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CLINICAL STUDIES ON THE TREATMENT OF *BARAṢ* (VITILIGO) IN UNANI SYSTEM OF MEDICINE – A SYSTEMATIC REVIEW

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ABSTRACT

Background: *Baraṣ* (vitiligo) is an acquired pigmentary, multifactorial, polygenic disorder, with a complex pathogenesis that is not yet well understood. Out of various propounded theories, some accepted suggestions are the autoimmune destruction of melanocytes, melanocytes adhesion, neurogenic damage, auto-toxicity, etc. Although several treatment modalities are available in the present scenario, but they have their own limitations and the treatment challenges persist as it is. In Unani System of Medicine, *Baraṣ* is a well-recognized disease entity and has been treated successfully since antiquity with various single and compound drugs. In recent years, various clinical trials have been conducted to validate the claims of Unani Medicine in the management of *Baraṣ*. ***Objectives:*** Our objective was to review the published scientific clinical studies, performed to evaluate the safety and efficacy of Unani drugs in the treatment of *Baraṣ* (vitiligo). ***Methods:*** We searched 4 databases for vitiligo, using the terms "*Bars* OR vitiligo", "*Baraṣ* OR vitiligo", "Unani medicine" and "vitiligo". We also hand searched journals available in the Library of CRIUM, Hyderabad. Additional efforts were made by general Google searches and reference searches of Unani treatment in *Baraṣ*. Prospective clinical trials included in this review were either randomized or non-randomized and controlled or single or double arm. ***Results:*** A total of 63 articles were reviewed; out of them 50 articles based on animal studies, epidemiological reports, incomplete report, studies of general concepts, were discarded resulting into 13 articles. Different Unani drugs were used in the trials. Although each clinical trial reported beneficial effect, but very few trials were controlled and randomized. ***Authors' conclusions:*** There are too many clinical trials conducted to evaluate the safety and efficacy of Unani drugs in the treatment of vitiligo. But, appropriately designed, high quality clinical trials were not carried out and there was lack of standardized scoring system. Hence, it is still needed to conduct the well-designed randomized controlled clinical trials with standardized scoring system to scientifically validate the efficacy of Unani drugs in the treatment of *Baraṣ* (vitiligo).

KEYWORDS: *Baraṣ*, Bars, Vitiligo, Unani, Clinical Studies.

INTRODUCTION

Baraṣ (vitiligo) is an acquired pigmentary disorder, characterized by milky, white, hypo-pigmented, sharply demarcated macules.[1] It affects about 0.5% to 2% of the world population,[2] and is prevalent more than 8% in some regions of India.[3] It has a familial incidence of 25 to 30%.[4] It is psychologically devastating and frequently recalcitrant skin disorder.[5] It is mostly seen in the 2nd and 3rd decades of life. It has in general been classified into two major forms: Segmental vitiligo (typically unilateral macules, in a segmented/ band shaped distribution) and Non-Segmental vitiligo (bilateral macules often distributed in an acrofacial pattern or scattered symmetrically all over the body).[1]

Aetiology of vitiligo is poorly understood and under debate. Various hypotheses are put forwarded such as stress, neural abnormalities, melatonin receptor dysfunction, impaired melanocyte migration, genetic susceptibility, biochemical defects, autoimmunity etc.; the same mechanism may not apply to all cases. Three major hypotheses of pathogenesis of vitiligo are neural, autoimmune and oxidative stress; however, no one fully explains the pathogenesis of vitiligo. The autoimmune theory is currently the leading hypothesis and is supported by strong evidence. Other than this increased oxidative stress theory, accumulation of hydrogen peroxide epidermis, auto cytotoxicity and others have the evidences also.[1]

Concept of Vitiligo in Unani System of Medicine

Various eminent Unani physicians had given a comprehensive description of vitiligo and discussed its aetiology and treatment in details.

