The Efficacy and Safety of Unani Coded Drug UNIM-046 in Cases of Bars (Vitiligo) - A Preliminary Clinical Trial

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Abstract

Vitiligo is an acquired idiopathic depigmentary condition characterized by the appearance of depigmented patches on the skin and/or mucous membrane. These patches may appear at various sites of the body, may be localized, segmental or generalized, of various colours e.g. hypopigmented, milky white or pink. This may affect both sex and all age groups. Though it does not affect the general health but considered a social stigma which leads to sociopsychological problems. This study was designed and carried out to evaluate the efficacy and safety of Unani drug UNIM-046 in vitiligo cases in RRIUM, Aligarh.

Out of 25 patients studied, 7 patients showed 40% repigmentation, 12 patients 41 to 70% repigmentation, 3 patients 71 to 90 % repigmentation and 3 patients 91 to 100% repigmentation on different affected parts of the body. In biochemical studies a significant reduction on the levels of Serum Total Protein ($P<0.01$) and Serum Albumin ($P<0.01$) was found; however UNIM-046 significantly increased the levels of Serum Globulin ($P<0.05$); while decreasing the A/G ratio ($P<0.001$) during follow-up in Bars patients. UNIM-046 significantly increases the levels of Serum Glutamate Pyruvate Transaminase (SGPT) ($P<0.01$), While a reduction in the level of Serum Glutamate Oxaloacetate Transaminase (SGOT) $P<0.01$) was observed whereas a significant increases in the levels of Serum Alkaline Phosphatase enzyme, (within normal limits) ($P<0.001$) was observed when compared with pre-treatment values. In haematological studies, a significant decrease in the levels of Erythrocyte Sedimentation Rate (ESR) ($P<0.01$), Red Blood Corpuscles (RBC) count ($P<0.01$) and lymphocyte Count ($P<0.01$) was observed. However, significant increase was observed in Eosinophil Count ($P<0.05$). Thus, test Unani formulation is suggested to be effective as well as safe for Bars patients.

Keywords: Bars, Vitiligo

Introduction

Vitiligo is an acquired idiopathic depigmentary condition characterized by the appearance of white patches on the skin or mucous membrane (Agrawal *et. al.*, 2001). These patches might be localized, segmental or generalized of various colours from milky white to pink. This disease does not affect the general physiology of the body but seriously threatens the social well being. It is a social stigma which leads to social embracement and psychological

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turmoil. It has been estimated that 1-2% of the world population is affected with this agony (Moser *et. al.,* 1999). In India the incidence among dermatology outdoor patients is estimated to be between 3 and 4 percent (Satish & Wahia*.,* 2000). The onset of the disease is reported before 20 years of age in 50% of the cases (Majumdar *et. al.*, 1993) and one third of the total cases of vitiligo were found having positive family history (Das *et. al.*, 1985).

In Unani system of medicine, the disease has been referred in the classics since antiquity and considered a skin disorder produced due to weakness of Quwwat-e-Mughayyara and Mushabbiha at tissue level due to coldness and / or preponderance of phlegm. Galen 130-200 AD) has the same view (Tabri Ahmad BinMohammed, ynm), Rabban Tabri (810-895 AD) (Tabri Abdul Hasan Ali Bin Sahl, 1981), underlined the Fasad-at-Dam (Impurity of blood) and Buroodat-at-Dam (Coldness of blood) to be responsible to this pathology. Avicenna (980-1037 AD) (Ibn Sina, 1906) also emphasizes the importance of Quwwat-e-Ghazia (Nutritive metabolism) which includes the Q. mughayyera and Q. Mushabbiha in pathogensis of the disease. The weaknesses of these faculties ultimately affect the natural process of the synthesis of melanin, a pigment in the melanocytes and responsible for normal skin colour. When the synthesis of melanin or distribution of melanocytes got affected, depigmentation or hypopigmentation occurs leading to vitiligo. Though the various theories regarding the pathogenesis of the disease have been put forward including immunological (Ongenae, *et.al.*; 2003), genetic (Xue *et.al.*, 2005), neural (Orecchia, G.; 2000) and biochemical but complete explanation is still obscured.

