Section A-Research paper

Clinical study of *Buthur Labaniyya* (Acne vulgaris) with therapeutic evaluation of a topical unani drug, *Shoniz* (*Nigella Sativa*) and *Sirka* (vinegar) in its management

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ABSTRACT

Background: Acne vulgaris is a common skin condition that primarily affects adolescents and significantly impacts their quality of life. It ranks as the 8th most prevalent disease globally, with an estimated prevalence of 9.4% in the global population. Despite the availability of various treatment options, acne remains a distressing issue for adolescents due to the presence of disfiguring marks and scars. This study aimed to evaluate the safety and efficacy of a topical Unani drug, Shoniz (*Nigella sativa*), and Sirka (*Grape vinegar*), in the management of acne. **Methods:** A randomized, open-label, standard controlled study was conducted with 60 patients diagnosed with acne, aged between 10 to 40 years, who met the inclusion criteria. The participants were randomly assigned to receive either local application of Shoniz (*Nigella sativa*) and Sirka (*Grape vinegar*) or Benzoyl peroxide 5% cream for a duration of 56 days. The study was conducted after obtaining ethical approval (Reference no. RRIUM/KU/2018-19/Tech/IEC dated 29/3/2019) and was registered in the Clinical Trials Registry India (CTRI) with registration number CTRI/2020/06/025718. Acne severity was assessed using a grading scale at baseline (day 0) and on days 15, 29, 43, and 57. Baseline investigations were conducted before and after the treatment period. **Results:** Objective parameters showed significant improvement within both the test and control groups (p-value < 0.0001). There was no significant difference between the test and control groups in terms of lesion improvement, indicating that the test drug (*Nigella sativa paste with Sirka*) was equally effective in treating acne compared to the control drug (Benzoyl peroxide cream). However, the test drug had a more significant effect on papules

compared to the control drug (p-value < 0.001). **Conclusion:** The local application of Shoniz (*Nigella sativa*) and *Sirka* (Grape vinegar) in paste form demonstrated effectiveness in improving acne and can be considered as a viable treatment option for this condition. The treatment was generally well tolerated by the participants.

Keywords: Buthur Labaniyya, Acne Vulgaris, Shoniz, Sirka, Nigella Sativa, Comedones.

Introduction:

Acne vulgaris is a very common condition with lifetime prevalence of approximately 85% and occurs mostly during adolescence. It can persist into adulthood, with a 50.9% prevalence rate of acne in women aged 20-29 years versus 26.3% in women aged 40-49 years. Female patients account for two thirds of visits made to dermatologists for acne.[1] Despite a number of treatment options available, acne still remains a nightmare for adolescents because of emotional stress, disfigurement and even permanent scarring of skin.[2] Acne vulgaris is hormonal in origin and results from a complex interplay of increased sebum production, ductal hypercornification, follicular colonization with *P. acnes*, and inflammation.[3] Genetics, family history of severe acne, diet (glycemic index), occlusive cosmetics, and occupational exposures also contribute to pathogenesis of acne.[1] Unani, an age – old traditional system of medicine, which is based on 'humoral theory' proposed by Hippocrates (480-370 B.C), the father of medicine, states that Acne vulgaris (*Buthūr Labaniyya*) lesions are the white eruptions on nose and cheeks which resemble condensed milk droplets.[4,5] These small white eruptions on nose and cheeks are caused by *madda sadeediya* (infected/suppurative matter) which comes towards the surface of the skin due to *bukhārāt-i-badan* (vapors of the body).[6]

For evaluating the patients of acne, a grading system has been framed by Indian authors which divides acne into four grades.[7] Commonly used drugs for treating bothersome acne are antibiotics like doxycycline and minocycline (oral); and topical drugs like retinoids and benzoyl peroxide. Although these are effective but there are side effects like nausea; pigmentation of skin, mucosae and nails, teratogenicity, vaginal candidiasis and resistance of *P. acnes* to antibiotics, photosensitivity and skin irritation.[8] In Unani system of medicine natural herbs which are comparatively safer have been in use for centuries for treating acne. These herbs, however, need to be evaluated on scientific parameters. To avoid side effects of conventional medicine, a study was conducted to evaluate the efficacy of *shonīz* and sirka paste in the treatment of acne.