Zakariyya Rāzī (850-925 AD) has given a detailed description of *Baraṣ* (vitiligo) in his most famous book *Kitābal-Hāwī*. He described that vitiligo is curable if after rubbing, affected skin becomes red and if after pricking the lesion, whitish fluid comes out, the possibility of recovery is remote and vice versa. If the white patches are limited and non-extensive and the colour of the patches is yellowish or reddish, early cure can be expected. He also added that the patches on the head and feet do not respond to treatment adequately. *Rāzī* also described that after using the external application, exposure to sunlight activates the process of pigmentation. He also reported that pricking by needle on vitiligo patches is also an effective measure to treat the *Baraṣ* (vitiligo).[6]

Most of the Unani physicians including *Jālinūs*, as mentioned in *Mu'ālajāt-i Buqrāṭiyāh*,[7] *Ibn Sīnā* in *Al-Qānūn fi'l-Ṭib*,[8] *Jurjānī* in his book *Ḍhakhīra Khawārizm Shāhī*,[9] *Hakīm Akbar Arzānī* in his book *Ṭibb-i Akbar*,[10] and *Sadīd al-Dīn Gāzrūni* in the book *Al-Sadīdī*,[11] described the cause of vitiligo as *Ḍu'af-i Quwwat-i Mughayyira-i Badan* (transformative faculty,[12] the power that brings changes, and shapes the nutrients into tissues) and *Mushabbiha-i Badan* (power of resemblance[12]). 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.[13][9][11]

In Unani system of medicine, there are four principal modes of treatment. These are *'Ilāj bi'l Tadbīr* (Regimen Therapy), *'Ilāj bi'l Ghidhā'* (Dietotherapy), *'Ilāj bi'l Dawā'* (Pharmacotherapy), and *'Ilāj bi'l Yad* (Surgery).[14]

There is a vast description of the management of *Baraṣ* in the classical Unani literature, and the principles of treatment of *Baraṣ* are based on *'Ilāj bi'l Tadbīr*, *'Ilāj bi'l Ghidhā'* and *'Ilāj bi'l Dawā'*. In *'Ilāj bi'l-Tadbīr*, psychotherapy is given to assure the patient for its non-contagious character and building self-confidence in patient. In Dieto-therapy, the diet having hot properties is used. Cold and moist foods, fish, milk and milk products are to be avoided. In Pharmacotherapy, most of the Unani Physicians advised initially, the treatment with *Tanqiya-i Badan* (Removal of harmful material from the body). *Tanqiya-i Badan* is performed in three steps; by administering *Munḍij-i Balgham* drugs till *Nuzj* appears, followed by three *Mushil* (Purges) alternated with three *Tabrīd* (Cooling agents/drugs).[15]

Hippocrates and *Ibn-i Sarābiyūn* suggested that after *Tanqiya*, digestive system should be corrected by consuming easily digestible diet.[16]

At present, Unani medicine, the form of traditional medicine especially in India, is acquiring more support in primary healthcare. Various clinical trials have been undertaken in the light of Unani concepts. Thus, the primary objective of this review was to conclude the evidences derived from published clinical studies on *Baraṣ* (vitiligo) in Unani system of medicine.

METHODS

We performed the comprehensive literature searches of relevant articles published up to 2017 through electronic searches of AYUSH Research Portal, PubMed, SCOPUS, and also by Google Scholar advanced search, using the terms "Bars OR vitiligo", "*Baraṣ* OR vitiligo", "Unani medicine" and "vitiligo". Additionally, reference searching also attempted through Clinical Trial Registry - India (CTRI) database. We also hand searched journals available in library, CRIUM, Hyderabad, including Hippocratic Journal of Unani Medicine, Indian Journal of Unani Medicine, Cureall journal of Unani Medicine, Proceedings of International Conferences in Unani Medicine.

After performing the exhaust searches on electronic databases, it is found that there are very few results in main databases. After assessing the resulting lists, randomized or non-randomized, controlled, single arm or multiple arms, all clinical studies were included in the review.

RESULTS

A total of 63 articles were reviewed; out of them 50 articles based on animal studies, epidemiological reports, incomplete reports, studies of general concepts, were discarded leading to inclusion of 13 articles. Different Unani drugs were used in the trials. Although each clinical trial reported beneficial effect, but there were few trials that were controlled and randomized. Detailed summary of these studies is given in the Table 1.