Keeping in view the sociopsychologiocal importance of the disease, the therapeutic potential of Unani drugs in this condition and the classical approaches of streamlining of the melanin synthesis. This study was designed and carried out as a clinical open trial with Unani Coded drug UNIM-046 in the cases of vitiligo. The objective of the study was to evaluate the therapeutic efficacy as well as the safety of the coded Unani drug UNIM-046 in the cases of vitiligo.

Materials and Methods

Subjects Selection

Forty eight patients attending in the out patients department (OPD), Regional Research Institute of Unani Medicine (RRIUM), Aligarh of either sex, age (10-60 yrs) were screened to assess the different biochemical and haematological

parameters. Out of forty eight patients, twenty five patients were selected for clinical trial. They were informed about the nature and objectives of trial and a written consent was obtained before enrolling them into the trial. UNIM-046 capsule and UNIM-046 cream were obtained from Central Council for Research in Unani Medicine, New Delhi.

Inclusion Criteria

Patients suffering from Bars (vitiligo) belonging to both sex and different age group (10-60 years) were selected for study. White patches on surfaces of skin neither elevated nor depressed having no exudation or scaling and no itching with hyperpigmented/ hypopigmented margin was taken as vitiligo patches without loss of sensitivity. Bars (Vitiligo) cases free from other systemic diseases, skin diseases and intestinal infestation were included in the study

Exclusion criteria

Pregnant women and patients with hepato-renal, cardiac and pulmonary malfunction, patients on active vitiligo treatment with other drugs, subjects with other skin diseases such as Leprosy, Pityriasis and albinism, subjects with known allergies, subjects who were unwilling to come for regular follow-up for the entire duration of the study and non-cooperative patients were excluded.

Diet restriction and recommendation

Diet plays an important role according to the Unani System of Medicine. As Unani classics relate Bars as a phlegmatic disorder which is attributed to cold and wet, hence any food articles which produces coolness and moistness in the body qualities were strictly prohibited.

Restricted Food Articles

Articles which produce Balgham (Phlegm) are milk and milk products, lemon and lime, tamarind, orange/ citrus fruits, parsley, custard apple, guava, prunes, cashew nuts, melon, water melon, Chinese dates, sour tomatoes and amla e.t.c. and articles which are supposed to bring changes in blood and make blood impure (Fasad-ud-dam) i.e. egg, fish, beef, brinjal and heavy and light mixed food was restricted.

Recommended Diet

Recommended food articles included Wheat, Indian Millet, Pulses, pure ghee obtained from butter, broad beans, French beans, Spinach, Bitter gourd,

Onion, Beet root, Carrot, Chillies, Black pepper, Maize, Figs (fresh and dry), Almond, Walnut, Dates, Mango, Apricots, Grapes, Potatoes, Rice, Papaya, Turnip, Mutton, Bird's flesh. Finally the diet was prescribed according to the patients need.

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 other 2.0-2.5 ml of blood samples were allowed to clot and serum was separated by centrifugation, which was used for various biochemical parameters. Biochemical and haematological investigations were carried out as follows.

Biochemical analysis

Biochemical parameters carried out are as follows. Serum Total Protein, Serum Albumin and Serum Globulin, Serum Glutamate Pyruvate Transaminase (SGPT, E.C. 2.6.1.2) and Serum Glutamate Oxaloacetate Transaminase (SGOT, E.C. 2.6.1.1.), Serum Alkaline Phosphatase enzyme (ALP).

Haematological analysis

Haematological parameters include: Haemoglobin (Hb %), Erythrocyte Sedimentation Rate (ESR), Total Leucocytes Counts (TLC), Red Blood Corpuscles (RBC) and Differential Leucocytes Counts (DLC): Polymorphs, Lymphocyte and Eosinophil Counts.

Drug, Dose and mode of administration

Compound Unani formulation coded drug UNIM-046 capsule, two capsules (500mg each) twice daily was given orally with water after meal to the patient. UNIM-046 cream was locally applied on affected area with exposure of early morning sun rays for 2-7 minutes daily.