Shonīz and *sirka* paste was selected because *shonīz* has detergent, anti-phlegmatic, anti-inflammatory, anti-oxidant and anti-bacterial properties[9,10,11,12,13] while *sirka* has desiccant,[11] resolvent,[14] astringent, demulcent,[15] antiseptic, deobstruent, and quickly infusible properties.[16]

Materials and methods:

An open, randomized, standard controlled trial was conducted in the year 2020 to 2021 at Regional Research Institute of Unani Medicine, Srinagar Kashmir, after gaining approval on 29-03-2019 from institutional ethical committee (Regional Research Institute of Unani Medicine, Central Council for Research in Unani Medicine, Ministry of AYUSH Government of India). A written informed consent was obtained from all the participating patients. Diagnosis and selection of the cases was made on the basis of case history, clinical features, and other necessary investigations along with safety parameters : Hb%, TLC,DLC,ESR, blood urea, serum creatinine, SGOT, SGPT, Serum alkaline phosphatase, Serum bilirubin, blood sugar; and USG (to exclude PCOS patients).

Case selection criteria:

Inclusion criteria

Patients in the age group of 10 to 40 years complaining of comedones, papules, pustules, itching and erythema were included.

Exclusion criteria

Patients <10 and > 40 years of age, pregnant & lactating females, mentally retarded persons, patients with severe acne, those on corticosteroid, anticonvulsant therapy or oral contraceptives, patients of acne rosacea, acne fulminans, acne necrotica, psoriasis, eczema etc. or patients of PCOD, diabetes mellitus, CKD and chronic liver disease, thyroid disease, those allergic to benzoyl peroxide , or those with history of treatment with benzoyl peroxide in past 30 days and patients who failed to give consent were excluded.

Intervention:

Test group: Paste of *shonīz* with grape *sirka* (diluted with water in the ratio of 1:1) was applied on acne lesions avoiding the area around eyes, till it dried and then washed with water. For the

first three days paste was applied only once a day followed by two time application afterwards.

Control group: Benzoyl peroxide 5% cream was applied on acne lesions once a day (avoiding area around eyes) and washed off after an hour for the first three days followed by two time application afterwards without removing the cream after an hour.

Both the drugs were continued for a period of 8 weeks at the most after taking written informed consent from the patients. Compliance was evaluated by the return of used packs.

Assessment:

All the patients having acne were assessed by using acne severity scale (modified as per acne grading system by Indian authors)[7] and photos of lesions at baseline (0^{th} day) and on 15^{th}, 29^{th}, 43^{th}, and 57^{th} day. Various safety parameters were also checked before (0^{th} day) and after study (57^{th} day) to evaluate the safety of the test drug.

Grade 1	Papules and few pustules
Grade 2	Pustules and few papules
Grade 3	Nodules with few pustules
Grade 4	Nodules and scarring

Data analysis:

Data was entered in a spread sheet and then exported to data editor of SPSS version 20.0 and Graph pad prism software. The continuous variables were expressed as mean ± standard deviation and categorical variables were expressed in terms of frequency and percentage. Chi-square test was employed for inter group comparison of categorical variables. Student's independent t-test was employed for inter-group analysis of data and for intra-group analysis paired t-test was applied subject to the condition that data is measured on continuous scale and satisfies assumption of normality. However, if the assumption of normality did not hold we applied Friedman's test for the intra group with different follow-ups and Mann-Whitney U test was employed for the intergroup (test vs. control) comparison of data at different follow-ups. . The graphical representation of data was presented by means of 3D bar and line graphs. A p-value of less than 0.05 was considered statistically significant.