Summary of Trials

Waheed MA et al, randomly assigned 75 participants in test and control group each. Participants in test group received, a coded Unani formulation – UNIM-005 in powder form for local application, after mixing with water followed by Sun exposure, and in control group bFGF (Basic Fibroblast Growth Factor) in liquid form was advised to apply in night around 8-9 PM followed by Sun exposure the next day. Participants received both treatments for 24 months and assessment of outcome was made by percentage of re-pigmentation. In segmental and focal type of vitiligo, a significant improvement was observed in test group as compared to control group, but in mucosal vitiligo there was less improvement in test group as compared to control group.[17]

Table 1: Summary of Clinical Studies

Study ID, Year and Design	Sample size	Interventions	Results
***Waheed M.A. et al* (2005)**[17] Randomized, controlled single blind clinical study	N = 150 Active = 75 Control = 75	**Group A** UNIM-005 for local application followed by Sun exposure **Group B** Basic Fibroblast Growth Factor (bFGF) for local application followed by Sun exposure	Mean percentage of re-pigmentation (%): **Group A** ***Segmental:*** 61.21 ± 18.12 ***Mucosal:*** 20.13 ± 13.18 ***Focal:*** 79.90 ± 0.23 **Group B** ***Segmental:*** 46.5 ± 4.89 ***Mucosal:*** 46.50 ± 4.89 ***Focal:*** 47.66 ± 4.70
***Zubair M* (2007)**[18] Randomized, Placebo controlled, single blind clinical study	N = 40 Test: 30 Control: 10	**Group A (Test)** *Safūf-i Baraṣ* filtered water 6 gm BD Local application of residue of powder followed by Sun exposure **Group B (Placebo)** Wheat flour capsule 1 BD	**Group A (Test)** Cured (100%): 3.40% cases Good response (71-90%): 26.80% cases Fair response (51-70%): 20% cases Slow response (41-50 %): 13% cases No response: 6.80% cases **Group B (Placebo)** No response
***Dilshad Ali* (2002)**[19] Non-randomized, single arm, open label clinical study	N = 40	***Safūf-i Baraṣ*** infusion 6 gm BD Local application of residue of infusion followed by Sun exposure	16 cases = Attained normal skin colour 19 cases Attained pink colour 5 cases = Remained white
***Anonymous* (2006)**[20] Non-randomized, single arm, double blind clinical study	N = 8000	**UNIM-001** 2 tablets of 500 mg each twice daily 1 hour after meal. **UNIM-003** Local application of powder mixing with water followed by Sun exposure Duration of therapy: 2 years	**Mean percentage of re-pigmentation** 112 cases = 100% repigmentation 139 cases = 91-99% repigmentation 461 cases = 71-90% repigmentation 1132 cases = 51-70% repigmentation 1810 cases = 41-50% repigmentation 3061 cases = ≤40% repigmentation 1285 cases = Nil response
***Anonymous* (2006)**[21] Non-randomized, single arm, double blind clinical study	N = 14000	**UNIM-004:** 2 tablets of 500 mg each twice daily. **UNIM-005:** Local application of powder mixing with water followed by Sun exposure	**Mean percentage of re-pigmentation** 296 cases = 100% repigmentation 526 cases = 91-99% repigmentation 1176 cases = 71-90% repigmentation 1864 cases = 51-70% repigmentation 4481 cases = 41-50% repigmentation 4081 cases = ≤40% repigmentation 1576 cases = Nil response
***Ansari K.B. et al* (2005)**[22] Non-randomized, double arm, double blind clinical study	N = 1278 Group. I – 644 Group II – 634	**Group I** UNIM-001: 500 mg BID, orally UNIM-003: Local application + exposure to Sunlight **Group II** UNIM-004: 500 mg BID, orally UNIM-005: Local application + exposure to Sunlight Duration of therapy: 1 year	**Mean percentage of repigmentation** ***Focal vitiligo*** Group I: 76.50 ±4.80, Group II: 81.12 ± 8.20 ***Mucosal vitiligo*** Group I: 47.40 ±4.67, Group II: 15.59 ± 3.28 ***Segmental*** Group I: 48.29 ±7.80, Group II: 61.13 ± 10.29 ***Acrofacial*** Group I: 62.26 ±1.12, Group II: 66.18 ± 12.13
***Anonymous* (2006)**[23] Non-randomized, double arm, double blind clinical study	N= 127 Group-1: Person with *Damwī* (Sanguine) temperament = 99 Group-2: Person with *Balghamī* (Phlegmatic) temperament = 28	**Group-I** UNIM-018+011+012+013 decoction X 40 days, UNIM-020: 3.5-7.0 gm daily UNIM-021 for local application followed by Sun exposure **Group-II** UNIM-010+011+012+013 UNIM-016: 2 gm daily after 5 days of MMT, UNIM-017: Local application followed by	**Percentage of repigmentation** **Group I** 71-90% in 01 case 51-70% in 01 case 41-50% in 12 cases up to 40% in 75 cases nil response in 10 cases **Group II** Up to 40% in 08 cases Nil response in 20 cases