Duration of treatment and follow-up

Duration of treatment of patients was 12- months. After registration of patients, a pre-treatment (0 days) and follow-up (3-months, 6-months, 9-months and 12-months) observations were made as per clinical diagnosis and by investigating Serum Glutamate Pyruvate Transaminase (SGPT), Serum Glutamate Oxaloacetate Transaminase (SGOT), Serum Alkaline Phosphatase

enzyme (ALP), Serum Total Protein and Serum Albumin, Serum Globulin and A/G ratio were done in biochemical investigations and Haemoglobin (Hb %), Erythrocyte Sedimentation Rate (ESR), Total Leucocytes Counts (TLC), Red Blood Corpuscles (RBC) and Differential Leucocytes Counts (DLC): Polymorphs Lymphocyte and Eosinophil Counts were done in haematological investigations.

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 less than 0.01.

Results and Discussions

Demographic Findings

Out of 37 patients of vitiligo, 29.73% patients were male and 70.27% female, which shows that female have higher incidence as compared to male. Shajil *et.al.*, 2006 had reported similar type of observations. 11-20 years of female and 21-30 years age group of male are more susceptible to vitiligo. Non-vegetarian had more incidences (56.75%) than vegetarian (43.24%). Middle income group had more incidences (59.45%) than low income group (40.54%). 26 cases (70.27%) have 0-5 years and 9 cases (24.32%) duration of this disease. The incidence was found more in Balghami patients 26 (54.05%) followed by Damvi 12 (32.43%).

Table 1: Showing distribution of patients according to Age and Sex.

Age group (in years)	Number & % of males	Number & % of Females	Total number & %
0-10	—	02 (5.41%)	02 (5.41%)
11-20	03 (8.11%)	15 (40.54%)	18 (48.64%)
21-30	05 (13.51%)	03 (8.11%)	08 (21.62%)
31-40	02 (5.41%)	02 (5.41%)	04 (10.81%)
41-50	01 (2.70%)	03 (8.11%)	04 (10.81%)
51-60	—	01 (2.70%)	01 (2.70%)
Total	11 (29.73%)	26 (70.27%)	37 (100.00%)

Table 2: Showing distribution of patients according to Dietary Habits.

S. No.	Dietary habits	Number of cases	%
1	Vegetarian	16	43.24%
2	Non-Vegetarian	21	56.75%
	Total	37	100.00%

Table 3: Showing distribution of patients according to Social status.

S. No.	Social status	Number of cases	%
1	HI group	—	—
2	MI group	22	59.45%
3	LI group	15	40.54%
	Total	37	100.00%

Table 4: Showing distribution of patients according to Chronicity of disease.

S. No.	Chronicity of disease (In years)	Number of cases	%
1	0-5	26	70.27%
2	6-10	9	24.32%
3	11-15	—	—
4	16-20	—	—
5	21-25	01	2.70%
6	26-30	—	—
7	31-35	01	2.70%
Total		37	100.00%

Table 5: Showing distribution of patients according to Temperament.

S. No.	Type of Temperament	Number of cases	%
1	Damvi	12	32.43%
2	Balghami	20	54.05%
3	Safravi	05	13.51%
4	Saudavi	—	—
	Total	37	100.00%

Pigmentation response

After completion of the treatment with Unani coded drug UNIM-046 (12th month), 7 (28 %) out of 25 patients showed 40% pigmentation, 12 (48%) patients showed 41-70% pigmentation, 3 (12 %) patients showed 71 to 90% pigmentation, 3 (12 %) patient showed 91 to 100% pigmentation affected on the different parts of the body in vitiligo patients.

Biochemical Studied

Serum Proteins

UNIM-046 significantly reduced the levels of Serum Total Protein 7.98% (P<0.01), 8.64% (P<0.001) and 6.12% (P<0.001) (3rd, 6th & 9th months), Serum Albumin 9.03% (P<0.05) and 14.0% (P<0.001) (3rd & 12th months), and A/G ratio 28.49% (P<0.05) (12th months) (Table-6), when compared with pre-treatment to the different (3rd to 12th months). A significant increase in the levels of Serum Globulin 13.7% (P<0.001) (12th month) (Table-1) were observed in Bars (Vitiligo) patients. *Verma et. al*., (2012) had reported similar type of observations in vitiligo patients treated with Unani coded drug UNIM-045.