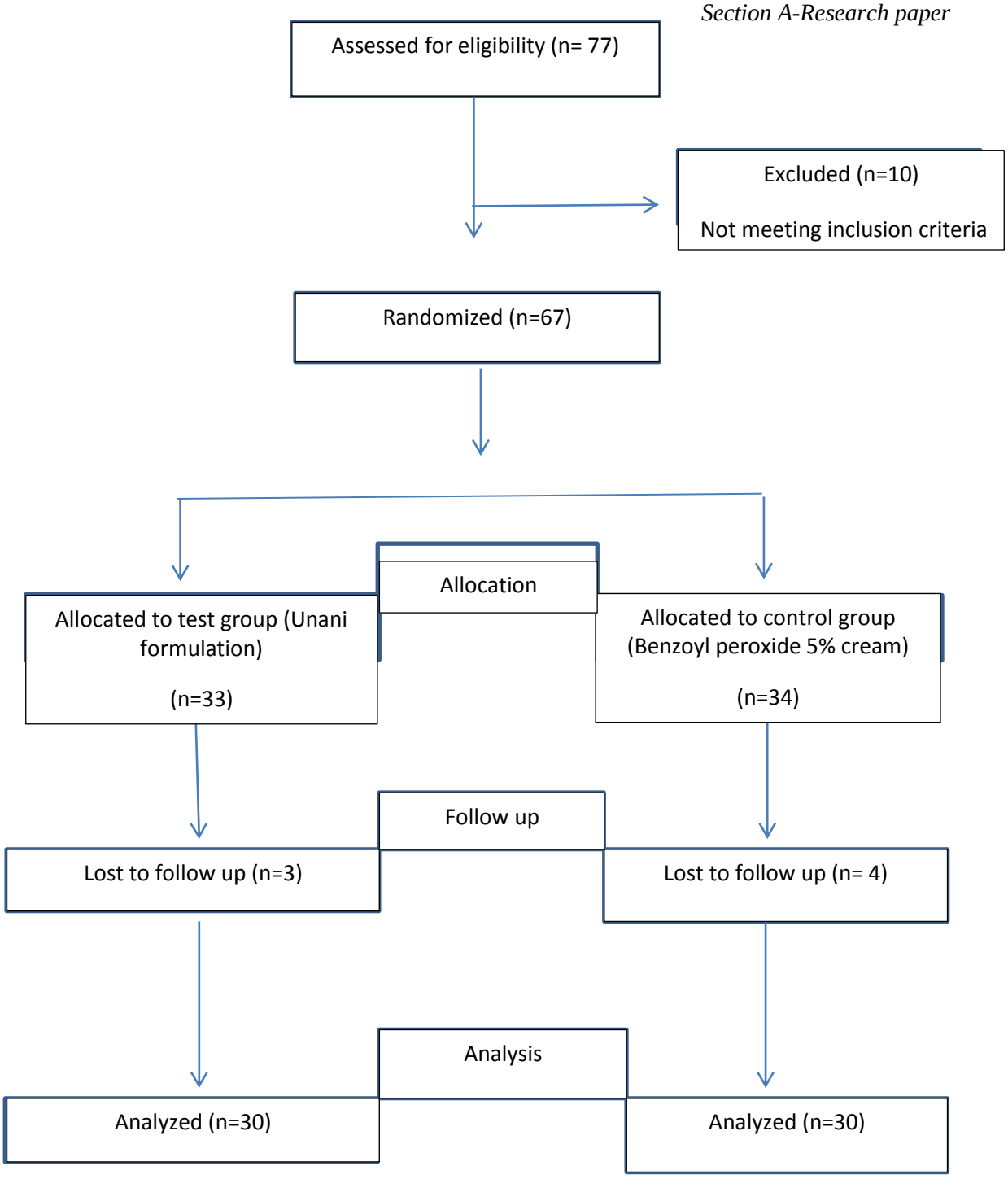

Figure 1: Patients deposition (Consort flow diagram)

Results:

Out of 67 randomly allocated patients only 60 were analyzed statistically. It was observed that the subjective parameters improved significantly both in test and control group but the

performance of test group treatment (*Shonīz* and *Sirka*) on papules was statistically higher (p value <0.001) as compared to control group treatment (Benzoyl peroxide 5% cream). In addition to this we also observed that acne lesions reduced significantly both in test and control group (p<0.0001*) but we found an insignificant difference between test group and control group with respect to the reduction of acne lesions which means that both the treatments are equally effective. In this study both the test and the control drugs were found to be safe. Safety parameters were within normal limits which were checked before and after treatment.

