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Original Article

# The effect of Unani antiacne formulation (*Zimade Muhasa*) on acne vulgaris: A single-blind, randomized, controlled clinical trial

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**Abstract**

***Objective*** To evaluate clinically the efficacy of *Zimade Muhasa*, a Unani anti acne formulation, for *Busoore labaniya* (Acne vulgaris) against 5% benzoyl peroxide.

***Methods*** The randomized, single-blind, standard controlled trial of 6 weeks evaluated the efficacy and tolerability of Unani topical antiacne formulation against standard control i.e. 5% benzoyl peroxide in 48 patients of either sex on the basis of Global Evaluation of Acne Scale (GEA Scale) along with arbitrary scale for assessment of effect over postinflammatory hyperpigmentation, scarring and fairness. In addition quality of life was assessed according to Cardiff Acne Disability Index (CADI) questionnaire. The alterations in improvement and possible complications were regularly assessed.

***Results*** After 6 weeks of treatment, compared with baseline both the treatment preparations decreased the acne lesions ($P<0.001$). Further, the test formulation improved postinflammatory hyperpigmentation ($P<0.001$), scarring ($P=0.025$) and complexion ($P=0.001$). There was significant ($P<0.001$) improvement in the quality of life in treatment groups at the end of study.

***Conclusion*** The test formulation was well-tolerated and equivalent to 5% benzoyl peroxide in alleviating acne lesions. Test formulation was also more effectual concerning the effects over scars, post inflammatory hyperpigmentation and fairness. This formulation can be used safely to treat active acne as well as in patients with post acne scarring. The clinical relevance may be clarified by longer duration treatment.

***Key words***
Acne vulgaris, Unani compound formulation, GEA Score, *Zimade Muhasa*.

## Introduction

Acne vulgaris is the most common dermatological disorder reported by adolescents.[1] Although, prevalent in 90% of adolescents, it persists in 12-14% of adults and about 25% experience permanent scarring by the time they approach 18 years of age.[2,3] Even though, acne has no direct impact on physical health, it contributes a significant psychosocial burden that encompasses poor body image, low self-esteem, social isolation and restriction of activities.[4] It is a complex disorder with multiple intrinsic and extrinsic factors that influence its final outcome.[5] An abounding literature is available regarding the antiinflammatory and antibiotic medications for the treatment of acne with proven efficacy. However, the regular use of these medications is associated with multiple side effects viz., cutaneous irritation and bleaching of clothes by benzoyl peroxide; irritant dermatitis due to

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topical retinoids; bacterial resistance following topical application of antibiotics; gastrointestinal upset and vaginal candidiasis as an aftermath of systemic antibiotics; musculoskeletal, mucocutaneous, ophthalmic involvement due to oral isotretinoin.[6]

Complementary and alternative medicine (CAM) is now getting more acceptance from the patients and health providers due to invidious effects of long-term use of contemporary medications. An estimate of about $33.5 billions was spent by the American people in 2007 on visits to CAM practitioners and purchase of CAM products.[7] A study in Turkey showed 52.1% of acne patients attending dermatology outpatient clinic of the Alanya Baskent University use complementary remedies.[8] A variety of clinical studies reported the role of herbs in relieving the acne manifestations viz. *Ocimum gratissimum, Gugulipid, Aloe vera, Berberis vulgaris, Tea tree oil* and *Nigella sativa oil*.[9-14] A polyherbal formulation was selected for the present study due to the fact that polyherbal therapies have synergistic, potentiative, agonistic or antagonistic pharmacological activities that work in congruous way to produce therapeutic activity with least side effects. The present herbomineral preparation (*Zimade Muhasa*) is described for acne management in ancient Greco-Arabic (Unani) literature.[15] Various *in vitro* studies of its ingredients have shown antiinflammatory, antimicrobial, antioxidant and immunomodulatory activity. The aim of present study was to investigate the efficacy of the respective formulation on modern scientific parameters.

## Methods

48 patients suffering from acne of either sex in the age group of 13-40 years attending the Medicine OPD of National Institute of Unani Medicine, Bangalore from February 2012 to January 2013 were recruited for the study. The subjects were randomly assigned in the test group (n=24) and the control group (n=24) using a computer generated randomization table. The study was approved by the Institutional Ethics Committee and duly signed informed consents were obtained from all the patients prior to the initiation of the study.

Patients who were under 13 years and above 40 years, pregnant and lactating women, patients on corticosteroid therapy, anticonvulsant therapy or taking oral contraceptives were excluded from the study. Other exclusion criteria included the patients with any systemic disease or concomitant disorders like acne rosacea, acne fulminans, acne necrotica, psoriasis, eczema etc. All the subjects were evaluated thoroughly prior to study. Blood samples were drawn for complete hemogram, random blood sugar, liver function and renal function assessment.