		Sun exposure Duration of therapy: 1 year	
***Verma RS et al* (2012)**[24] Non-randomized, single arm, double blind clinical study	N = 23	**UNIM-045:** two Capsules twice daily orally **UNIM-045:** Cream for local application followed by Sun exposure Duration: 1 year	1 Case (4%): Complete repigmentation 8 Cases (35%): 71-90% repigmentation 8 Cases (35%): 41-70% repigmentation 6 Cases (26%): 40% repigmentation
***Tariq SSH et al* (2012)**[25] Non-randomized, single arm, open label clinical study	N = 40	**Bābchi *(Psoralea corylifolia)*:** *Zulāl* (filtered water) prepared by 5 gm powder + 50 ml water was given orally. Residue also applied locally on vitiligo patches	Patients with depigmented white patches: repigmentation in 71.4% cases Patients with depigmented pink patches: repigmentation in 66.6% cases
***Shareef MA et al* (2003)**[26] Non-randomized, single arm, open label clinical study	N = 240 A = 115 B = 125	**Group A** Powder of *Sadāb* 1.5 gm BD orally with water Powder of *Sadāb* with Vinegar also applied locally **Group B** Powder of *Atrīlāl* 1.5 gm BD orally with water Powder of *Atrīlāl* with Vinegar also applied locally	**Mean percentage of repigmentation** **Group A** 26 cases = Excellent response (75-100%) 32 cases = Good response (50-75%) 57 cases = Fair response (<50%) **Group B** 48 cases = Excellent response 21 cases = Good response 56 cases = Fair response
***Hussain S.J. et al* (1991)**[27] Non-randomized, single arm, open label clinical study	N = 30	Tablets prepared by powdered *Atrīlāl* was given 2 TDS orally after meals Duration of therapy: 6 months to 2 years	7 Patients: +++ (Complete repigmentation) 16 Patients: ++ (Follicular stippling) 7 Patients: + (Marginal repigmentation)
***Ishaquddin M* (2007)**[28] Non-randomized, single arm, open label clinical study	N = 40	Filtered water of 10 gm Powder of Combination of ***Gandhak Āmla Sār*** *(Sublimated sulphur),* ***Gerū*** *(Red ochre),* ***Gulnār Fārsī*** *(Punica granatum),* and ***Bābchi*** seeds *(Psoralea corylifolia),* administered orally in two divided doses Residue of powder was applied on lesion after mixing with vinegar Duration of therapy: 90 days	**Improvement in** Depigmented white patches: 50% Depigmented pink patches: 40% White discharge on pricking: 60%
***Anonymous* (2005)**[29] Non-randomized, single arm, double blind clinical study	N = 2186	Munḍij: Decoction of UNIM-040+041+042 (5+5+5 gm) for 7-90 days according to *Nuzj* appeared *Mushil* (purgative) and *Tabrīd* (cooling drugs) were given alternate days for 3 days.	Up to 40% repigmentation occured in all 2186 cases

Zubair M, enrolled 30 participants in test group, and 6 gm of *Safūf-i Baraṣ* was given twice daily in the form of *Zulāl* (filtered water), and its residue was advised to apply locally. In control group (placebo), 10 participants were enrolled and advised to take 1 wheat flour capsule (placebo) twice daily for 4 months' duration. Significant difference in response was found, favouring test drug over the placebo, with 3.4% cured, good response in 26.8%, fair response in 20% and slow response in 13% cases, while no response was seen in cases receiving placebo. However, small sample size (n=40) may have been compromised the validity of study. There were no serious adverse effects reported by the author.[18]Another author, *Dilshad Ali* also used the same intervention on 40 participants for 4 months, but without any control and randomization, resulting into the 16 cases to normal skin colour, 19 cases to slow response and 5 cases to no response.[19]