Table 1: Showing comparison based on papules among test and control group before treatment

Papules at Base Line	Test		Control		p-value
	No.	%age	No.	%age	
Present	30	100	30	100	-
Absent	0	0	0	0	
Total	30	100	30	100	

Table 2: Showing comparison based on papules among test and control group after treatment

Papules after treatment	Test		Control		p-value
	No.	%age	No.	%age	
Present	2	27	9	30	<0.001*
Absent	28	73	21	70	
Total	30	100	30	100	

Table 2 presents a comparison based on the presence of papules among the test and control groups after treatment. The table includes the number and percentage of individuals in each group who had papules present or absent after treatment. In the test group, 2 individuals (27% of the group) had papules present, while in the control group, 9 individuals (30% of the group) had

papules present. The p-value column indicates the statistical significance of the differences observed. An asterisk (*) indicates a highly significant result, with a p-value of less than 0.001. Overall, the table provides a comparison of the occurrence of papules between the test and control groups after treatment

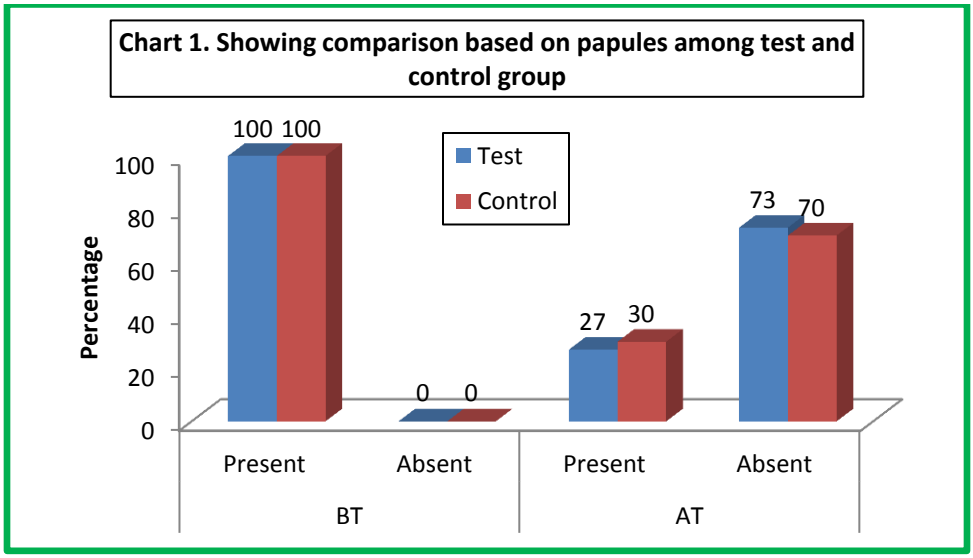

Table 3: Showing inter and intra group comparison of two treatments based on grading Scale of acne at different follow-ups							
Test	**Grading**	**Baseline**	**F1**	**F2**	**F3**	**F4**	P-value
	Minimum	1	1	1	0	0	< 0.0001*
	Median	2	2	1	1	0	
	Maximum	3	3	2	2	2	
Test Applied: Friedman Test							
Control	**Grading**	**Baseline**	**F1**	**F2**	**F3**	**F4**	
	Minimum	1	1	1	0	0	< 0.0001*
	Median	2	2	1	1	0	
	Maximum	3	3	3	2	2	
P-value (test vs. control) Mann Whitney Test		0.772	0.772	0.144	1	0.913	

Table 3 provides an inter and intra group comparison of two treatments based on the grading scale of acne at different follow-ups. The table includes the test name, grading scale, and the baseline, F1, F2, F3, and F4 follow-up periods. The values presented are the minimum, median, and maximum scores for each group. The p-value column indicates the statistical significance of

the differences observed. The Friedman test was used to compare the treatments within each group. The control group is also included for comparison, and the Mann Whitney test was used to determine the p-value for the test group versus the control group. The asterisk (*) signifies a p-value of less than 0.0001, indicating a highly significant result.