Liver Function Tests

A significant increase in the level of the Serum Glutamate Pyruvate Transaminase (SGPT) 26.61% (P<0.05), 18.15% (P<0.01) and 12.21% (P<0.05) (3rd, 6th & 9th months), Serum Glutamate Oxaloacetate Transaminase level (SGOT) 14.67% (P<0.05), however significant decrease 11.94% (12th month) but within normal level was observed, when compared with pre-treatment to the different follow-up (Table-7). UNIM-046 significantly increased but within normal level of Serum Alkaline Phosphatase enzyme, 21.11% (P<0.05), 24.40% (P<0.001) and 28.33% (P<0.001) (6th, 9th & 12th months) were observed when compared with pre-treatment to the different follow-up (Table-7) in bars (vitiligo) patients.

Haematological Studies

In haematological studies UNIM-046 significantly decrease the levels of haemoglobin 3.72% ((P<0.01)) and 5.31 % (P<0.01) (9th & 12th months), Red blood corpuscles 7.27% (P<0.01) and 5.20% (P<0.05) (3rd & 6th months) and lymphocyte counts 11.85% (P<0.05), 16.71(P<0.001) (6th & 9th months) however a significant increase in the level of eosinophil counts 51.69% (P<0.01), 31.46% (P<0.05) and 30.30% (P<0.05) (3rd, 9th & 12th months) (Table-8) were observed, when compared with pre-treatment to different follow-ups in bars (vitiligo) patients. No concrete inference might be taken from these findings since sample size is small. However, the drug was found safe in general.

Conclusion

The drug UNIM-046 showed considerable repigmentation effect in vitiligo cases and it was found safe on biochemical as well as haematological

parameters. No untoward effect of the drug was noticed on clinical, biochemical and haematological parameters during the course of treatment

Table 6: Effect of Unani coded drug UNIM- 046 (Oral and local) on the level of Serum Total Protein, Serum Albumin, Serum Globulin and A / G ratio.

Group → / Parameter ↓	(Pre-treatment)	3 -Month	6-Month	9-Month	12-Month
Serum Total Protein (gm/dl)	7.52 ± 0.16	6.92 ± 0.90**	6.87 ± 0.14***	7.06 ± 0.16*	7.19 ± 0.17▪
Serum Albumin (gm/dl)	4.43 ± 0.14	4.03 ± 0.14*	4.19 ± 0.10▪	4.14 ± 0.11▪	3.81 ± 0.10***
Serum Globulin (gm/dl)	2.92 ± 0.18	2.93 ± 0.16▪	2.76 ± 0.16▪	2.67 ± 0.17▪	3.32 ± 0.15*
A/G Ratio	1.72 ± 0.16	1.49 ± 0.11▪	1.71 ± 0.15▪	1.76 ± 0.14▪	1.23 ± 0.08***

*P<0.05 significant **P<0.01 significant, ***P<0.001 highly significant

Table 7: Effect of Unani coded drug UNIM- 046 (Oral and local) on the levels of SGPT, SGOT and Serum Alkaline Phosphatase.

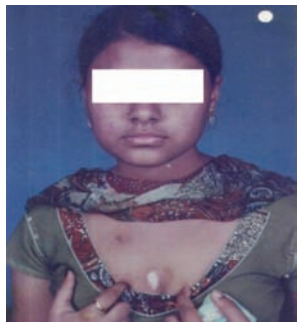
Group → / Parameter ↓	(Pre-treatment)	3 -Month	6-Month	9-Month	12-Month
SGPT (IU/L)	26.95 ± 2.06	34.12 ± .22**	31.84 ± 2.05**	30.24 ± 1.80*	26.32 ± 1.24▪
SGOT (IU/L)	29.99 ± 1.22	34.39 ± 1.63*	31.23 ± 2.64▪	28.16 ± 1.33▪	26.41 ± 0.81**
Serum Alkaline Phosphatase (IU/L)	69.60 ± 4.92	81.52 ± 5.87▪	84.29 ± 5.57*	86.58 ± .84***	89.32 ± .82***

