response of Melanocyl (Methoxsalen) Tablet in vitiligo patients. pre-treatment= 0-day, post-treatment=240-days

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