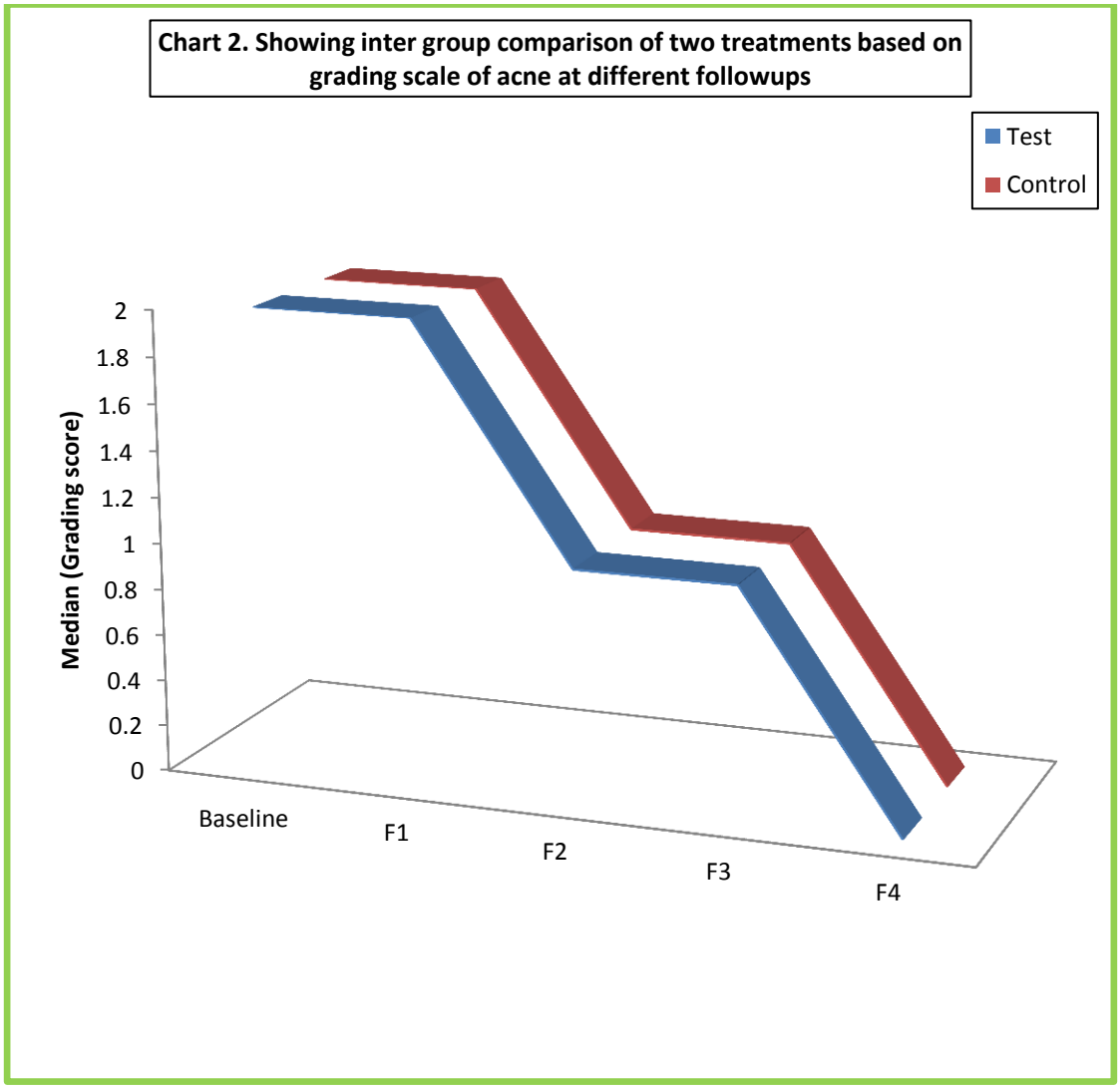

Table 4: Showing comparison of safety parameters in test group

Safety Parameters		Mean	SD	P-value
Hb	BT	13.28	1.709	NS
	AT	13.17	1.431	

TLC	BT	7186	2140	NS
	AT	6651	1658	
Neutro	BT	63.67	7.289	NS
	AT	60.68	7.231	
Lympho	BT	32.67	7.237	NS
	AT	35.61	6.953	
Eosino	BT	1.933	0.7849	NS
	AT	1.9	0.6618	
Mono	BT	1.833	1.053	NS
	AT	1.767	0.504	
Baso	BT	0	0	-
	AT	0	0	
ESR	BT	36.6	19.62	NS
	AT	28.32	18.5	
RBS	BT	90.92	19.73	NS
	AT	91.38	14.6	
B. Urea	BT	24.32	5.136	NS
	AT	22.63	4.784	
S. Creatinine	BT	0.719	0.1737	NS
	AT	0.7337	0.1917	
SGOT	BT	33.11	44.22	NS
	AT	25.41	16.28	
SGPT	BT	42.5	50.5	NS
	AT	31.54	25.75	
S. ALP	BT	110	34.48	NS
	AT	106.8	28.04	
S. Bilirubin	BT	0.784	0.4904	NS
	AT	0.7997	0.5052	
Test applied Paired t-test				

Table 4 and 5 presents a comparison of safety parameters in a test and control group. The table includes various safety parameters such as Hb, TLC, Neutro, Lympho, Eosino, Mono, Baso, ESR, RBS, B. Urea, S. Creatinine, SGOT, SGPT, S. ALP, and S. Bilirubin. The table displays the mean and standard deviation (SD) values for each parameter in the "BT" (Before Treatment) and "AT" (After Treatment) groups. A paired t-test was used to determine these differences. The p-value column indicated the statistical insignificance for each parameter with p-value>0.05

Table 5: Showing comparison of safety parameters in control group

Safety Parameters		Mean	SD	P-value
Hb	BT	13.69	1.69	NS
	AT	13.49	1.845	

TLC	BT	6547	1398	NS
	AT	6348	1711	
Neutro	BT	61.83	6.773	NS
	AT	60.5	8.48	
Lympho	BT	34.73	7.216	NS
	AT	35.37	8.352	
Eosino	BT	2.133	0.6814	NS
	AT	2.067	0.6397	
Mono	BT	1.7	0.6513	NS
	AT	2	0.5252	
Baso	BT	0	0	-
	AT	0	0	
ESR	BT	30.07	18.2	NS
	AT	17.1	13.22	
RBS	BT	87.97	10.33	NS
	AT	98.14	15.76	
B. Urea	BT	23.69	5.296	NS
	AT	22.94	6.883	
S. Creatinine	BT	0.7007	0.1927	NS
	AT	0.8047	0.2054	
SGOT	BT	20.75	6.883	NS
	AT	26.17	17.1	
SGPT	BT	25.93	13.33	NS
	AT	30.72	40.73	
S. ALP	BT	121.6	70.7	NS
	AT	117.4	84.01	
S. Bilirubin	BT	0.9173	0.6983	NS
	AT	0.997	0.8821	
Test applied Paired t-test				

Discussion:

Over the past decade, the treatment of many diseases by various forms of complementary and alternative form of medicine has been rising.[17] One of the forms of complementary and alternative medicine is the Unani system of medicine wherein, multiple management options have been described in classical literature for treatment of acne vulgaris. However, there is paucity of studies where the efficacy and safety of locally applied Unani drugs in acne vulgaris is evaluated. The present Unani drug was taken from classical literature and had been clinically evaluated for its efficacy and safety and compared with Benzoyl peroxide cream 5% w/w.[4] The results indicate that the Unani treatment improved comedones, papules, pustules, itching and

erythema and led to reduction in the acne severity scale grading.[7] As per Unani system of medicine acne vulgaris (*Buthūr Labaniyya*) is caused by suppurative matter which is expelled towards the surface of skin due to bodily vapors.[4] *Kharabi khūn* (blood dyscrasia), improper digestion, intake of foods having hot temperament, constipation, sudden arrest of bleeding in *Bawāsīr* (piles), menstrual irregularity and pregnancy have been regarded as the causes of acne.[18] *Buthūr Labaniyya* occurs due to hyperactivity of sebaceous glands which produce excess oily secretion i.e. sebum that accumulates in their openings and leads to inflammation and suppuration. This suppurative material reaches to the skin surface by vapors of the body. The suppurative matter doesn't dissolve due to its viscous nature and accumulates layer by layer. Air is said to increase its viscosity gradually by drying up its lighter ingredients resulting in blockage of openings of these sebaceous glands. Medicatrix naturae tries to remove morbid material through skin in the form of papules or swellings. The morbid matter is driven away from vital organs to external ones to avoid any damage to vital organs. *Buthūr* are formed as a result of excess accumulation of this morbid/vicious material in the body which is expelled by medicatrix naturae towards the skin.[19,20]