A single arm clinical study with large sample size (n=14,000) was conducted with 2 Coded poly-herbal Unani formulations, UNIM-004: two tablets (500 mg

each) twice daily after meals and to apply the UNIM-005 powder mixing with water early in the morning followed by Sun exposure for 24 months' duration. The outcome measured by mean percentage of re-pigmentation was 100% in 112 cases, 91-90% in 139 cases, 71-90% in 461 cases, 51-70% in 1132 cases, 41-50% in 1810 cases, less than 40% in 3061 cases, and nil response in 1285 cases. No adverse effects were reported.[21]

Another non randomized, single arm clinical study was conducted on 8000 participants. Participants in this study received, a coded polyherbal Unani formulation – UNIM-001 in the dose of 2 tablets (500 mg each) twice daily 1 hour after meals, and UNIM-003 powder for local application in early morning after mixing with water followed by Sun exposure for 24 months. A significant improvement was seen having 100% mean percentage of re-pigmentation in 296 cases, 91-99% in 526 cases, 71-90% in 1176 cases, 51-70% in 1864 cases, 41-50% in 4481 cases, less than 40% in 4081 cases and nil response in 1576 cases. The main lacuna in the study was lack of randomization and control group.[20]

Ansari K.B. et al, conducted a comparative clinical study on 634 and 644 participants in Group I and Group II respectively and compared the effect of two combinations of coded Unani formulations (Group-I: UNIM-001 + UNIM-003 and Group II: UNIM-004 + UNIM-005). Only focal, mucosal, segmental and acrofacial type of vitiligo participants were included. The doses and duration of treatment were same as described in above two studies, and significant results were reported in both groups. In focal vitiligo, mean percentage of re-pigmentation was 76.50 ±4.80 in Group I and 81.12 ± 8.20 in Group II. In Mucosal vitiligo it was 47.40 ±4.67 in Group I and 15.59 ± 3.28 in Group II, so it was more significant in Group I as compared to Group II. In segmental vitiligo, Group-II showed more significant repigmentation, i.e., 61.13 ± 10.29 as compared to 48.29 ±7.80 in Group-I. In acrofacial vitiligo, also Group II had more significant result, i.e., 66.18 ± 12.13 as compared to 62.26 ±1.12 in Group I. Author reported the drugs safe and effective in this study.[22]

Another double arm clinical study was conducted on 127 patients of vitiligo aged 20-50 years, with disease chronicity of 1 year. Interventions were given on the principles of Unani medicine described by famous Unani physician *Avicenna* in his treatise *"Canon of Medicine"*. Accordingly, *Munḍij-Mushil* (MM) Therapy was given in vitiligo patients of *Damwī* and *Balghamī* temperament. In Group I (*Damwī* temperament, n = 99), coded Unani formulations UNIM-018 (decoction of 26 g Unani drugs) + UNIM-011 (250 mg tablet) + UNIM-012 (decoction of 36 g Unani drugs) + UNIM-013 (decoction of 31 g Unani drugs) were given in the form of decoction for 40 days, it is called as *Munḍij Mushil* Therapy. After 5 days' gap, UNIM-020 (*Ma'jūn*) was given in the dose of 3.5-7 gm, every day orally with external application of UNIM-021 followed by Sun exposure. In Group-II (*Balghamī temperament, n = 28*): UNIM-010 (decoction of 30g Unani drugs) + UNIM-011+012+013 were given in the same dose as in Group I, then coded Unani formulation UNIM-016 was given in the dose of 2 gm daily orally. After 5 days of MM Therapy, UNIM-017 was applied locally followed by Sun exposure. Duration of the trial was 1 year. The percentage of re-pigmentation in *Damwī (Group-I)*was 71-99% in 1 case, 51-70% in 1 case, 41-50% in 12 cases and up to 40% in 75 cases and nil response in 10 cases, while in *Balghamī* (Group-II) repigmentation was up to 40% in 8 cases and nil in 20 cases. The response to treatment was better in *Damwī* temperament group, but not up to the mark. Also the SOPs for MM Therapy were not established.[23]