The control group was provided with 5% benzoyl peroxide gel (Persol AC 5 gel®, WALLACE manufactures) in wrappings. The test group was given Unani preparation (*Zimade Muhasa*) in powdered form in the similar wrappings. The Unani formulation comprised of *Iris germanica* var. *florentina*, *Azadirachta indica*, *Abrus precatorius*, *Albizia lebbeck* and *lake salt*. The ingredients of the test formulation were provided by the department of pharmacy of the institute and preparation was carried out at the institute's pharmacy.

All the subjects were advised to apply the provided medicaments daily overnight on clean face over the affected area for 6 weeks. Subjects provided with test formulation were advised to prepare the paste of 2 gm of powder with lukewarm water. Compliance to therapy was assessed at every follow-up by examining the packets in which medication was dispensed at previous visit. Participants whose

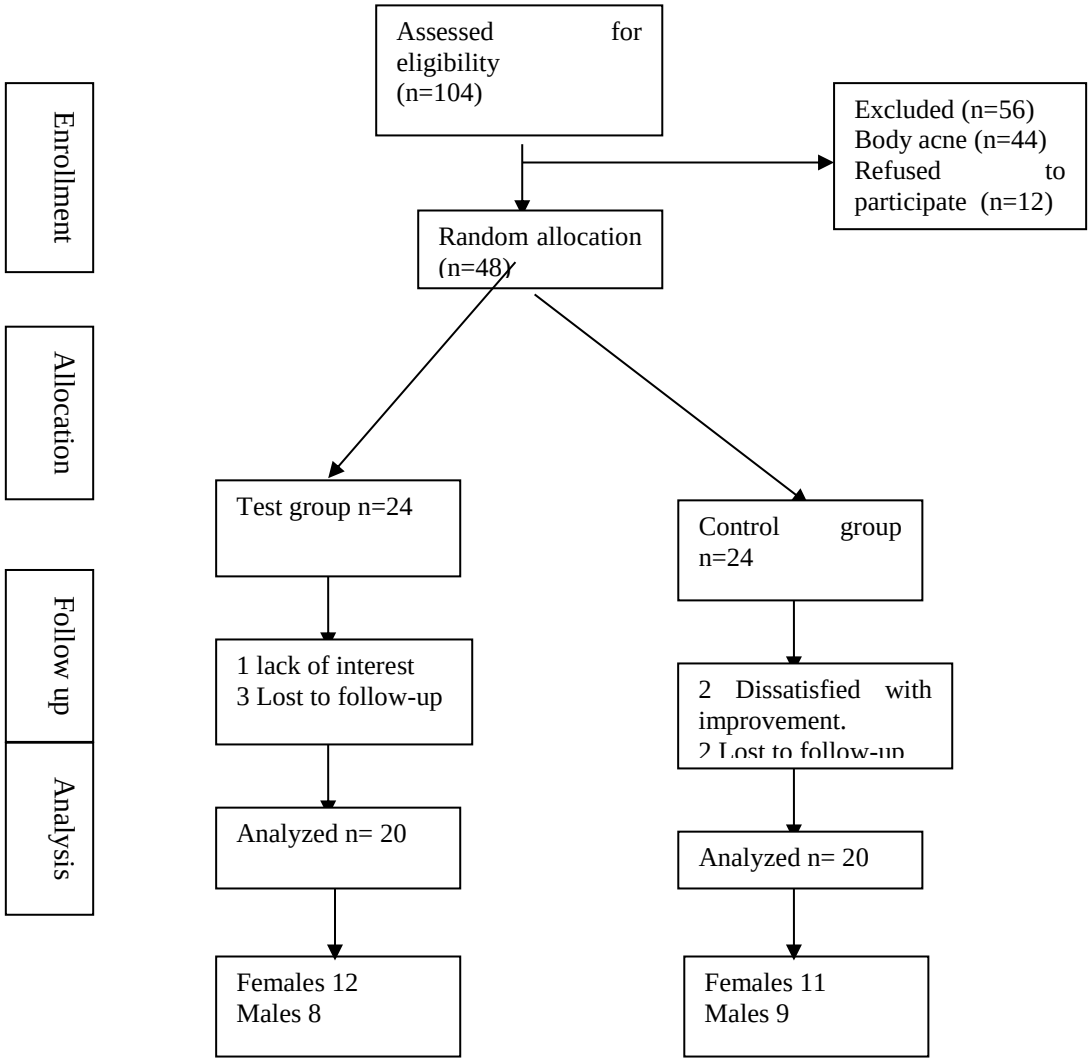


**Figure 1** CONSORT flow diagram of patients to study centre.

compliance with treatment was <80% of provided dose were considered drop out.