The topical formulation used in the present study consists of paste of *Shonīz* seeds (*Nigella sativa*) with *sirka* (grape vinegar). *Nigella sativa* has *Jāli* (detergent), *Qāṭi ʿ-i-Balgham* (anti-phlegmatic), *Muʿarriq* (diaphoretic), *Muḥallil-i-Awrām* (anti-inflammatory), antioxidant, *Daf'e Jaraseem* (antibacterial), deodorant, *Muḥallil* (resolvent), and *Mufattiḥ sudad* (deobstruent) properties.[9,10,11,12,13] While *Sirka* has *Mujaffif* (desiccant),[11] *Qāṭi ʿBalgham* (phlegm dissolving/anti-phlegm),[21] *Muḥallil* (resolvent), *Rādi ʿ* (repellent),[14] *Qābīd* (astringent), *Mulaṭṭif* (demulcent),[15] *Dāfi ʿ-i-Ta ʿaffun* (antiseptic), *Qāṭi ' akhlāṭ-i-ghalīẓ*, *Munḍij* (concoctive), *Sarīun-nufūdh* (quickly infusible) and *Mufattiḥ sudad* (deobstruent) properties.[16] These properties of the Unani formulation makes it a good choice for the treatment of acne vulgaris. In acne vulgaris inflammatory papules and pustules are seen and these drugs used here help to reduce inflammation and remove excess sebum and clear the skin pores. These effects of Unani drugs are in accordance with the description given in Unani literature.[9,22] Tests to check treatment effects of Unani formulation on blood, liver and renal function in patients with acne vulgaris have been carried out to observe any systemic adverse effects. No significant changes were observed in these laboratory investigations and all the parameters remained well within the normal limits in both test and control groups. No other adverse drug reactions were observed

during the study indicating the safety of the topical Unani formulation. However we could observe that the topical application of Unani formulation could be refined in a way that it may be formed as an ointment base form for easy application to skin. Very few systematic studies have been conducted on the treatment of acne vulgaris with Unani formulations. However the present formulation has been reported for the first time. The topical Unani formulation of *Shonīz (Nigella sativa*), *Naushadar* (*ammonium chloride)* and *Bura Armani* mixed with *sirka* has been used in the management of acne vulgaris and found to be safe and effective.[6] Similarly polyherbal Unani formulation (*Zimade mohasa*) has also been found to be effective in the treatment of acne vulgaris.[23] An effective and safe treatment with *Tila-i- Muhasa* has been reported for acne vulgaris patients.[24] More recently treatment with one of the herbs used in complementary medicine, *Shahtra* (*Fumaria indica*) orally along with the topical use of *Zimad Muhasa* has been shown to be effective in patients with moderate to severe acne vulgaris.[25] These time tested potential Unani formulations can be a good source of active ingredients for drug discovery programme for the treatment of acne vulgaris. Moreover, *Nigella sativa* has been found to be potentially effective in many dermatological conditions.[26]

Limitations:

The small sample size and lack of post-follow up decreases the robustness of the study. Because of time limitations we could not follow the patients after completion of trial and the recurrence rate was unknown. Thus the interpretation of statistical tests should be taken with caution. Moreover, the Unani topical application used in the present study should have been redesigned in ointment base to make it more patient friendly. We propose that the post-trial follow up of the acne vulgaris patients may be undertaken in future.

Conclusion:

In summary, safety and efficacy of test Unani formulation (paste of *shonīz* with *sirka*) were consistently similar with that of control group (Benzoyl peroxide cream 5% w/w). So the test drug formulation can be used safely and effectively for the treatment of acne vulgaris and studies with more sample size and post-trial follow up may be carried out.

Author contributions:

Gousia Mehraj recruited the patients and collected all the clinical data. Dr. Adil Rashid analyzed the data. Prof. Naquib-ul-Islam along with Dr. Shameem Ahmed Rather supervised the trial.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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