Verma et al, conducted a single blind, single arm clinical study on23 participants of vitiligo aged 10-60 years. A coded Unani drugUNIM-045 was given in the dose of 2 capsules twice a day and UNIM-045 cream for local application followed by Sun exposure in the morning for 1 year. The percentage of repigmentation was 100%, 71-90%, 41-70% and 40% in 1, 8, 8 and 6 participants respectively. Though good improvement was reported, but it is less significant due to small sample size (n=23).[24]

The subjects of vitiligo aged 10 – 60 years, (n=40) recruited by *Tariq SSH et al*, in a single arm open label clinical study. *Zulāl* (filtered water) obtained by mixing 5 gm *Bābchi (Psoralea corylifolia)* powder in 50 ml water and keeping it overnight, and filtering it in the morning was given orally daily. The *Thufl* (residue) of this powder was advised to apply locally. Repigmentation was achieved in 71.4% and 66.6% cases with white depigmented patches and pink depigmented patches respectively. However, author concluded that effect of drug was significant without any adverse effect, but no standard parameters for assessment of efficacy were adopted.[25]

Shareef MA et al, assigned 115 and 125 vitiligo patients in Group A and B respectively with age group 01-70 years. Group A received 1.5 gm powder of *Sadāb (Ruta graveolens)* twice daily orally and powder of *Sadāb* after mixing with vinegar was advised to apply locally. Patients in Group B received 1.5 gm powder of *Atrilāl (Ammi majus)* twice daily orally and *Atrilāl* mixed with vinegar was applied locally. Response to treatment was more significant in Group B than in Group A. Repigmentation achieved was 75-100%, 50-75% and below 50% in 48, 21 and 56 participants respectively in Group B and 26, 32, and 57 participants respectively in Group A. Author reported significant re-pigmentation in both groups and no adverse effects were reported.[26]

A single arm clinical study with MM Therapy was conducted on 2,186 patients of vitiligo. Decoction of UNIM-040+041+042 (5+5+5 gm) boiled in 120ml water

was given early in the morning empty stomach till the *Nuzj* appeared in the urine. After this, *Mushil* (purgative) and *Tabrīd* (cooling drugs) were given alternate days for 3 days. Duration of therapy ranged from 7-90 days according to *Nuzj* appeared. Repigmentation achieved was 40% in all 2,186 participants, and no adverse effects were reported. According to this study, improvement was seen in each and every case in a very short duration, showing a holistic approach to treatment of vitiligo with MM Therapy as described in Unani classical text.[29]

Ishaquddin M, conducted a single arm, open label clinical study on 40 vitiligo patients of either sex aged 10-60 years. Intervention given was filtered water of 10 gm Powder of combination of *Gandhak Amlā Sār* (Sublimated sulphur), *Gerū* (Red ochre), Gulnār Fārsī *(Punica granatum)*, and Bābchi seeds *(Psoralea corylifolia)* that was obtained by keeping the mixture overnight and filtering it in the morning, administered orally in two divided doses. Residue of powder was applied on lesion after mixing with vinegar for 90 days. This resulted into the improvement in 50% of white patches.[28]

Hussain S.J. et al, enrolled 30 participants in single arm clinical study on vitiligo. The powdered *Atrilāl* was given in the dose of 2 tablets (750 mg each) thrice daily orally after meals for a period of 6 months to 2 years. Seven cases showed complete re-pigmentation, 16 cases showed follicular stippling and 07 cases showed marginal re-pigmentation. Author did not report any adverse effect of the drug.[27]

DISCUSSION

The objective of this systematic review was to combine and summarize the data from individual randomized controlled clinical trials performed to evaluate the safety and efficacy of Unani drugs in the treatment of vitiligo, but most of such trials were uncontrolled and non-randomized. Only two randomized controlled clinical trials could be found, which also varied in study design, outcome measures, and methodology. However, outcomes of these studies revealed significant results but these trials are not enough to provide the evidence. Some other single arm/ double arm studies without any control group were conducted and showed good results. But, these studies also varied widely in methodology, design, intervention and outcome measures. Different re-pigmentation ranges were set by different authors. The meta-analysis of the studies could not be done as no standard scoring system was applied to measure the outcome.