*P<0.05 significant, **P<0.01 significant,***P<0.001 highly significant

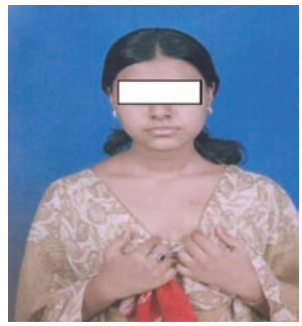
Table 8: Effect of Unani coded drug UNIM- 046 (Oral and local) on Haemogram.

Group → / Parameter ↓	(Pre-treatment)	3 -Month	6-Month	9-Month	12-Month
Haemoglobin (gm %)	12.63 ± 0.17	12.29 ± 0.24▪	12.19 ± 0.26▪	12.16 ± 0.20*	11.96 ± 0.21**
ESR (mm /hr)	22.16 ± 1.77	13.28 ± 1.70**	24.20 ± 3.11*	20.88 ± 3.14▪	18.36 ± 2.56▪
R.B.C. (10 6 /mm3)	3.85 ± 0.08	3.57 ± 0.09**	3.65 ± 0.09*	3.79 ± 0.08▪	3.74 ± 0.08▪
T.L.C. (103/mm3)	6.75 ± 0.32	6.46 ± 0.47▪	6.48 ± 0.45▪	6.39 ± 0.41▪	6.30 ± 0.35▪
Polymorphs (%)	62.64 ± 1.88	58.24 ± 1.98▪	66.40 ± 1.56▪	66.00 ± 1.73▪	62.56 ± 1.71▪
Lymphocyte (%)	33.76 ± 1.85	36.72 ± 1.96▪	29.76 ± 1.41*	28.12 ± 1.34**	33.12 ± 1.59▪
Eosinophil (%)	3.56 ± 0.32	5.40 ± 0.58**	4.08 ± 0.33▪	4.68 ± 0.5*4	4.64 ± 0.44*

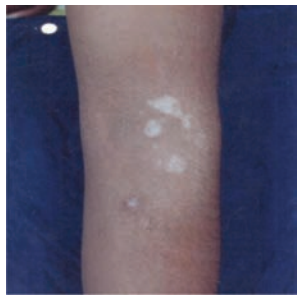
*P<0.05 Significant, **P<0.01 significant



Pre-treatment



After-treatment
(12-Month)



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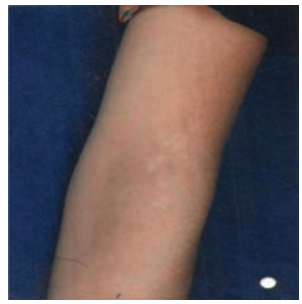
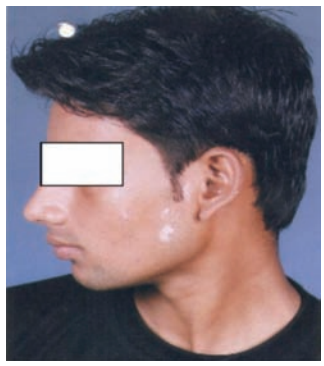


After- treatment
(12-Month)



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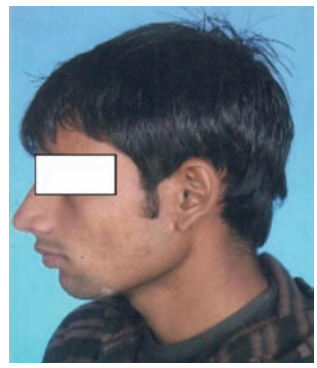

After- treatment
(12-Month)

Fig. 1 Photographs showing response to the Unani coded Drug UNIM-046 in Bars (Vitiligo) lesions

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