Subjects were also advised not to modify their routine during the study period. The study duration was divided into 3 visits of follow-up of 15 days each. At every follow-up, patients were asked about the condition of their symptoms and subjected to assess the clinical findings. Every patient was interviewed separately. Concomitant treatment was not allowed during the period of study in either of the groups.

The efficacy of the test and control groups was assessed by subjective and objective parameters. Subjective parameters comprised mitigation in acne lesions (comedones, papules, pustules, nodules, cysts, pigmentation and scars), quality of life and fairness. The efficacy of the subjective parameters in both the groups was based on the arbitrary 4-point grading scale (0- no symptoms; 1- mild symptoms; 2- moderate symptoms; and 3- severe symptoms). Effect on fairness of skin was assessed by a 5-point arbitrary grading score. The grades range from 0 to 4; 0 as non responders and 1, 2, 3 and 4 as responders.

Objective parameters include alleviation in acne lesions according to Global Acne Severity (GEA) Scale devised by Global

Evaluation Acne group.[16] Besides; all patients included in the study completed the Cardiff Acne Disability Index questionnaire for the assessment of quality of life.

Analysis of Covariance (ANCOVA) was used to find the significance of study parameters between the groups. Comparison of the continuous variables was accomplished with the student's t test. Chi-square/ Fisher exact test was used to find the significance of study parameters on a categorical scale between groups. Wilcoxon signed rank test was used to find the significance within the group. The continuous variables in the entire manuscript are presented in the form of mean±standard deviation. *P* value <0.05 has been accepted as statistically significant.

## Results

A total of 40 patients of 104 patients completed the study protocol (**Figure 1**). The main reason for attenuation was irregular use of medication; family reasons and irregular follow-up. No significant difference was observed between the two groups regarding the basic demographic data (**Table 1**).

Among 48 recruited patients, a total of 8 patients; 4 from each group desisted from the study either dissatisfaction with treatment or lack of interest. The mean ± SD scores of both groups are shown in **Table 2**. In the test group, a significant difference was observed regarding the alleviation of comedones (*P*<0.001), papules (*P*<0.001), pustules (*P*<0.001), nodules (*P*<0.02), postinflammatory pigmentation (*P*<0.001), scars (*P*<0.025) and improvement in complexion (*P*<0.001) during 6 weeks of intervention. The GEA Score of the test group improved significantly during the treatment period (*P*<0.001).

In the control group, a statistically significant difference was observed in the improvement regarding comedones (*P*<0.001), papules (*P*<0.001) and pustules (*P*=0.085). A statistically nonsignificant difference was found regarding the efficacy on nodules

**Table 1** Baseline socio-demographic characteristics of subjects in test and control group.

| *Parameters* | *Test group* | *Control group* | *P value* |
|---|---|---|---|
| Mean age (years) | 21.65±4.95 | 20.65±5.12 | 0.534 |
| Gender (male/female) | 8/12 | 9/11 | 0.749 |
| Socioeconomic status (upper/upper middle/lower middle/ lower class) | 4/14/1/1 | 1/9/0/0 | 0.107 |
| Marital status (unmarried/ married) | 17/3 | 16/4 | 1.000 |
| Occupation (house wife/student/employee/ Business/salesman) | 4/12/2/0/2 | 4/14/1/1/0 | 0.664 |
| Family history | 7/20 | 7/20 | 1.000 |
| Diet pattern (veg/ mixed) | 4/16 | 6/14 | 0.465 |
| Seasonal variation (Summer/ winter aggravation) | 5/2 | 3/1 | 1.000 |
| Habitation (urban/rural) | 18/2 | 19/1 | 0.559 |

**Table 2** Change in variables before and after intervention

| *Lesions* | *Test group* | | *P value* | *Control group* | | *P value* |
|---|---|---|---|---|---|---|
| | *Baseline* | *6 weeks* | | *Baseline* | *6 weeks* | |
| Comedones | 1.70±0.80 | 0.65±0.49 | <0.001 | 1.85±0.81 | 0.75±0.79 | <0.001 |
| Papules | 2.00±0.92 | 0.40±0.50 | <0.001 | 1.85±0.67 | 0.90±0.85 | <0.001 |
| Pustules | 1.50±0.69 | 0.55±0.60 | <0.001 | 1.40±0.75 | 0.95±0.83 | 0.058 |
| Nodules | 0.40±0.68 | 0.05±0.22 | 0.020 | 0.15±0.37 | 0.20±0.41 | 0.564 |
| Pigmentation | 2.10±0.91 | 0.65±0.49 | <0.001 | 1.45±0.76 | 1.25±0.72 | 0.206 |
| Scars | 0.55±0.89 | 0.30±0.47 | 0.025 | 0.80±0.95 | 0.80±0.95 | 1.000 |
| Quality of life | 12.25±2.45 | 4.95±0.94 | <0.001 | 12.00±1.78 | 5.80±3.64 | <0.001 |
| GEA score | 3.50±0.95 | 0.85±0.75 | <0.001 | 2.95±0.69 | 1.00±1.12 | <0.001 |