CONCLUSION

Various clinical studies evaluating the safety and efficacy of Unani drugs in the treatment of vitiligo have been carried out, but well-designed randomized controlled clinical trials (RCTs) still need to be conducted to scientifically validate the safety and efficacy of Unani drugs in the treatment of *Baraṣ* (vitiligo). Some scanning devices like Vectra WB360 may be used for accurate 3D imaging solution[30]; and validated tools like Vitiligo Area Scoring Index (VASI), vitiligo European Task Force (VETF)[31] and Vitiligo Diseases Activity score (VIDA), may be used for the assessment of response to treatment.

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REFERENCES

1. Christopher G, Barker J, Bleiker T, Robert C, Creamer D. Rook's Textbook of Dermatology [Internet]. 9th editio. Wiley-Blackwell; 2016. Available from: http://doi.wiley.com/10.1002/9781118441213
2. Krüger C, Schallreuter KU. A review of the worldwide prevalence of vitiligo in children/adolescents and adults. Int J Dermatol [Internet]. 2012 Oct [cited 2018 Apr 4]; 51(10): 1206–12. Available from: http://doi.wiley.com/10.1111/j.1365-4632.2011.05377.x
3. James WD (William D, Elston DM, Berger TG, Andrews GC. Andrews' Diseases of the skin : clinical dermatology. Saunders Elsevier, 2011; 910 p.
4. Sams WM, Lynch PJ. Principles and practice of dermatology [Internet]. Churchill Livingstone; 1990 [cited 2018 Apr 9]. 1014 p. Available from: https://www.mendeley.com/research-papers/principles-practice-dermatology/?utm_source=desktop&utm_medium=1.17.13&utm_campaign=open_catalog&userDocumentId=%7B1ce3b56e-614a-49cb-a1e8-5b076624ed19%7D
5. Yaghoobi R, Omidian M, Bagherani N. Vitiligo: a review of the published work. J Dermatol [Internet]. 2011 May [cited 2018 Apr 9]; 38(5): 419–31. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21667529
6. Rāzī ABM ibn Z. Kitab al-Hawi f'il Tibb (Arabic version) Vol-23. Hyderabad: Dairatul Marif, Osmania University, 1970; 72-75 p.
7. Ṭabrī A Ḥasan A bin M. Al-Mu'ālajat al-Buqrāṭiya (Vol-II). New Delhi: Central Council For Research in Unani Medicine, 1997; 199-200 p.
8. Ibn Sīnā al-S al-RA 'Ali al-H ibn 'Abd A. Al-Qānūn fi'l Ṭibb. 1st ed. Kantoori GH, editor. Lahore: Shaikh Muhammad Basheer and Sons, Urdu Bazar; 351-353 p.
9. Jurjāni AH. Dhakhīra Khawārizm Shāhī. Khan HHH, editor. New Delhi: Idara Kitab-us-Shifa, 2075, Kucha Chelan, Darya Ganj, 2010; 8: 18.
10. Arzānī HA. Ṭibb-i Akbar. Husain AHM, editor. Deoband, 247554: Faisal publications, Jama Masjid,

731-732 p.
11. Gāzrūnī S al-D. Al-Sadīdī (Arabic). Lucknow: Maṭba Munshi Nawal Kishor, 61-62 p.
12. Standard Unani Medical Terminology. New Delhi: Central Council For Research in Unani Medicine, 2012; 32 p.
13. Rāzī ABM ibn Z. Kitāb al-Mansūri (Urdu translation). New Delhi: Central Council For Research in Unani Medicine, 1991; 207 p.
14. DC NC. UNANI | National Health Portal Of India [Internet]. Therapeutic approaches and treatment modalities. 2016 [cited 2018 Apr 21]. Available from: https://www.nhp.gov.in/unani_mty
15. Standard Unani Treatment Guidelines for Common Diseases. New Delhi: Central Council For Research in Unani Medicine, 2014; 180-182 p.
16. Ali MI, Khan MMA, Shakera AR. Seminar on Bars (Leucoderma) 10th - 11th March, 1979, Hyderabad. In Hyderabad: Central Council For Research in Unani Medicine, 1979; p. 6.
17. Abdul Waheed M, Ramaih A, S.J. H, Jabeen F, Ahmad N. Drug UNIM-005 (herbal compound drug) and bFGF (basic fibroblast growth factor) in the treatment of stable vitiligo lesions. Hippocrat J Unani Med., 2005; 1(1): 41–5.
18. Zubair M. Clinical Study and Management of Bars with Unani Formulation. Rajiv Gandhi University of Health Sciences, 2007.
19. Dilshad Ali, Mannan A, Misbahuddin S. Bars aur uskey ilaj mein safoof bars ki ifadiat ka jaiza. Vol. 2, Unani Medicus - An International Journal. Aligarh Muslim University, 2015.
20. Clinical trials of Unani drugs on Baras: Trial-1; UNIM-001+UNIM-003 (Oral medicine with paste for local application). In: Monograph on Bars (Vitiligo): [Internet]. New Delhi: Central Council For Research in Unani Medicine, 2006; p. 47–56. Available from: http://ccrum.res.in/writereaddata/UploadFile/tr4_1350.pdf
21. Clinical trials of Unani drugs on Baras: Trial-2; UNIM-004+UNIM-005 (Oral medicine with paste for local application). In: Monograph on Bars (Vitiligo): New Delhi: Central Council For Research in Unani Medicine, 2006; 57–65.
22. Ansari KB, Ahmad M, Waheed MA, Hussain SJ. Unani drugs UNIM-001+003 and UNIM-004+005 in the treatment of Vitiligo of different somatic appearances. In: Proceedings International Conference on Unani Medicine. Vigyan Bhawan, New Delhi: Central Council For Research in Unani Medicine, 2005; 113–7.
23. Avicenna's Approach to Management of Bars (Vitiligo): Trial of Munzij & Mushil and topical & oral drugs in vitiligo cases of Balghami (phelgmatic) and Damavi (sanguine) temperament. In: Monograph on Bars (Vitiligo). New Delhi: Central Council For Research in Unani Medicine, 2006; 125.
24. Verma R, Khan P, Naseem M, Ali Khan L. A Clinical study of the Unani formulation UNIM-045 for anti-Vitiligo effect. [Internet]. Vol. 7, Hippocratic Journal of Unani Medicine, 2013; 31-40 p. Available from: http://ccrum.res.in/writereaddata/UploadFile/Hippocratic2_1448.pdf
25. Tariq SSH, Aleem S, Latafat T. Clinical evaluation of Babchi (Psoralea corylifolia Linn.) in Bars (Vitiligo) - An Open Study. Hippocrat J Unani Med [Internet]., 2012; 7(1): 13–8. Available from: http://ccrum.res.in/writereaddata/UploadFile/Hippocratic_1982.pdf
26. Shareef MA, Hussain SJ, Parveen S, Lateef A, Zaidi ST., Ahmed Z, et al. Clinical screening of Atrilal and Sadab on Bars (Vitiligo) cases - A comparative study. Cureall J Unani Med., 2003; 1(3 & 4): 28–31.
27. Hussain SJ, Taiyab M, Zakiuddin. Effect of Atrilal on Biochemical Changes in Cases of Vitiligo. Indian J Unani Med., 1991; 1(1): 18–28.
28. Ishaquddin ARM, Badarudduja K, A M. Clinical evaluation of a combination of gandhak amla sar, geru, gulnar and babchi in vitiligo (leucoderma). Vol. 2, Unani Medicus - An International Journal. Aligarh Muslim University, 2015.
29. Clinical trials of Unani drugs on Baras: Trial-8; Munzij and Mushil Therapy (UNIM-040+041+042). In: Monograph on Bars (Vitiligo): New Delhi: Central Council For Research in Unani Medicine, 2006; 120–4.
30. Hayashi M, Okamura K, Araki Y, … MS-J of, 2016 undefined. A novel three dimensional imaging method for the measurement of area in vitiligo and chemical leukoderma. jdsjournal.com [Internet]. [cited 2018 Apr 19]; Available from: https://www.jdsjournal.com/article/S0923-1811(16)30713-7/fulltext
31. Komen L, da Graça V, Wolkerstorfer A, de Rie MA, Terwee CB, van der Veen JPW. Vitiligo Area Scoring Index and Vitiligo European Task Force assessment: reliable and responsive instruments to measure the degree of depigmentation in vitiligo. Br J Dermatol [Internet]. 2015 Feb [cited 2018 Apr 19]; 172(2): 437–43. Available from: http://doi.wiley.com/10.1111/bjd.13432