GEA= Global acne severity (GEA) scale

**Table 3** Adverse effects of the test and control medicaments.

| *Adverse effects* | *Test group* | *Control group* | *P value* |
|---|---|---|---|
| Dryness | 07/20 | 9/20 | 0.748 |
| Peeling | 02/20 | 0/20 | 0.487 |
| Burning | 0/20 | 3/20 | 0.231 |
| Itching | 13/20 | 9/20 | 0.341 |

(*P*=0.564), postinflammatory pigmentation (*P*=0.206), scars (*P*=0.142) and improvement in complexion. A significant difference was observed in the GEA Score between first and last session. In this study, a highly significant difference was observed in the improvement in the quality of life in both groups before and after intervention.

Four adverse effects were noted during the study (**Table 3**). The difference between the test and control group regarding the adverse effects was not significant. Neither of the adverse effect was severe.

## Discussion

In the present study, the Unani antiacne compound formulation (*Zimad Muhasa*) and benzoyl peroxide significantly decreased the acne issues in our subjects over a period of 6 weeks. There was no significant difference observed between two therapies regarding the alleviation of acne lesions and improving quality of life, but test formulation was more effective in improving postinflammatory pigmentation, scars and fairness.

This study provided sufficient data regarding scientific affirmation that the present herbomineral preparation is safe, effective and tolerable in acne patients and is also comparable to control i.e. benzoyl peroxide.

Acne is a multifactorial disorder. The main pathogenic components are: abnormal follicular keratinization with retention of keratinous plug in the follicle, increased sebum production, presence of *Propionibacterium acnes* and inflammation.[5] Recent discoveries in acne pathogenesis have evinced the role of oxidative stress in the causation of acne. Researchers have shown that squalene in sebum upon oxidation releases irritating free radicals into the tissues which along with peroxides initiate and maintain the damaging inflammatory pathway.[17] The alleviation in the acne lesions with the test formulation appears to be due to resolvent, antiseptic, astringent, detergent and desiccant properties of the ingredients as described in Unani pharmacological literature.[18,19,20] *Azadirachta indica* leaves has been tested for antibacterial, antiinflammatory, antioxidant, wound healing and skin renewal effects on animal models.[21,22,23,24,25,26] Animal studies on *Albizia lebbeck* bark has revealed antimicrobial, antiinflammatory, antioxidant and immunomodulator activity.[27-30] Experimental studies on *Abrus precatorius* seeds have confirmed the antiinflammatory, antimicrobial, wound healing, anti oxidative and immune stimulatory activity.[31-35] Also antioxidative activity was previously reported. Studies on *Iris germanica florentina* in animal models were found to be a potent antiinflammatory, antimicrobial, antioxidant and immunomodulatory herb.[36,37,38]

The significant improvement in the postinflammatory pigmentation as evident from the study may be because of detergent property of the ingredients as described in exemplary Unani texts.[39,40,41,42] It may also be contributary to antiinflammatory and wound healing activities of the respective herbs.

In this study, the improvement in the complexion appears to be by the virtue of skin whitening effects of the ingredients. In ancient

literature, the drugs possessing detergent properties exhibit skin whitening effects.[18] Recent studies have revealed skin whitening activity of herbs possessing antioxidant properties.[43] Hence, the observations of this study appear to be mediated through the antioxidant property of *Abrus precatorius, Iris germanica florentina*, *Azadirachta indica* and *Albizzia lebbeck*.[34,37,24,29]

Current studies suggest that flavonoids in herbs inhibit production of proinflammatory eicosanoids and pro inflammatory cytokines, including TNF alpha that play a crucial role in acne pathogenesis. Furthermore, several studies also suggested the role of growth factors and inflammatory cytokines in the development of acne lesions and the immune system has the capacity of developing them. Consequently, the herbs with immunomodulatory effects may prove advantageous.[38]

Hence forth, the present study is one among the studies conducted for evaluation of anti acne preparation (*Zimade Muhasa*) from the Unani system of medicine on human subjects. The findings are sufficient enough to encourage the use of the present Unani preparation as an alternate for the management of acne vulgaris.

## Conclusion

Acne is a common inflammatory dermatosis of skin that usually affects the face of adolescents. Although, this skin condition involves effectually all adults at least once during life, effective treatment is a major concern. The local application of the Unani anti acne preparation (Zimade Muhasa) for 6 weeks is well-tolerated and also markedly improved the outcome of the disorder. Nonetheless, the tolerable side effects may affirm the application of the present preparation as an alternative treatment for the management of acne. A double-blind, long-term clinical trial, with adequate sample size to establish the exact treatment duration, its additional applications and to assess the plausible obnoxious effects are recommended.

**Conflict of interest** None declared

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